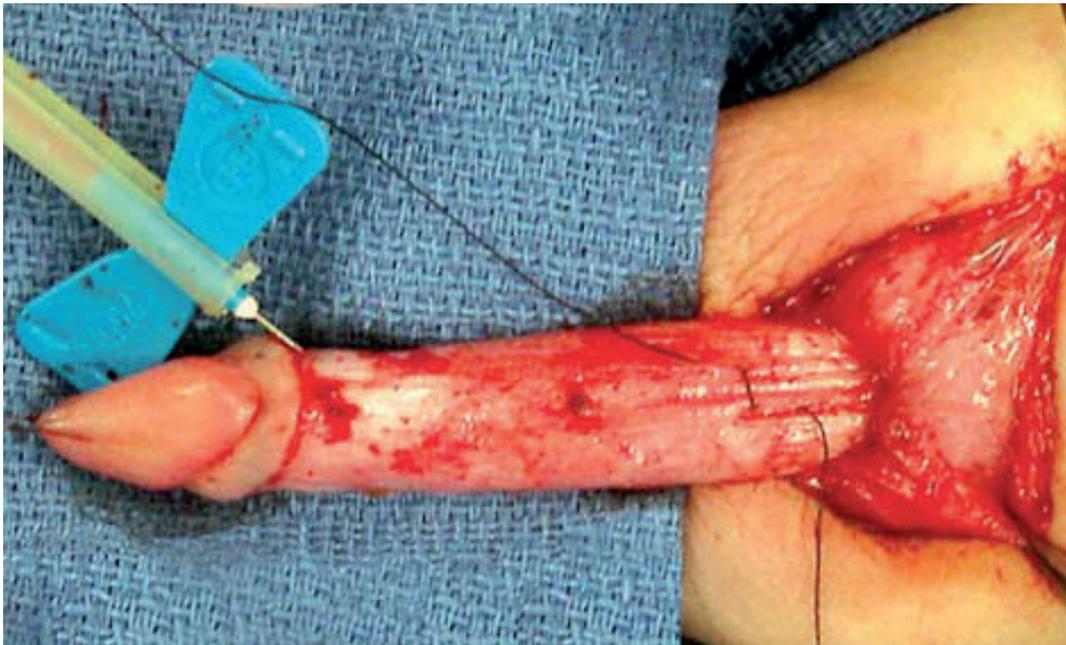


ISSN 1677-5538

# International

# Braz J Urol

Official Journal of the Brazilian Society of Urology  
Official Journal of the Thai Urological Association  
Volume 35, Number 1, January - February, 2009



*Diagonal plication suture for correction of penile torsion (Page 56)*

XXXI Brazilian Congress of Urology  
November 7 - 11, 2009 - Goiânia - GO - Brazil

Full Text Online Access Available  
[www.brazjurol.com.br](http://www.brazjurol.com.br)  
INDEXED BY  
PubMed

# International Braz J Urol

## **EDITOR'S COMMENT**

### **A Really International Urological Journal**

The January – February 2009 issue of the International Braz J Urol presents interesting contributions from many different countries, and as usual, the editor's comment highlights some papers.

Also, it is a great pleasure to confirm that the International Braz J Urol is a truly international Journal. In this issue, concerning articles and editorials, we present contributions from 12 different countries from different continents.

Doctor Tyagi and colleagues, from William Beaumont Hospital, Royal Oak, Michigan, USA, investigated on page 76 the presence of functional  $\beta_1$ ,  $\beta_2$  and  $\beta_3$ -adrenoceptor in urothelium and detrusor muscle of human bladder through in vitro pharmacology of selective  $\beta_3$  adrenoceptor agonist solabegron. They confirmed the presence of mRNA for  $\beta_1$ ,  $\beta_2$  and  $\beta_3$ -adrenoceptor in both human urothelium and detrusor. In an in vitro functional bladder assay, solabegron and other agonists for  $\beta$ -adrenoceptors such as procaterol and isoproterenol evoked potent concentration-dependent relaxation of isolated human bladder strips. It was concluded that selective  $\beta_3$ -adrenoceptor agonist may be a potential new treatment for the overactive bladder OAB syndrome. Also, the authors speculated that the existence of  $\beta_3$ -adrenoceptor mRNA in the urothelium, in addition to the detrusor muscle suggest multiple site of actions for the  $\beta_3$ -adrenoceptor in the lower urinary tract. Dr. Atsushi Otsuka, from Hamamatsu University School of Medicine, Shizuoka, Japan, provided an editorial comment to this article.

Doctor Castilho and colleagues, from Catholic University of Campinas evaluated on page 24 the long-term follow-up (minimum 18 months) of 24 patients undergoing laparoscopic adrenalectomy for pheochromocytoma. The authors found intra-operative complications in 4 patients (16.7%) and postoperative complications in 2 (8.3%). Eighteen (90%) of the 20 patients who had symptomatic hypertension, returned to normal blood pressure immediately after surgery, during the hospital stay. The authors found that the initial positive results obtained in the treatment of 24 patients were confirmed after a mean follow-up of 74 months. It was concluded that laparoscopic adrenalectomy for pheochromocytoma is a safe and effective procedure, providing the benefits of a minimally invasive approach. Dr. Tobias-Machado & Dr. Maria Bicudo, from ABC Medical School, São Paulo, Brazil, Dr. Cassio Andreoni, from Federal University of São Paulo, Brazil and Dr. M Fau & Dr. Laurent Brunaud, from University of Nancy, France, provided important editorial comments on laparoscopic treatment of pheochromocytoma.

Doctor Lopes and co-workers, from Federal University of Bahia, Salvador, Bahia, Brazil, presented on page 49 the use of a bovine pericardium graft in corporoplasty for penile prosthesis implantation. Bovine pericardium was used to cover large areas of implanted penile prostheses in 5 patients with a history of ero-

## **EDITOR'S COMMENT** - *continued*

sion, infection and fibrosis and the use of the tunica albuginea was unfeasible. The authors concluded that bovine pericardium might substitute synthetic and autologous material with the additional advantages of lower cost and greater availability. Dr. Paulo H. Egydio, from the Center for Peyronie's Disease, São Paulo, Brazil and Dr. Nicolaas C. Lumen, from Ghent University Hospital, Belgium, provided interesting editorial comments on this paper.

Doctor Natalin and colleagues, from Columbia University, New York, USA, compared on page 36 the ureteroscopic treatment outcomes of ureteral and renal stones, stratified for stone size and location, between overweight, obese and non-obese patients. A total of 107 patients underwent flexible or semi-rigid ureteroscopy with Ho:YAG laser lithotripsy and met criteria for review and analysis. The authors found an overall, initial stone-free rates of 91%, 97%, and 94% in normal, overweight and obese individuals respectively. When compared to non-obese patients, there were no significant differences. For renal and proximal ureteral stones, the stone-free rate in overweight and obese individuals was 94% in both groups; and a stone-free rate of 100% was found for distal stones, also in both groups. It was concluded that ureteroscopic treatment of stones in obese and overweight patients is an acceptable treatment modality, with success rates similar to non-obese patients. Dr. Mauricio Rubinstein, from Federal University of State of Rio de Janeiro, RJ, Brazil and Dr. Eduardo Mazzucchi, from University of Sao Paulo, USP, Brazil

Doctor Nadu and collaborators, from Tel Aviv University, Israel, reported on page 9 the outcomes of laparoscopic surgery combined with endourological assistance for the treatment of renal stones in patients with associated anomalies of the urinary tract. The authors studied 13 patients with ureteropelvic junction obstruction, horseshoe kidney, ectopic pelvic kidney, fused-crossed ectopic kidney, and double collecting system. Treatment included laparoscopic pyeloplasty, pyelolithotomy, and nephrolithotomy combined with flexible nephroscopy and stone retrieval. Intraoperative complications were lost stones in the abdomen diagnosed in 2 patients during follow up. Mean number of stones removed was 12 (range 3 to 214). Stone free status was 77% (10/13) and 100% after one ancillary treatment in the remaining patients. It was concluded that laparoscopic and endourological techniques can be successfully combined in a one-procedure solution that deals with complex stone disease and repairs underlying urinary anomalies. Dr. Nasser Simforoosh, from Shaheed Beheshti University of Medical Sciences, Tehran, Iran and Dr. Manickam Ramalingam, from K.G. Hospital and Post Graduate Institute, Coimbatore, India, provided important editorial comments on this paper. in the abdomen diagnosed in 2 patients during follow up. Mean number of stones removed was 12 (range 3 to 214). Stone free status was 77% (10/13) and 100% after one ancillary treatment in the remaining patients. It was concluded that laparoscopic and endourological techniques can be successfully combined in a one-procedure solution that deals with complex stone disease and repairs underlying urinary anomalies. Dr. Nasser Simforoosh, from Shaheed Beheshti University of Medical Sciences, Tehran, Iran and Dr. Manickam Ramalingam, from K.G. Hospital and Post Graduate Institute, Coimbatore, India, provided important editorial comments on this paper.

  
**Francisco J.B. Sampajo, M.D.**  
Editor-in-Chief

# Renal Parenchyma Thickness: A Rapid Estimation of Renal Function on Computed Tomography

Daniel M. Kaplon, Michael S. Lasser, Mark Sigman, George E. Haleblian, Gyan Pareek

*Section of Minimally Invasive Urologic Surgery, Department of Surgery, Division of Urology, The Warren Alpert School of Medicine of Brown University, Providence, Rhode Island, USA*

---

## ABSTRACT

*Purpose:* To define the relationship between renal parenchyma thickness (RPT) on computed tomography and renal function on nuclear renography in chronically obstructed renal units (ORUs) and to define a minimal thickness ratio associated with adequate function.

*Materials and Methods:* Twenty-eight consecutive patients undergoing both nuclear renography and CT during a six-month period between 2004 and 2006 were included. All patients that had a diagnosis of unilateral obstruction were included for analysis. RPT was measured in the following manner: The parenchyma thickness at three discrete levels of each kidney was measured using calipers on a CT workstation. The mean of these three measurements was defined as RPT. The renal parenchyma thickness ratio of the ORUs and non-obstructed renal unit (NORUs) was calculated and this was compared to the observed function on Mag-3 lasix Renogram.

*Results:* A total of 28 patients were evaluated. Mean parenchyma thickness was 1.82 cm and 2.25 cm in the ORUs and NORUs, respectively. The mean relative renal function of ORUs was 39%. Linear regression analysis comparing renogram function to RPT ratio revealed a correlation coefficient of 0.48 ( $p < 0.001$ ). The linear regression equation was computed as  $\text{Renal Function} = 0.48 + 0.80 * \text{RPT ratio}$ . A thickness ratio of 0.68 correlated with 20% renal function.

*Conclusion:* RPT on computed tomography appears to be a powerful predictor of relative renal function in ORUs. Assessment of RPT is a useful and readily available clinical tool for surgical decision making (renal salvage therapy versus nephrectomy) in patients with ORUs.

**Key words:** kidney; obstruction; kidney cortex; computed tomography

**Int Braz J Urol. 2009; 35: 3-8**

---

## INTRODUCTION

The most comprehensive radiographic modality for renal imaging is computed tomography (CT). As CT technology has advanced with the development of helical scanners, the resulting superior spatial and temporal resolution no longer limits the role of CT to assess static anatomic parameters (1). In recent years, multiple studies have demonstrated a clear role for utilizing CT to assess renal perfusion and glomerular filtration rate (GFR) (2,3). Langheinrich et al. dem-

onstrated that GFR can be measured accurately with triphasic CT (4). In addition, Patlak et al. developed a model for determining tissue function based on contrast transfer between tissues; this technique has been extrapolated to renal function in several studies (5). The information provided by these functional studies may be useful in defining recoverability of renal function, an important concept in assessing the viability of an obstructed renal unit (ORU). Other investigators have also studied anatomical details for assessing renal function with a recent report analyzing the role

of renal parenchyma thickness (RPT) on ultrasound as a predictor of recoverability of renal function (6).

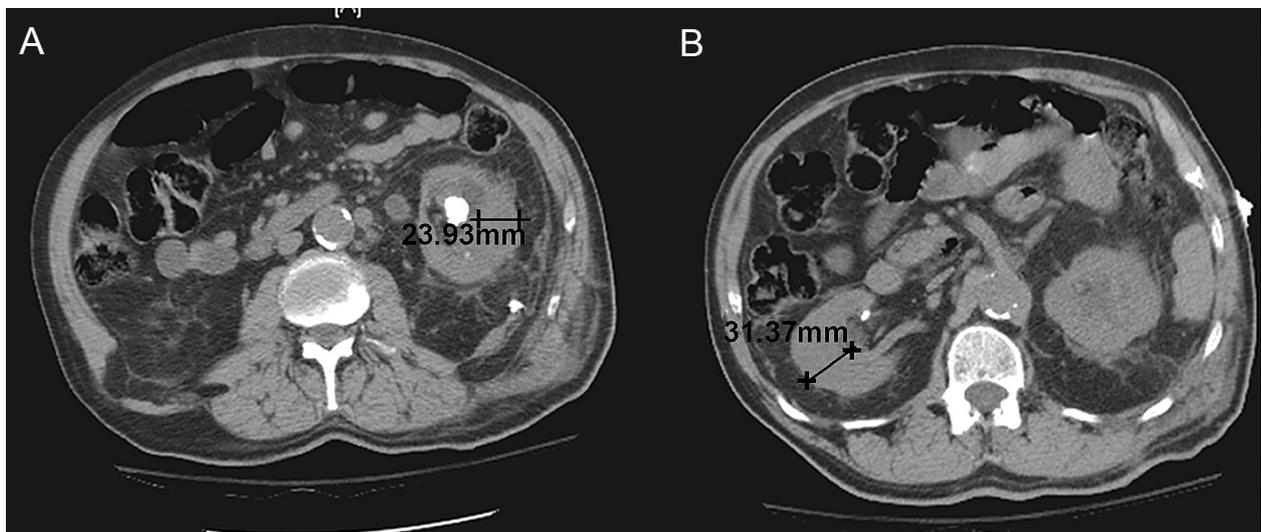
We sought to define the relationship between RPT on computed tomography and renal function on Mag-3 Lasix renogram in chronically obstructed renal units (ORUs) in order to define a minimal thickness ratio associated with adequate function. Our goal was to provide an efficient and pragmatic clinical tool for surgical decision making in patients with chronic ORUs.

## MATERIALS AND METHODS

Institutional review board approval was obtained prior to the commencement of the study. Fifty two consecutive patients undergoing lasix renograms between 2004 to 2006 were reviewed. From this cohort those who had a concomitant CT scan within 6 months were extracted. Patients with bilateral hydronephrosis, solitary kidney, and medical renal disease were excluded from review. In addition, those patients whose history suggested acute obstruction were excluded as well. Of this cohort, 28 patients had a diagnosis of unilateral obstruction and were included for analysis. Mean and median age was 49 and 48, respectively.

A General Electric Hi-Speed Advantage CT scanner was used to evaluate all patients in the study. RPT was measured at a hilar image on CT scan of the ORU and compared to a corresponding image of the NORU (Figure-1). The parenchyma thickness at the exact cranio-caudal midpoint of each kidney was measured using calipers on a CT workstation. The measurement was taken at an angle exactly perpendicular to the axis of the kidney. All measurements were performed by a single investigator. Two additional measurements were obtained in each kidney: one 2 cm cranial to the midpoint and one 2 cm caudal to the midpoint. For all scans, the parenchyma was measured from the renal capsule to the edge of the collecting system. The mean of the three measurements was then taken for each kidney and defined as the RPT. The renal parenchyma thickness ratio of the ORUs and non-obstructed renal unit (NORUs) was calculated and this was compared to the observed function on Mag-3 lasix Renogram. Regression analysis was performed using WESSA statistical software (Wessa, P. (2009), Free Statistics Software, Office for Research Development and Education, version 1.1.23-r3, URL <http://www.wessa.net/>).

Correlation between RPT ratio and function was determined. Further analysis of the linear regression curve allowed for calculation of the RPT ratio



**Figure 1** – Measurement of renal parenchyma thickness for obstructed renal unit (A) and non-obstructed renal unit (B).

correlating to a renal function of 20%, which at our institution represents the general cutoff for performing renal salvage surgery.

**RESULTS**

A total of 28 patients were evaluated. Mean patient age was 49 years (range 13-90 years). Obstruction was secondary to ureteropelvic junction obstruction (n = 12), calculus disease (n = 5), malignancy (n = 2), stricture (n = 1), ureterocele (n = 1), and non-specified hydronephrosis (n = 6). Seventeen patients were evaluated with noncontrast CT scan and 10 patients with contrast CT scan.

Mean parenchyma thickness was 1.82 cm and 2.25 cm in ORUs and NORUs, respectively. The mean renal function of ORUs was 39% and the mean renal function of NORUs was 61%.

Linear regression analysis comparing renogram function to ratio of thicknesses between the ORUs and NORUs revealed a correlation coefficient of .48 (p < 0.001) (Figure-2). The linear regression equation was computed as Renal Function = . 0.48 + 0.80 \* RPT ratio \* RPT ratio. A thickness ratio of 0.68 correlated with 20% renal function.

**COMMENTS**

Computed tomography has become a first-line assessment tool for patients presenting with renal obstruction and has proven to be the most effective modality for diagnosing the etiology of obstruction (7). Not only is CT widely used, it also provides a clear depiction of the renal anatomy and may provide additional valuable and quantifiable clinical information regarding renal function. An important parameter assessed on CT is the “health” of the renal parenchyma. Often in the outpatient setting RPT on CT scan may suggest diminished renal function. When this is observed, patients often undergo radionuclide scans for a more formal evaluation of differential renal function. This information then helps the clinician and the patient make decisions about the appropriate course of treatment. Thus, our goals were to determine if a relationship between RPT on computed tomography and renal function on Mag-3 lasix renogram in ORUs exists and if so, to define a minimal thickness ratio associated with adequate function.

Recently, many studies have examined various parameters on CT in order to predict renal function. Evidence has shown the differential renal parenchyma volume measured by noncontrast CT provides

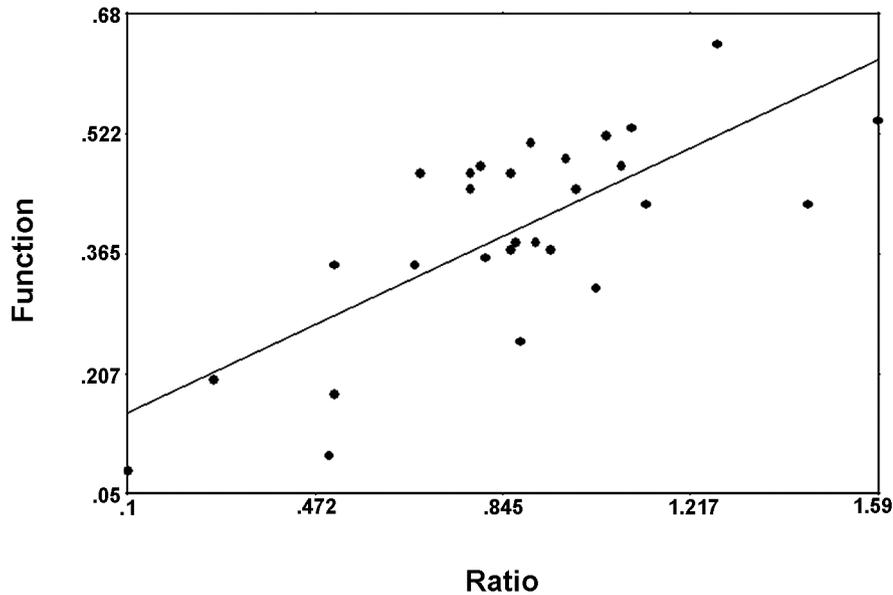


Figure 2 – Linear regression showing renal parenchyma thickness ratio vs. renogram function.

a fairly accurate prediction of differential creatinine clearance (7). El-Dein et al. demonstrated that contrast enhanced spiral CT is as accurate as nuclear renography for calculating total and separate renal function (8). There are, however, major drawbacks to these forms of renal function estimation. Primarily, these studies required sophisticated software to calculate total renal volume based on CT reconstructions (8). Such scans must be performed as a dedicated study as data from existing scans may not be adequate for the sophisticated reconstructions and volume rendering required. In instances where reconstruction can be performed on existing scans, it is often a time consuming and costly endeavor. Measurement of RPT ratios, however, can be performed in a retrospective manner on existing scans, either with or without contrast.

Multiple recent studies have demonstrated the ability to calculate GFR using contrast enhanced CT. Most of these studies rely on a variation of the Patlak model, which involves using the transfer of contrast into tissue as a marker for function (5). While this method has been validated and provides an estimate of GFR, its practical use is limited by the complexity of calculation required to arrive at the GFR value. In addition, Hackstein has suggested that the Patlak model can overestimate GFR in several situations (3).

In patients with asymmetric renal disease such as renal artery stenosis and obstruction, measurement of unilateral function is not possible by calculation of global creatinine or inulin clearance because these parameters are influenced by the contralateral renal unit (1). Determination of individual kidney function has been historically performed either by percutaneous nephrostomy and creatinine clearance or by nuclear scintigraphy. Both of these modalities have limitations, with the former being invasive and the latter being often unreliable in cases of obstruction (9). More sophisticated models for predicting unilateral renal function include electron beam CT, three-dimensional ultrasound, and gadolinium magnetic resonance (1).

The major limitation of this study is that the nuclear renogram is used as the gold-standard test for function. We chose the nuclear renogram because it is the most commonly used test for function of ORUs at most institutions, including our own. It is important to realize, however, that nuclear renogram can actually

overestimate function in cases of obstruction (9). A more accurate assessment of renal function could be assessed via a percutaneous nephrostomy with subsequent creatinine clearance, but this was not possible due to the retrospective nature of this study. In addition, the population studied here is small. Admittedly, only 3 patients in our series had renal function less than 20% by renogram, so a larger population will be needed to further validate these results. In addition, it must be noted that patients with abnormalities of the measured area of the kidney such as focal scarring or fetal lobulation would not be good candidates for this method of measurement.

To date, no study has used parenchyma thickness alone to compare function to nuclear renography. We assessed a group of patients in whom all had a chronic unilateral abnormality and a presumed normal contralateral renal unit. This study describes an approach that allows for rapid estimation of renal function using a single measurement, which can be done without sophisticated reconstructions. The thickness ratio of the ORU to NORU correlates quite well with the relative function as predicted by nuclear renogram.

## CONCLUSION

Renal parenchyma thickness ratio on computed tomography appears to be a powerful predictor of relative renal function in chronic ORUs. Assessment of RPT ratio is a useful clinical tool for surgical decision making in patients with ORUs. It relies on straight-forward measurements that can be made on existing CT scans without the need for complex calculations, reconstructions, or secondary studies.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Daghini E, Juillard L, Haas JA, Krier JD, Romero JC, Lerman LO: Comparison of mathematic models for

- assessment of glomerular filtration rate with electron-beam CT in pigs. *Radiology*. 2007; 242: 417-24.
- O'Dell-Anderson KJ, Twardock R, Grimm JB, Grimm KA, Constable PD: Determination of glomerular filtration rate in dogs using contrast-enhanced computed tomography. *Vet Radiol Ultrasound*. 2006; 47: 127-35.
  - Hackstein N, Bauer J, Hauck EW, Ludwig M, Krämer HJ, Rau WS: Measuring single-kidney glomerular filtration rate on single-detector helical CT using a two-point Patlak plot technique in patients with increased interstitial space. *AJR Am J Roentgenol*. 2003; 181: 147-56.
  - Hackstein N, Wiegand C, Rau WS, Langheinrich AC: Glomerular filtration rate measured by using triphasic helical CT with a two-point Patlak plot technique. *Radiology*. 2004; 230: 221-6.
  - Patlak CS, Blasberg RG, Fenstermacher JD: Graphical evaluation of blood-to-brain transfer constants from multiple-time uptake data. *J Cereb Blood Flow Metab*. 1983; 3: 1-7.
  - Khalaf IM, Shokeir AA, El-Gyoushi FI, Amr HS, Amin MM: Recoverability of renal function after treatment of adult patients with unilateral obstructive uropathy and normal contralateral kidney: a prospective study. *Urology*. 2004; 64: 664-8.
  - Ng CF, Chan LW, Wong KT, Cheng CW, Yu SC, Wong WS: Prediction of differential creatinine clearance in chronically obstructed kidneys by non-contrast helical computerized tomography. *Int Braz J Urol*. 2004; 30: 102-7; discussion 108.
  - El-Ghar ME, Shokeir AA, El-Diasty TA, Refaie HF, Gad HM, El-Dein AB: Contrast enhanced spiral computerized tomography in patients with chronic obstructive uropathy and normal serum creatinine: a single session for anatomical and functional assessment. *J Urol*. 2004; 172: 985-8.
  - Steckler RE, McLorie GA, Jayanthi VR, Gilday DL, Ash JM, Churchill BM, et al.: Contradictory supra-normal differential renal function during nuclear renographic investigation of hydronephrosis. *J Urol*. 1994; 152: 600-2; discussion 602-3.

---

*Accepted after revision:  
October 2, 2008*

---

**Correspondence address:**

Dr. Daniel M. Kaplon  
Dept. of Surgery/Division of Urology  
Rhode Island Hospital  
2 Dudley Street, Suite 174  
Providence, 02905, RI, USA  
Fax: + 1 401 444-6947  
E-mail: kaplonda@gmail.com

## EDITORIAL COMMENT

Non-invasive estimation of split renal function has been a major challenge for many years, since renal scintigraphy has some limitations (including overestimation of function in obstructive diseases). Helical Computed Tomography (CT), which is

considered the most important, self-comprehensive imaging study for renal evaluation, has previously been used to predict split renal function, based on morphological and perfusional criteria (1). However, most of the models require the injection of iodinated

contrast media, which may be a significant limitation in patients with impaired renal function (given the nephrotoxicity of the contrast agent). Even contrast-enhanced Magnetic Resonance Imaging (MRI), formerly considered a safe method for renal function estimation in patients with impaired renal function, has become a limited exam in this scenario given the apparent association of gadolinium injection and the development of nephrogenic systemic fibrosis in this group of patients.

Summerlin et al. recently published an article showing that split renal function can be correctly calculated using 3D renal volumes obtained on CT images, with good correlation to the results of split post-contrast renal attenuation and renal scintigraphy (2). The article from Dr. Kaplon et al. proposes a practical and straightforward method of calculating split renal function based solely on renal parenchyma

thickness, regardless of the use of intravenous contrast media. Given the simple measurements technique, and since it does not involve complicated mathematical models for analysis, it is intuitive to predict that the method could be extrapolated to other imaging techniques, such as ultrasound and non-enhanced MRI, and further investigations will certainly be conducted on these new possibilities.

#### REFERENCES

1. Hackstein N, Buch T, Rau WS, Weimer R, Klett R: Split renal function measured by triphasic helical CT. *Eur J Radiol.* 2007; 61: 303-9.
2. Summerlin AL, Lockhart ME, Strang AM, Kolettis PN, Fineberg NS, Smith JK: Determination of split renal function by 3D reconstruction of CT angiograms: a comparison with gamma camera renography. *AJR Am J Roentgenol.* 2008; 191: 1552-8.

***Dr. Ronaldo Hueb Baroni***  
*Institute of Radiology*  
*University of Sao Paulo, USP*  
*Sao Paulo, SP, Brazil*  
*E-mail: rbaroni@einstein.br*

# Laparoscopic Surgery for Renal Stones: Is it Indicated in the Modern Endourology Era?

Andrei Nadu, Oscar Schatloff, Roy Morag, Jacob Ramon, Harry Winkler

*Department of Urology, The Chaim Sheba Medical Center, Tel Hashomer, Israel and The Sackler School of Medicine, Tel Aviv University, Israel*

---

## ABSTRACT

*Purpose:* To report the outcomes of laparoscopic surgery combined with endourological assistance for the treatment of renal stones in patients with associated anomalies of the urinary tract. To discuss the role of laparoscopy in kidney stone disease.

*Materials and Methods:* Thirteen patients with renal stones and concomitant urinary anomalies underwent laparoscopic stone surgery combined with ancillary endourological assistance as needed. Their data were analyzed retrospectively including stone burden, associated malformations, perioperative complications and outcomes.

*Results:* Encountered anomalies included ureteropelvic junction obstruction, horseshoe kidney, ectopic pelvic kidney, fused-crossed ectopic kidney, and double collecting system. Treatment included laparoscopic pyeloplasty, pyelolithotomy, and nephrolithotomy combined with flexible nephroscopy and stone retrieval. Intraoperative complications were lost stones in the abdomen diagnosed in two patients during follow up. Mean number of stones removed was 12 (range 3 to 214). Stone free status was 77% (10/13) and 100% after one ancillary treatment in the remaining patients. One patient had a postoperative urinary leak managed conservatively. Laparoscopic pyeloplasty was successful in all patients according to clinical and dynamic renal scan parameters.

*Conclusions:* In carefully selected patients, laparoscopic and endourological techniques can be successfully combined in a one procedure solution that deals with complex stone disease and repairs underlying urinary anomalies.

**Key words:** *kidney; laparoscopy; nephrolithiasis; genitourinary abnormalities*

**Int Braz J Urol.** 2009; 35: 9-18

---

## INTRODUCTION

Endourological techniques have revolutionized the treatment of urinary stones to the point they have rendered open stone surgery anachronistic (1). Procedures like open ureterolithotomy, open nephrolithotomy, or open pyelolithotomy have become anecdotal. However, patients with large stone burdens and associated renal malformations are prone to require multiple endourological procedures in order to have their stones retrieved and anomalies repaired.

Thus in these selected patients, open stone surgery can certainly be considered reasonable (2). In centers with established experience in advanced reconstructive laparoscopy, this can be a feasible option if the goals of stone clearance and correction of malformations could be achieved in a single procedure. Incorporating laparoscopic techniques confer these patients surgical efficacy combined with the advantages of minimally invasive surgery.

In the present paper, we describe our experience and evaluate the outcomes of laparoscopic sur-

**Table 1** – Patients characteristics.

N of Patients	Preoperative Diagnosis
6	UPJO + multiple pelvic and calyceal stones
2	UPJO + horseshoe kidney + multiple stones
1	UPJO + two stones 3 cm each in the renal pelvis + a calyceal diverticulum with a 2 cm stone
1	UPJO + ectopic pelvic kidney + 2 cm upper pole stone
1	UPJO + situs inversus + crossed-fused ectopic kidney + tens of stones in lower moiety
1	UPJO + pelvic kidney + obstructive hydrocalyx + multiple pelvic and calyceal stones
1	Double collecting system + 9 cm complete staghorn stone in the lower moiety

UPJO = ureteropelvic junction obstruction.

gery in combination with endourological procedures involving a variety of cases of renal stones in the setting of underlying urinary tract malformations.

## MATERIALS AND METHODS

The data of twenty-nine patients who underwent laparoscopic procedures for kidney stones between January 2004 and May 2007 were retrospectively analyzed. Retrieved data included indications for intervention, stone burden, associated malformations, perioperative complications and outcomes in terms of functional results and stone free status. Fifteen patients underwent laparoscopic nephrectomy due to non functioning kidneys and were not included in the present study. One patient underwent laparoscopic pyelolithotomy without harboring underlying malformations and thus was also excluded. The remaining thirteen patients underwent laparoscopic stone removal and reconstructive procedures combined with ancillary endourological assistance as needed. Preoperative stone scenario and associated anomalies are detailed in Table-1 and Figures-1 to 3. All cases were discussed with the endourology unit and considered unlikely that stones and underlying anomalies could be efficiently addressed with a single endourological procedure. Three patients had previous unsuccessful endourological procedures, with inability to gain percutaneous access and significant residual stones after nephroscopy among main causes of failure.

Patients underwent preoperative anatomical and functional evaluation with non contrast CT scan and either intravenous pyelography or diuretic renal scans in cases of suspected ureteropelvic junction (UPJ) obstruction. Postoperative assessment consisted of x-rays, ultrasound, and/or CT as appropriate. A diuretic renal scan was performed in patients who underwent concomitant pyeloplasty.

Surgical procedures and their technique are summarized below. Combinations were used to deal with specific patient necessities.



**Figure 1** – Patient with situs inversus and left to right crossed-fused ectopic kidney with ureteropelvic junction obstruction and multiple stones in the ectopic kidney (lower moiety). This patient underwent laparoscopic pyelolithotomy and pyeloplasty.

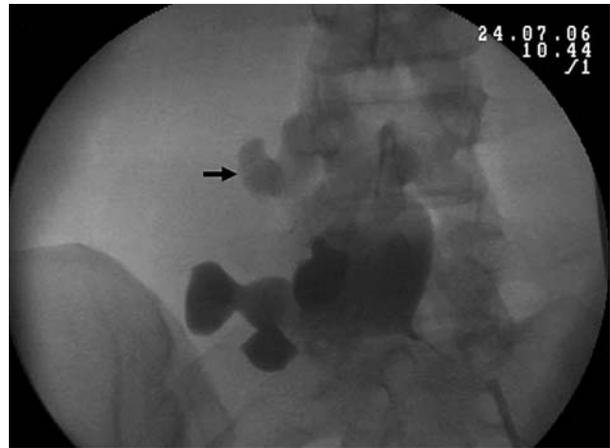


**Figure 2** – Left: Complete 9 cm staghorn stone in the lower moiety of a complete duplicated pelvicalyceal system. Right: Intravenous urography performed 3 months after laparoscopic anatomic nephrolithotomy showing dye descending through both right excretory systems.

## SURGICAL TECHNIQUE

### Laparoscopic Pyeloplasty and Pyelolithotomy / Flexible Nephroscopy

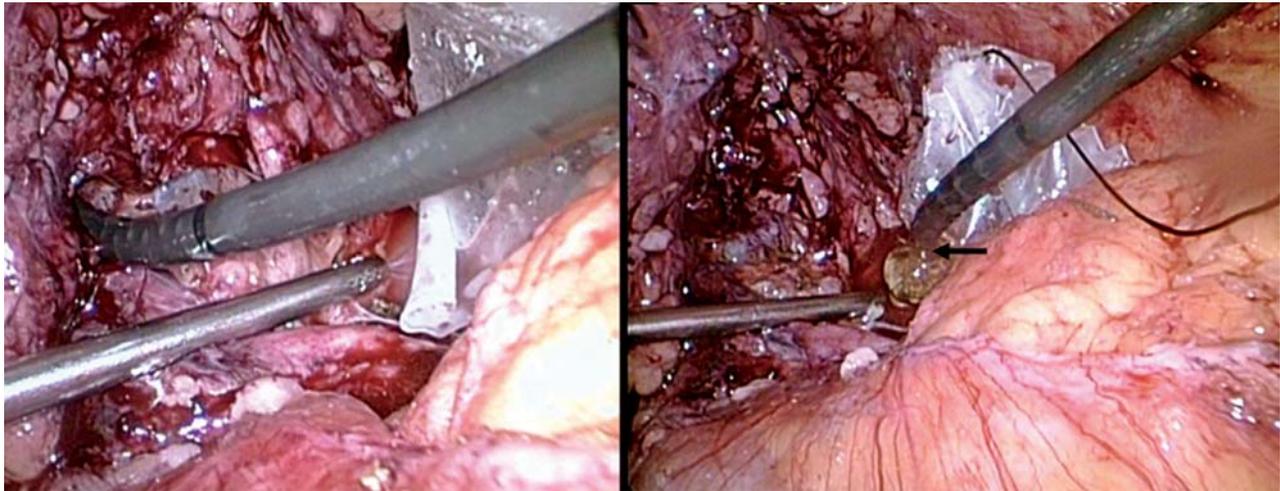
The operative room setting includes one laparoscopic cart and one endourological cart to enable simultaneous laparoscopy and nephroscopy. Using a four port transperitoneal approach, the ureter is identified and followed cranially, the UPJ is exposed and the renal pelvis dissected. The renal pelvis is opened above the UPJ, the ureter is spatulated on its lateral aspect and dismembered. Stones in the renal pelvis are removed with an atraumatic grasper and placed in a laparoscopic bag. A flexible cysto-nephroscope is passed through one of the 10 mm ports and guided laparoscopically through the opening in the renal pelvis. The kidney is systematically inspected and calyceal stones removed with a basket or fragmented with Holmium:YAG laser lithotripsy. A double J stent is introduced in an antegrade fashion, the renal pelvis is reduced as needed, and ureteropelvic anastomosis is performed with two (one posterior and one anterior) 4/0 polyglactin running sutures. A percutaneous drain is placed and the bag with stones removed (Figure-4).



**Figure 3** – Retrograde pyelography of a patient with an ectopic pelvic kidney, ureteropelvic junction obstruction and a 2 cm stone in the upper pole (arrow). Intraoperatively, infundibular stricture was encountered and the patient underwent laparoscopic pyeloplasty, and “cut to the light” nephrolithotomy.

### Laparoscopic Nephrolithotomy

A “cut for the light” technique was used when calyceal stones were associated with infundibular stricture, obstructed hydrocalyx, or calyceal diverticulum. After widely incising the renal pelvis, the



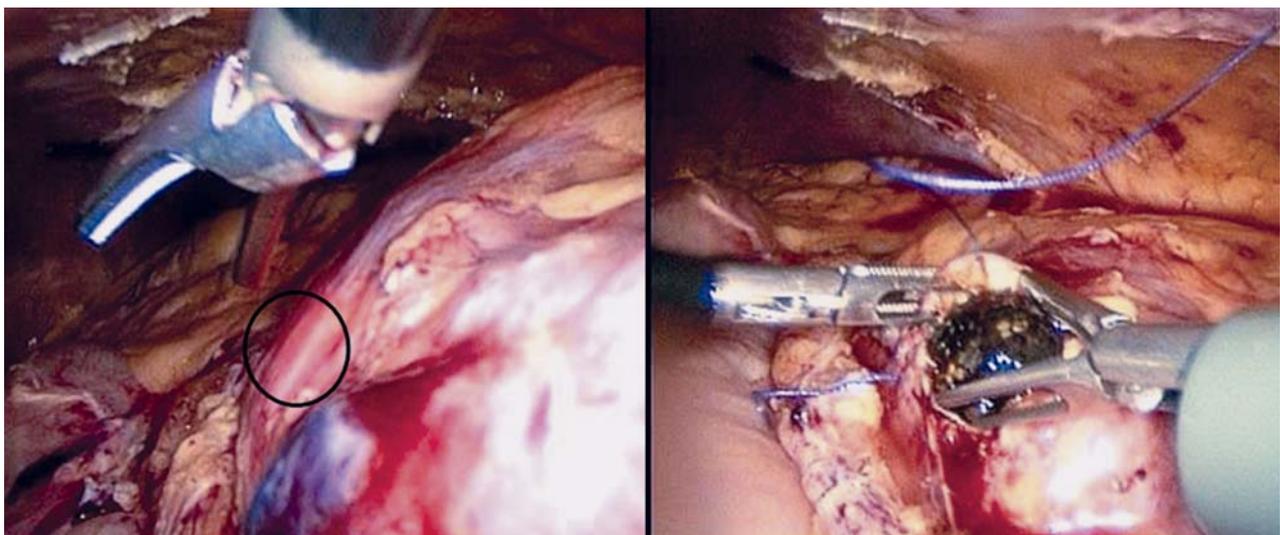
**Figure 4** – Left: Flexible nephroscopy through the laparoscopic pyelotomy. Right: Basket extraction of encountered stones (arrow). Intermittent suction prevents fluid accumulation in the abdomen.

flexible cysto-nephroscope is brought at the obstructed calyx containing the stone and a small laparoscopic nephrotomy is made in the kidney as indicated by the endoscopic light. The stone is removed and the kidney sutured with one layer 2/0 polyglactin (Figure-5).

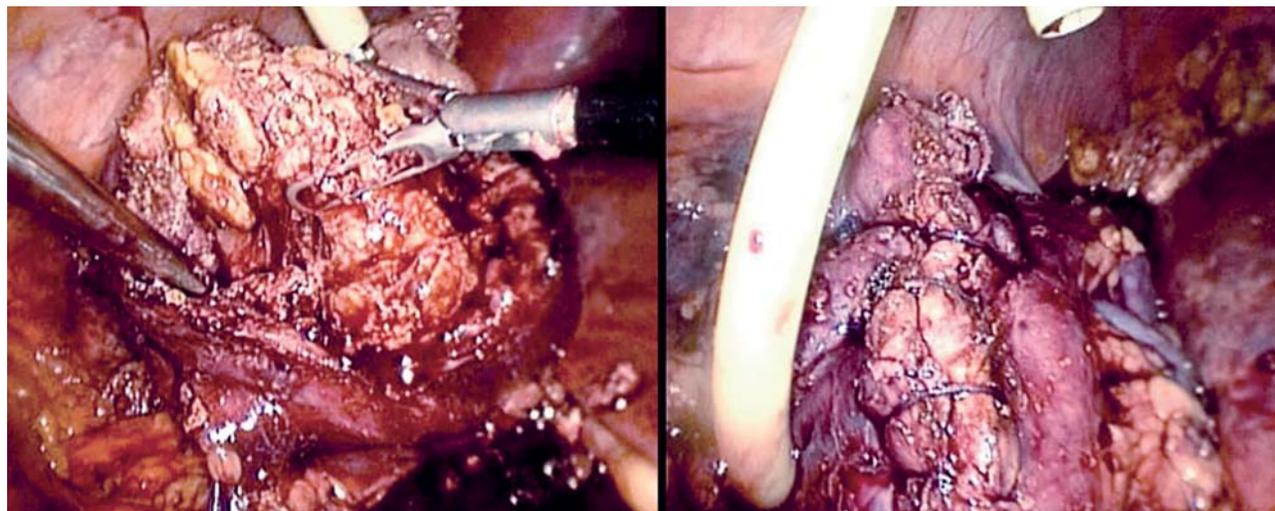
#### Laparoscopic Anatomic Nephrolithotomy

The kidney is dissected from the surrounding fat, the vascular elements identified and clamped en

bloc with a laparoscopic Satinsky clamp. The renal parenchyma and collecting system are incised longitudinally on the postero-lateral aspect of the kidney; the staghorn stone is mobilized with graspers, removed and placed in an endobag. A 16 F Foley catheter is placed as a nephrostomy tube by making a small incision in the kidney away from the nephrotomy line. The kidney is sutured with a running 2/0 polyglactin single layer that includes renal capsule, parenchyma,



**Figure 5** – Left: Endoscopic light transilluminates the location of an obstructed upper pole calyx (area inside the circle). Right: The kidney is incised over the lighted parenchyma and the stone removed laparoscopically.



**Figure 6** – Left: Laparoscopic anatomic nephrolithotomy, stone extraction. Right: One layer LapraTy™ assisted suturing of the kidney.

and collecting system in a “no-knot” technique with the aid of Lapra-Ty clips (Ethicon-Johnsons & Johnsons), Figure-6.

## RESULTS

Mean age at surgery was 36 years (range 18-56), ASA score 2 (range 1-2), and average number of stones removed was 12 (range 3 to 214). Laparoscopic pyeloplasty combined with pyelolithotomy and flexible nephroscopy was performed in ten patients, laparoscopic pyeloplasty with pyelolithotomy and endoscopic-assisted nephrolithotomy was performed

in two; and laparoscopic anatomic nephrolithotomy was performed in one patient (Table-2).

A double J stent and percutaneous drain was left postoperatively in all patients. Additionally, a nephrostomy drain using a 16 Fr Foley catheter was placed in two patients. All the procedures were completed laparoscopically with no conversions to open surgery. Intraoperative complications included two patients with lost stones in the abdomen diagnosed during follow up (Figure-7) and variable degrees of irrigation fluid accumulation secondary to nephroscopy in several others. One patient had a postoperative urinary leak in the context of an indwelling double J stent, which was not replaced at the time of surgery,

**Table 2** – Procedures performed and their indication.

Procedure	Indication
1. LP combined with LPL and flexible nephroscopy	Patients with UPJO and associated pelvic and calyceal stones
2. LP combined with LPL and endoscopic-assisted LNL	Patients with UPJO and stones in an obstructed hydrocalyx or calyceal diverticulum
3. Laparoscopic anatomic nephrolithotomy	Patient with double collecting system and complete stag-horn of the lower moiety

*LP = laparoscopic pyeloplasty; LPL = laparoscopic pyelolithotomy; UPJO = ureteropelvic junction obstruction; LNL = laparoscopic nephrolithotomy.*



*Figure 7 – Lost stones in the abdomen incidentally discovered during follow-up.*

and most probably chronically obstructed. Leakage was discovered during early postoperative period as urinary extravasation through the percutaneous drain. Cystoscopic replacement of the double J stent effectively treated the complication and the patient was discharged during the following days without evidence of further leakage.

Stone free status was obtained in ten patients (77%), and the remaining three were rendered stone free after one ancillary procedure (shockwave lithotripsy - SWL) in two patients and retrograde nephroscopy in another).

In all twelve patients with UPJ obstruction the pyeloplasty was considered successful according to clinical (disappearance of pain) and diuretic renal scan parameters. The mean washout half-life time in the diuretic renal scan improved from 43 to 22 minutes.

Warm ischemia time for laparoscopic anatomic nephrolithotomy was 43 minutes; the patient was rendered stone free and renal function remained within preoperative values.

## COMMENTS

Endourology has revolutionized the treatment of urinary stones. Notwithstanding, underlying anatomic anomalies, extremely large stone burdens

or a combination of them can significantly decrease the success rate of endourological procedures (3,4). The surgical approach in these special cases should efficiently address the large stone burden and associated malformations in a single procedure. Although open surgery is an alternative, laparoscopic surgery might be a feasible option additionally conferring the advantages of minimally invasive surgery.

Micali et al. reported 17 patients who underwent laparoscopic stone extraction, including 11 with renal calculi and 9 with associated anomalies (UPJ obstruction) with stone size up to 6 cm; fifteen patients were eventually rendered stone free and one patient had a postoperative urinoma. These authors concluded that indications for laparoscopy included stones associated with anatomical abnormalities requiring reconstruction and calculi for which endourological procedures had failed (5). Ramakumar et al. reported 90% three month stone-free rate in 19 patients who underwent laparoscopic pyelolithotomy and pyeloplasty (6). Similar results were recently reported by Srivastava et al. (7) and Stein et al. (8) with 75 and 80% stone-free rates respectively.

Nambirajan et al. reported their experience with eighteen patients who underwent different laparoscopic procedures with concomitant stone removal, including pyeloplasties, partial nephrectomies, and calyceal ablations. Stone-free status was achieved in 93% of cases. The authors concluded that laparoscopy is effective for complex renal stones and that the need for open surgery should be rare in the future (9). Meria et al. compared laparoscopic pyelolithotomy to percutaneous nephrolithotomy (PNL) in 32 patients with pelvic stones without underlying malformations. Stone free rates were not significantly different (88 vs. 82%). However, the laparoscopic group had higher operative time, urological complications (12% urine leak), and conversion to open surgery was required in two patients. They concluded that indications for each technique must be determined although PNL remains the gold standard for large pelvic stones (10). It is our belief and current practice that SWL, retrograde and percutaneous techniques are the first approaches to treat kidney stones due to their excellent results and minimal morbidity. The role of laparoscopy is not to replace any of these options, but to compliment them in situations where decreased success or increased

morbidity is expected, specially as regards large stone burdens coexisting with underlying malformations. As showed in our series and as reported by other authors (11,12), laparoscopic and endourological techniques can be successfully combined in the same procedure to improve the stone free rate and simultaneously resolve synchronous anomalies.

Tunc et al. published a study on 150 patients with stones in anomalous kidneys treated with SWL, including 57 duplex, 45 horseshoes, 30 malrotated, 14 pelvic, and 4 crossed ectopic. The overall stone-free rate was 68%, with the worst results obtained in crossed ectopic kidneys with stone clearance of only 25% (13). Pure percutaneous approach has also been reported in anomalous kidneys. Although highly effective with an overall stone-free rate of 83%, the anterior displacement of the collecting system together with an unpredictable vascular supply and interposition of bowel between the kidney and the abdominal wall makes the procedure technically demanding. Moreover, it requires a highly precise imaging system (i.e. CT guided) to minimize risk of visceral damage during kidney puncture and tract creation (14). Pure endoscopic management has also been accomplished for anomalous kidneys. Weizer et al. reported a 75% stone-free rate (15), meanwhile Braz et al. reported an 81% stone-free rate at three months, however 62% required ancillary treatments (16). Due to urinary stasis, these patients suffer from poor spontaneous stone passage, with persistence or growth of residual fragments in 60% of cases.

Laparoscopic techniques seem especially useful for stones located in anomalous kidneys. Our overall stone-free rate was 77% (10/13), and reached a 100% after one ancillary treatment (i.e. SWL or nephroscopy). Additionally, anomalies to be addressed (i.e. UPJ obstruction) were successfully repaired with optimal functional outcome.

There are several operative pitfalls that need special consideration when combining laparoscopy with endourological procedures. The operating room and the space around the operating table become limited when the laparoscopic and endourological towers need to be brought to work simultaneously. The laser cart and endourological instrumentation table pose additional ergonomic problems. One serious limitation is the difficulty to obtain fluoroscopic images during

stone removal. Introduction of a C arm becomes a challenge in the described set-up and even if possible the images obtained in the insufflated abdomen of a patient in lateral decubitus are far from informative. Deflating the abdomen may improve the imaging but is unpractical and time consuming, and even after this, images are of poor quality due to patient position and free fluid in the abdomen, thus seriously limiting the ability to identify small residual stones.

Irrigating fluid that flows freely into the abdomen during the nephroscopy is of some concern and might be a limiting factor. Although some of it can be suctioned, still large quantities of fluid accumulate and occupy the space of the pneumoperitoneum. As fluid accumulates between bowel loops it cannot be directly aspirated. We overcame this difficulty by placing the patient in a “head down” position for two minutes, allowing the fluid to accumulate under the diaphragm where it becomes easily aspirated with the laparoscopic suction.

Identifying stones inside obstructed calyces can become a real challenge. Intraoperative ultrasound can be useful in these situations (9) however; it poses additional restrictions to the already cumbersome operative scenario. We found a solution relying on “cut for the light” technique, where the light of the endoscope marks the stone containing calyx and the location for the parenchymal incision. In the two cases performed, the light of the endoscope precisely delineated the place for the nephrotomy (Figure-5).

Kaouk et al. created a porcine model to address the feasibility of laparoscopic anatomic nephrolithotomy (17), Deger et al. reported the first case in humans (18), and recently Simforoosh et al. (19) reported their series of five patients, with 3/5 being rendered stone-free. Interestingly, no postoperative urinary extravasation occurred albeit no internal stent was placed. We performed a laparoscopic anatomic nephrolithotomy in a young patient with a duplex system and a complete staghorn of the lower moiety with optimal results and no perioperative complications. The kidney was repaired with one running suture including parenchyma and collecting system with no postoperative urinary extravasation.

An interesting aspect of laparoscopic pyelolithotomy concerns stones lost in the abdomen. It is not infrequent during retrieval of multiple small stones to

have them fall out of the renal pelvis or the endobag, and locating them in the abdomen is challenging and time consuming. There is no report in the urological literature regarding this issue; however there are well described complications of lost stones in the abdomen after laparoscopic cholecystectomy. They include intraperitoneal and abdominal wall abscess, fistula, and prolonged fever (20). Regarding the infectious status of struvite staghorn stones, lost stones should remain of concern. However, two patients in our series had lost stones in the abdomen and after completing more than two years of follow-up, they remain completely asymptomatic.

We are aware of the limitations of this paper, which consist of a small, retrospective series of patients. However, considering the limited data published up to date we believe our experience contributes to the developing of this novel and poorly studied approach.

## CONCLUSIONS

Although classical endourological procedures should remain as the gold standard for the great majority of renal stones, however patients with large stone burdens and underlying malformations might benefit from a combined laparoscopic and endourological one procedure solution that deals with complex stone disease and repairs associated anomalies.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Matlaga BR, Assimos DG: Changing indications of open stone surgery. *Urology*. 2002; 59: 490-3; discussion 493-4.
2. Alivizatos G, Skolarikos A: Is there still a role for open surgery in the management of renal stones? *Curr Opin Urol*. 2006; 16: 106-11.
3. Grasso M, Conlin M, Bagley D: Retrograde ureteropyeloscopic treatment of 2 cm. or greater upper urinary tract and minor Staghorn calculi. *J Urol*. 1998; 160: 346-51.
4. Semerci B, Verit A, Nazli O, Ilbey O, Ozyurt C, Cikili N: The role of ESWL in the treatment of calculi with anomalous kidneys. *Eur Urol*. 1997; 31: 302-4.
5. Micali S, Moore RG, Averch TD, Adams JB, Kavoussi LR: The role of laparoscopy in the treatment of renal and ureteral calculi. *J Urol*. 1997; 157: 463-6.
6. Ramakumar S, Lancini V, Chan DY, Parsons JK, Kavoussi LR, Jarrett TW: Laparoscopic pyeloplasty with concomitant pyelolithotomy. *J Urol*. 2002; 167: 1378-80.
7. Srivastava A, Singh P, Gupta M, Ansari MS, Mandhani A, Kapoor R, et al.: Laparoscopic pyeloplasty with concomitant pyelolithotomy--is it an effective mode of treatment? *Urol Int*. 2008; 80: 306-9.
8. Stein RJ, Turna B, Nguyen MM, Aron M, Hafron JM, Gill IS, et al.: Laparoscopic pyeloplasty with concomitant pyelolithotomy: technique and outcomes. *J Endourol*. 2008; 22: 1251-5.
9. Nambirajan T, Jeschke S, Albqami N, Abukora F, Leeb K, Janetschek G: Role of laparoscopy in management of renal stones: single-center experience and review of literature. *J Endourol*. 2005; 19: 353-9.
10. Meria P, Milcent S, Desgrandchamps F, Mongiat-Artus P, Duclos JM, Teillac P: Management of pelvic stones larger than 20 mm: laparoscopic transperitoneal pyelolithotomy or percutaneous nephrolithotomy? *Urol Int*. 2005; 75: 322-6.
11. Fariña Pérez LA, Cambronero Santos J, Meijide Rico F, Zungri Telo ER: Laparoscopic pyelolithotomy in a pelvic kidney. *Actas Urol Esp*. 2004; 28: 620-3.
12. Whelan JP, Wiesenthal JD: Laparoscopic pyeloplasty with simultaneous pyelolithotomy using a flexible ureteroscope. *Can J Urol*. 2004; 11: 2207-9.
13. Tunc L, Tokgoz H, Tan MO, Kupeli B, Karaoglan U, Bozkirli I: Stones in anomalous kidneys: results of treatment by shock wave lithotripsy in 150 patients. *Int J Urol*. 2004; 11: 831-6.
14. Matlaga BR, Shah OD, Zagoria RJ, Dyer RB, Stroom SB, Assimos DG: Computerized tomography guided access for percutaneous nephrostolithotomy. *J Urol*. 2003; 170: 45-7.
15. Weizer AZ, Springhart WP, Ekeruo WO, Matlaga BR, Tan YH, Assimos DG, et al.: Ureteroscopic management of renal calculi in anomalous kidneys. *Urology*. 2005; 65: 265-9.
16. Braz Y, Ramon J, Winkler H: Ureterorenoscopy and holmium laser lithotripsy for large renal stone burden: A reasonable alternative to percutaneous nephrolithotomy. *Eur Urol*. 2005; (Suppl 4): 264. (Abstract 1047).

17. Kaouk JH, Gill IS, Desai MM, Banks KL, Raja SS, Skacel M, et al.: Laparoscopic anatomic nephrolithotomy: feasibility study in a chronic porcine model. *J Urol.* 2003; 169: 691-6.
18. Deger S, Tuellmann M, Schoenberger B, Winkelmann B, Peters R, Loening SA: Laparoscopic anatomic nephrolithotomy. *Scand J Urol Nephrol.* 2004; 38: 263-5.
19. Simforoosh N, Aminsharifi A, Tabibi A, Noor-Alizadeh A, Zand S, Radfar MH, et al.: Laparoscopic anatomic nephrolithotomy for managing large staghorn calculi. *BJU Int.* 2008; 101: 1293-6.
20. Memon MA, Deeik RK, Maffi TR, Fitzgibbons RJ Jr: The outcome of unretrieved gallstones in the peritoneal cavity during laparoscopic cholecystectomy. A prospective analysis. *Surg Endosc.* 1999; 13: 848-57.

---

*Accepted after revision:  
October 24, 2008*

---

**Correspondence address:**

Dr. Oscar Schatloff  
Department of Urology  
The Chaim Sheba Medical Center  
Tel Hashomer, 52621, Israel  
Fax: + 972 3 535-1892  
E-mail: oscar.schatloff@gmail.com

## EDITORIAL COMMENT

Authors present interesting series of patients with urinary stone disease managed mainly by laparoscopic method. The presented cases have some kind of anomaly necessitating laparoscopic approach rather than using routine endourological procedures like percutaneous nephrostolithotomy or urethroscopic means.

Laparoscopy is gaining more popularity in managing urinary stone disease (1-3). This is especially true when associated anomalies like ureteropelvic junction obstruction, or fusion anomalies exists (4).

Even though results of laparoscopic approach in managing stone disease in the present series and other reported series seems satisfactory (1-5), longer follow-up and more cases are necessary to better elucidate the exact role of laparoscopy in today's management of stone disease.

## REFERENCES

1. Simforoosh N, Aminsharifi A, Tabibi A, Noor-Alizadeh A, Zand S, Radfar MH, et al.: Laparoscopic anatomic nephrolithotomy for managing large staghorn calculi. *BJU Int.* 2008; 101: 1293-6.
2. Basiri A, Simforoosh N, Ziaee A, Shayaninasab H, Moghaddam SM, Zare S: Retrograde, antegrade and laparoscopic approaches for the management of large, proximal stones: A randomized clinical trial. *J Endourol.* 2008; 22: 2677-80.
3. Meria P, Milcent S, Desgrandchamps F, Mongiat-Artus P, Duclos JM, Teillac P: Management of pelvic stones larger than 20 mm: laparoscopic transperitoneal pyelolithotomy or percutaneous nephrolithotomy? *Urol Int.* 2005; 75: 322-6.
4. Mosavi-Bahar SH, Amirzargar MA, Rahnavardi M, Moghaddam SM, Babbolhavaeji H, Amirhasani S:

Percutaneous nephrolithotomy in patients with kidney malformations. *J Endourol.* 2007; 21: 520-4.

5. Simforoosh N, Basiri A, Danesh AK, Ziaee SA, Shari-faghdas F, Tabibi A, et al.: Laparoscopic management

of ureteral calculi: a report of 123 cases. *Urol J.* 2007; 4: 138-41.

***Dr. Nasser Simforoosh***

*Shaheed Labbafinejad Hospital*

*Urology Nephrology Research Center*

*Shaheed Beheshti University of Medical Sciences*

*Tehran, Iran*

*E-mail: simforoosh@iurtc.org.ir*

## EDITORIAL COMMENT

Laparoscopy is an established modality in management of renal stones in selected situations. On most occasions, laparoscopy is nephron sparing - namely - pyelolithotomy as compared with percutaneous nephrostolithotomy (PCNL).

The authors have successfully used laparoscopy combined with endourological procedures in anomalous kidneys, mainly ureteropelvic junction obstruction. This is a retrospective study. Larger and prospective studies will help in developing concrete guidelines.

It is to be noted that a renal angiogram or CT angiogram is a complimentary investigation in planning reconstructive laparoscopic surgery in anomalous kidneys.

The authors have not done an infundibuloplasty in cases of infundibular stenosis with calyceal diverticulum and; the collecting system was not closed separately in patients with staghorn calculus where

an anatomic pyelolithotomy was done. It would be interesting to see the configuration of the collecting system using a CT scan during follow-up.

In most centers, pyeloplasty is done with interrupted sutures. The authors have used running sutures for the anterior and posterior walls.

Meria et al. had shown similar results with different modalities (PCNL and laparoscopy) in management of stone disease in non-anomalous kidneys; however the complication rate in was higher in laparoscopy compared to ESWL and PCNL. Hence, they concluded that ESWL or PCNL should be the first option in non-anomalous kidneys.

Practical problems of C arm usage; ultrasound usage and free flow of irrigating fluid into the peritoneal cavity with laparoscopy are problems to be looked into.

Combining laparoscopy with PCNL and pure endoscopy gives a better result in stone disease.

***Dr. Manickam Ramalingam***

*Department of Urology*

*K.G. Hospital and Post Graduate Institute*

*Coimbatore, India*

*E-mail: uroram@yahoo.com*

# The Role of Liver Transplantation Techniques in the Surgical Management of Advanced Renal Urothelial Carcinoma with or without Inferior Vena Cava Thrombus

Wolfgang H. Cerwinka, Murugesan Manoharan, Mark S. Soloway, Gaetano Ciancio

*Department of Urology (WHC, MM, MSS) and Department of Surgery (GC), Division of Transplantation, University of Miami Miller School of Medicine, Miami, Florida, USA*

---

## ABSTRACT

*Purpose:* Standard radical nephrectomy for large masses is significantly facilitated by liver transplantation techniques, which have been successfully employed over the last ten years at our institution. Large and locally-advanced urothelial carcinoma of the kidney with or without extension into the inferior vena cava is rare. The purpose of this study was to present the surgical management of large and locally-advanced urothelial tumors arising from the renal pelvis using liver transplantation techniques and to evaluate patient outcome.

*Materials and Methods:* Diagnostic work-up and surgical management of 4 patients with large and locally-advanced renal urothelial carcinoma were retrospectively reviewed. Two out of four patients with urothelial carcinoma presented with inferior vena cava thrombus. Mean tumor size was 11.6 cm. All patients underwent surgery, 2 patients with the presumed diagnosis of renal cell cancer. Liver transplantation techniques were an integral part in all radical nephrectomies.

*Results:* No intraoperative complications and postoperative mortality occurred. Mean operative time was 7.5 hours, estimated blood loss was 1.5 L, and an average of 4.8 units of blood was transfused intraoperatively. Three patients succumbed to cancer recurrence at a mean postoperative time of 6.3 months; 1 patient is still alive 24 months after surgery.

*Conclusions:* Large and locally-advanced renal masses of urothelial origin can be successfully removed by a combination of radical nephrectomy with liver transplantation techniques. Since long-term outcome of such patients has been poor, accurate preoperative diagnosis is essential to consider neoadjuvant treatment and to plan nephroureterectomy.

**Key words:** *urothelial carcinoma; kidney, nephrectomy; liver transplantation*

**Int Braz J Urol. 2009; 35: 19-23**

---

## INTRODUCTION

Urothelial carcinoma (UC) of the renal pelvis represents approximately 10% of all primary renal malignancies and its prognosis correlates with histological grade and stage (1,2). Advanced disease stages, such as invasion into renal parenchyma or perirenal fat with or without tumor extension into the inferior vena cava (IVC) carry a poor prognosis (3). IVC involvement is rare with only a few cases

reported in the literature (4). Extirpation of these large renal masses poses a particular challenge to the urologic surgeon because adequate surgical exposure and subsequent nephrectomy rely on mobilization of adjacent organs such as liver and spleen. In cases of tumor extension into the IVC, additional exposure of the retrohepatic and suprahepatic IVC is necessary. Locally-advanced renal cell carcinomas (RCC) have been safely and completely removed by combining radical nephrectomy with surgical techniques derived

from liver transplantation over the last ten years at our institution (5).

The purpose of this study was to present the surgical management of large and locally-advanced urothelial tumors arising from the renal pelvis employing liver transplantation techniques and to evaluate patient outcome.

## MATERIALS AND METHODS

Four patients with locally-advanced UC of the renal pelvis ( $\geq T3$ ), two with extension into the IVC, were treated at our institution between 2003 and 2005. Pertinent preoperative work-up (imaging, laboratory), tumor characteristics (grade, stage), surgical approach, perioperative management, and patient outcome were reviewed. All four patients underwent standard preoperative evaluation including abdominal CT scans, chest X-rays or chest CT scans, and liver function tests. Bone scans and abdominal MRIs were obtained in 2 patients. Tumor thrombus extent was staged according to the Mayo Foundation classification (6). Cystoscopy and cytology were performed in 1 of 3 patients with a history of hematuria.

Liver transplantation techniques, in combination with nephrectomy for large and locally-invasive renal masses, have been previously described in detail (5). In brief, a bilateral subcostal incision, with superior midline T-extension is performed and a Rochard self-retaining retractor placed. This tri-radiate incision permits access to the liver, diaphragm, hepatic veins, and suprahepatic IVC and is the favored approach for orthotopic liver transplantation. Liver and IVC are mobilized in piggyback fashion. Liver mobilization begins with dissection, ligation and division of the ligamentum teres. The falciform ligament is then divided by cautery. This incision is carried around each portion of the divided falciform ligament to the right superior coronary ligament and divides the left triangular ligament. The visceral peritoneum on the right side of the hepatic hilum and the infrahepatic IVC are incised with the right inferior coronary and hepatorenal ligaments. At this stage, nephrectomy of most bulky masses can be safely carried out, however, in cases of IVC involvement, mobilization continues. The liver is gradually rolled to the left using the same

techniques as in liver transplantation. In this fashion, the infrahepatic, intrahepatic, and suprahepatic portions of the IVC are completely exposed. The three hepatic veins are identified, their orifices inspected, and tumor removed. Following the removal of the tumor thrombus and IVC, the clamp is repositioned below the hepatic veins thus permitting continued hepatic venous drainage during the removal of the IVC and tumor thrombus. Exposure of the left kidney begins by mobilization of the descending colon. The spleen is dissected off the diaphragm and mobilized en bloc with the pancreas toward the midline. To gain access to the upper pole of the left kidney the left liver lobe is mobilized. The study was approved by the Institutional Review Board.

## RESULTS

Three male and one female patient underwent surgery for large but clinically localized UCs of the renal pelvis; mean age was 65 years (range 59-74). Preoperative diagnosis was UC in 2 cases: One patient had undergone radical cystectomy with ileal conduit 6 years earlier suggesting upper tract UC; another patient underwent cystoscopy showing tumor protruding from the ureteral orifice. The remaining two patients with IVC thrombus entered surgery with the presumed diagnosis of RCC.

A bilateral subcostal incision with midline T-extension was the surgical approach in all 4 cases. Mean operative time was 7.5 hours, mean estimated blood loss was 1.5 L, and an average of 4.8 units of blood was transfused. Three nephrectomy specimens were bivalved in the operating room, which changed the diagnosis in one case and ureterectomy was consequently performed; the remaining specimen was not bivalved and the ipsilateral ureter was left in situ. Gross examination of the specimens demonstrated UC arising from the renal pelvis and invasion of the proximal ureter. None of the patients required cardiopulmonary bypass. There was neither an intraoperative complication nor an operative mortality. Postoperative morbidity occurred in 2 patients secondary to pulmonary embolism on postoperative day 2 and 61. Three patients underwent adjuvant chemotherapy; one could not proceed because of low

performance status. Three patients expired of disease recurrence at a mean of 6.3 months after surgery; one patient is alive without evidence of disease 24 months later (Table-1). All 4 patients were diagnosed with high-grade urothelial carcinoma arising from the renal pelvis. Tumor characteristics are shown in Table-2. Mean tumor size was 11.6 cm. In 2 patients the tumor extended into the IVC and in 2 patients lymph nodes were involved.

**COMMENTS**

To our knowledge this is the first study describing the application of liver transplantation techniques for the resection of large UCs of the kidney with and without IVC thrombus. The surgical technique described herein allowed excellent exposure and safe removal of the tumor in all 4 patients (5). Liver transplantation techniques proved essential for the resection of IVC thrombi in 2 patients and sig-

nificantly improved exposure to the retroperitoneum allowing complete removal of the remaining two renal masses with a mean size of 12 cm. Albeit RCC of such size is amenable to conventional nephrectomy, UC of the renal pelvis is known to induce significant perirenal inflammation and desmoplastic reaction and is frequently associated with lymph node metastasis (7). Secondary to these adverse tumor characteristics operative time was considerably prolonged with a mean of 7.5 hours. No intraoperative complications or postoperative mortality occurred. In a series of 3 patients with renal UC and IVC thrombus, a midline approach was selected in 2 patients (one surgery was aborted due to extensive liver involvement) and an extended subcostal incision in the third. One of these patients was without evidence of disease 9 months after surgery, two died of respiratory failure within 2 months postoperatively (8).

Prognosis for upper tract UC, stage for stage, is reportedly inferior to that of bladder UC. While 5 year overall survival rates for stage T2, T3, and T4

**Table 1** – Treatment and outcome of patients with advanced urothelial carcinoma of the renal pelvis.

Patient	EBL (mL)	Blood Transfusions	Operative Time	Morbidity	Adjuvant Chemotherapy	Recurrence	Survival
1	3000	11	7.6 hours	PE day 2	Cisplatin/Gemcitabine	Local	8 months
2	2000	5	8.3 hours		Cisplatin/Gemcitabine		Alive at 24 months
3	650	1	8.5 hours	PE day 61		Local	2 months
4	500	2	5.7 hours		MVAC	Metastatic	10 months

EBL = estimated blood loss; PE = pulmonary embolism; MVAC = methotrexate, vinblastine, doxorubicin, cisplatin.

**Table 2** – Tumor characteristics. High-grade urothelial carcinoma of the renal pelvis was the diagnosis in all cases.

Patient	Side	Margins	Tumor Size (cm)	Inferior Vena Cava Thrombus	TNM Stage	Positive Lymph Nodes
1	Right	Negative	8 x 6 x 6	Retrohepatic below hepatic veins	T3 N0 Mx	0
2	Left	Positive	11 x 6 x 5.5		T3 N0 Mx	0
3	Right	Positive	15.4 x 10.2 x 8	Infrahepatic	T4 N2 Mx	6
4	Right	Negative	12 x 5 x 4		T3 N2 Mx	2

bladder UC are 72%, 40%, and 33%, they are 60%, 15% and 15% for upper tract UC (3,9). Neoadjuvant chemotherapy for patients with  $\geq$  T2 bladder UC in prospective randomized clinical trials has demonstrated survival benefits (10,11). However, there is no evidence supporting neoadjuvant chemotherapy for upper tract UC. None of our patients received neoadjuvant chemotherapy; however, we speculate that it may have improved patient survival as previously demonstrated for bladder UC (intact vasculature, improved resectability, early control of occult metastases, better performance status). Neoadjuvant chemotherapy may furthermore result in better outcome than adjuvant chemotherapy because many patients do not receive optimal dosing of systemic chemotherapy after nephrectomy (12). One out of four patients with UC in our series was unable to commence adjuvant chemotherapy because of low performance status. Despite complete tumor resection, 3 out of 4 patients died of disease recurrence within 10 months after surgery, of whom 2 had undergone adjuvant chemotherapy.

Consideration of neoadjuvant chemotherapy relies on correct preoperative diagnosis. Two out of four patients in this study entered surgery with the presumptive diagnosis of RCC. Despite the presence of hematuria in 3 out of 4 patients, only 1 underwent cystoscopy, which established the correct diagnosis. Therefore, the finding of a large renal mass with or without IVC thrombus in patients with history of hematuria requires a complete hematuria work-up (13). According to the literature only 30% of patients with upper tract UC underwent surgery with the correct preoperative diagnosis. Several factors may contribute to the fact that large renal UC is frequently mistaken for RCC preoperatively (4). 1. UC arising from the renal pelvis is uncommon with an incidence of 7% to 15% of all primary renal malignancies (1,2). 2. RCC represents 85% of all primary renal malignancies and extends into the IVC in 4-10% (14,15). 3. A significant history of cigarette smoking and hematuria exists for both RCC and UC. 4. While upper tract UC presents with non-specific findings on imaging studies, CT scan may be a useful tool to differentiate renal UC from RCC (4,16). 5. IVC thrombus formation of UC is exceedingly rare with 21 cases reported in the literature (4). Meta-analyses evaluating the management of UC with IVC extension showed that in approximately

30% of patients a preoperative MRI was obtained. Only 20% had a positive cytology and all patients, in whom a retrograde pyelography was performed, demonstrated a renal pelvic/ureteral filling defect. In 60% of cases, nephrectomy without ureterectomy was performed and average survival was 6 months (17,18). Renal UC has a propensity to recur in the ipsilateral ureter at a rate of 30 to 40% and mandates radical nephroureterectomy (19,20). In one of our patients, with the presumed diagnosis of RCC, the ureter was left in situ.

## CONCLUSIONS

Large and locally-advanced urothelial carcinomas of the renal pelvis can be successfully removed by enhancing standard radical nephrectomy with liver transplantation techniques; however, survival is poor. Preoperative diagnosis of renal urothelial carcinoma requires a high index of suspicion and is essential to consider neoadjuvant treatment and to plan nephroureterectomy.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Guinan P, Vogelzang NJ, Randazzo R, Sener S, Chmiel J, Fremgen A, et al.: Renal pelvic cancer: a review of 611 patients treated in Illinois 1975-1985. Cancer Incidence and End Results Committee. *Urology*. 1992; 40: 393-9.
2. Störkel S, Eble JN, Adlakha K, Amin M, Blute ML, Bostwick DG, et al.: Classification of renal cell carcinoma: Workgroup No. 1. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). *Cancer*. 1997; 80: 987-9.
3. Ozsahin M, Zouhair A, Villà S, Storme G, Chauvet B, Tausky D, et al.: Prognostic factors in urothelial renal pelvis and ureter tumours: a multicentre Rare Cancer Network study. *Eur J Cancer*. 1999; 35: 738-43.
4. Kawashima A, Takao T, Takaha N, Nishimura K, Nonomura N, Okuyama A, et al.: Renal pelvic cancer

- with tumor thrombus in the vena cava inferior: a case report. *Hinyokika Kyo*. 2004; 50: 869-72.
5. Ciancio G, Hawke C, Soloway M: The use of liver transplant techniques to aid in the surgical management of urological tumors. *J Urol*. 2000; 164: 665-72.
  6. Neves RJ, Zincke H: Surgical treatment of renal cancer with vena cava extension. *Br J Urol*. 1987; 59: 390-5.
  7. Kondo T, Nakazawa H, Ito F, Hashimoto Y, Toma H, Tanabe K: Primary site and incidence of lymph node metastases in urothelial carcinoma of upper urinary tract. *Urology*. 2007; 69: 265-9.
  8. Leo ME, Petrou SP, Barrett DM: Transitional cell carcinoma of the kidney with vena caval involvement: report of 3 cases and a review of the literature. *J Urol*. 1992; 148: 398-400.
  9. Stein JP, Lieskovsky G, Cote R, Groshen S, Feng AC, Boyd S, et al.: Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. *J Clin Oncol*. 2001; 19: 666-75.
  10. Grossman HB, Natale RB, Tangen CM, Speights VO, Vogelzang NJ, Trump DL, et al.: Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. *N Engl J Med*. 2003; 349: 859-66. Erratum in: *N Engl J Med*. 2003; 349: 1880.
  11. Advanced Bladder Cancer Meta-analysis Collaboration: Neoadjuvant chemotherapy in invasive bladder cancer: a systematic review and meta-analysis. *Lancet*. 2003; 361: 1927-34.
  12. Lerner SE, Blute ML, Richardson RL, Zincke H: Platinum-based chemotherapy for advanced transitional cell carcinoma of the upper urinary tract. *Mayo Clin Proc*. 1996; 71: 945-50.
  13. Grossfeld GD, Wolf JS Jr, Litwan MS, Hricak H, Shuler CL, Agerter DC, et al.: Asymptomatic microscopic hematuria in adults: summary of the AUA best practice policy recommendations. *Am Fam Physician*. 2001; 63: 1145-54.
  14. Marshall FF, Dietrick DD, Baumgartner WA, Reitz BA: Surgical management of renal cell carcinoma with intracaval neoplastic extension above the hepatic veins. *J Urol*. 1988; 139: 1166-72.
  15. Chow WH, Devesa SS, Warren JL, Fraumeni JF Jr: Rising incidence of renal cell cancer in the United States. *JAMA*. 1999; 281: 1628-31.
  16. Gatewood OM, Goldman SM, Marshall FF, Siegelman SS: Computerized tomography in the diagnosis of transitional cell carcinoma of the kidney. *J Urol*. 1982; 127: 876-87.
  17. Williams JH, Frazier HA 2nd, Gawith KE, Laskin WB, Christenson PJ: Transitional cell carcinoma of the kidney with tumor thrombus into the vena cava. *Urology*. 1996; 48: 932-5.
  18. Miyazato M, Yonou H, Sugaya K, Koyama Y, Hatano T, Ogawa Y: Transitional cell carcinoma of the renal pelvis forming tumor thrombus in the vena cava. *Int J Urol*. 2001; 8: 575-7.
  19. Strong DW, Pearse HD, Tank ES Jr, Hodges CV: The ureteral stump after nephroureterectomy. *J Urol*. 1976; 115: 654-5.
  20. Murphy DM, Zincke H, Furlow WL: Management of high grade transitional cell cancer of the upper urinary tract. *J Urol*. 1981; 125: 25-9.

---

*Accepted after revision:  
October 06, 2008*

---

**Correspondence address:**

Dr. Wolfgang H. Cerwinka  
 Children's Healthcare of Atlanta  
 Emory University  
 5445 Meridian Mark Road, Suite 420  
 Atlanta, GA, 30342, USA  
 Fax: + 1 404 252-1268  
 E-mail: wcerwinka@gaurology.com

## Pheochromocytoma: A Long-Term Follow-Up of 24 Patients Undergoing Laparoscopic Adrenalectomy

Lísias N. Castilho, Fabiano A. Simoes, Andre M. Santos, Tiago M. Rodrigues, Carlos A. dos Santos Junior

*Section of Urology, Catholic University of Campinas, Campinas, Sao Paulo, Brazil*

---

### ABSTRACT

*Purpose:* Pheochromocytomas are tumors derived from chromaffin cells that often secrete catecholamines and cause hypertension. The clinical diagnosis of pheochromocytoma depends on the presence of excessive production of catecholamines. Conventional imaging modalities that have been used in the preoperative evaluation include CT, MRI, and 131I-MIBG scintigraphy. Surgical resection is the definitive treatment for patients with pheochromocytoma. The goal of this study was to evaluate the long-term follow-up of 24 patients undergoing laparoscopic adrenalectomy for pheochromocytoma.

*Materials and Methods:* From January 1995 to September 2006, 24 patients underwent laparoscopic adrenalectomy for adrenal pheochromocytoma. Twenty (83.3%) patients had arterial hypertension. The inclusion criteria of patients in this retrospective study were laparoscopic approach, unilateral or bilateral adrenal tumor, pathological diagnosis of pheochromocytoma and a minimum follow-up of 18 months.

*Results:* Intra-operative complications occurred in 4 (16.7%) patients. Two (8.3%) patients had postoperative complications. Two patients (8.3%) had blood transfusion. The mean postoperative hospital stay was 3.8 days (range 1 to 11). Eighteen (90%) of the twenty patients who had symptomatic hypertension, returned to normal blood pressure immediately after surgery, during the hospital stay. In one patient, the high blood pressure levels remained unchanged. Another patient persisted with mild hypertension, well controlled by a single antihypertensive drug.

*Conclusions:* Our results confirmed that laparoscopic adrenalectomy for pheochromocytoma is a safe and effective procedure, providing the benefits of a minimally invasive approach. In our study, the initial positive results obtained in the treatment of 24 patients were confirmed after a mean follow-up of 74 months.

*Key words:* laparoscopy; pheochromocytoma; adrenalectomy

*Int Braz J Urol. 2009; 35: 24-35*

---

### INTRODUCTION

Pheochromocytomas (PCCs) are tumors derived from chromaffin cells that produce and often secrete catecholamines. Over 90% of PCCs are in the abdomen, most frequently in the chromaffin cells of the adrenal medulla. Approximately 10% are found in extra-adrenal sites where they are called paragangliomas due to their association with sympathetic nervous system ganglia in the chest, abdomen, or pelvis (1).

The estimated incidence ranges from 0.005% to 0.1% of the general population and from 0.1% to 0.2% of the adult hypertensive population. The highest incidence occurs during the fourth and fifth decades of life, and is nearly identical in both sexes (1).

Approximately 10% of pheochromocytomas are hereditary. Hereditary tumors are frequently multiple or bilateral and rarely malignant. Familial syndromes associated with PCCs include multiple endocrine neoplasia type 2 (MEN 2), von Hippel-Lindau

disease (VHL), and the neuroectodermal dysplasias consisting of neurofibromatosis, tuberous sclerosis, and Sturge-Weber syndrome (2). Approximately 10 to 15% of pheochromocytomas exhibit malignant behavior. In order to diagnose malignant PCCs, one must document invasion of adjacent organs or metastatic disease. The most frequent sites of metastases are the liver, lung, and bone, particularly the spine, skull, and ribs. There is no absolute clinical, imaging, or laboratory criteria to predict malignancy; however, patients with malignant disease tend to have larger tumors and higher urinary metanephrine levels (2).

Conventional imaging modalities that have been used in the preoperative evaluation of patients with a biochemically confirmed pheochromocytoma include CT, MRI, and Iodine-131-metaiodobenzylguanidine (<sup>131</sup>I-MIBG) scintigraphy. CT easily detects tumors of 1 cm or more with high sensitivity, which varies between 93% and 100% for adrenal gland tumor detection and approximately 90% for extra-adrenal disease identification (Figure-1). MRI is also sensitive. Characterization of adrenal masses is done with chemical shift MRI based on the absence of fat in PCCs. In addition, the hypervascularity of pheochromocytomas makes them appear characteristically bright, with a high signal on T2-weighted images (Figure-2). <sup>131</sup>I-MIBG scanning works by administering a radiolabeled amine for which chromaffin tissue is selectively avid. Since it is a physiologic study, MIBG can identify pheochromocytomas regardless of their location. This modality may be useful in patients with biochemical evidence of a pheochromocytoma that has not been localized by CT or MRI or in the follow-up evaluation of patients with suspected or documented recurrent or metastatic disease (2).

Surgical resection is the definitive treatment for patients with pheochromocytoma. Prior to the surgery, the patient must be adequately prepared with alpha-adrenergic blockade and complete restoration of fluid and electrolyte balance. Alpha-blockade works to oppose catecholamine-induced vasoconstriction and sometimes must be associated with the beta-adrenergic blockade with propranolol and expanding volume (3).

Pheochromocytoma was initially considered a contraindication to laparoscopic approach due to the fear of hypertensive crisis associated with the

pneumoperitoneum. However, an increasing series of laparoscopy using the transperitoneal or retroperitoneal approach have been reported and proved to be a safe procedure with similar blood loss and no difference in blood pressure or heart rate increments when compared with open adrenalectomy (3). Patients also experience faster resolution of postoperative ileum, decreased analgesic requirements, a shorter length of hospital stay, and a shorter convalescence with a more rapid return to normal activity (3-5).



Figure 1 – CT scan showing a 2 cm left adrenal mass.

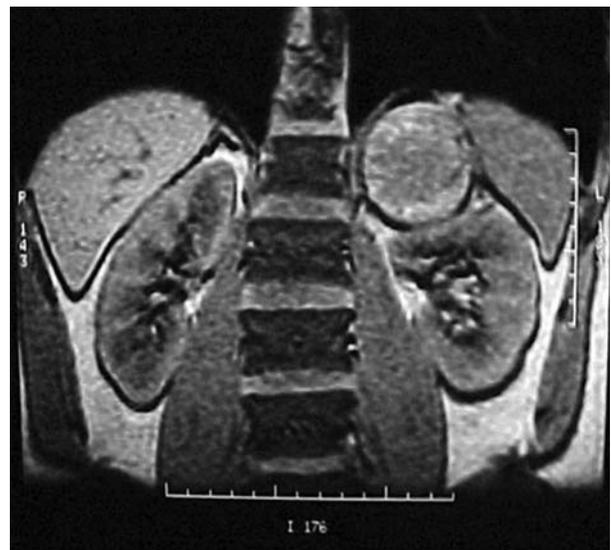


Figure 2 – MRI showing large adrenal mass - hypersignal in T2.

The goal of this study was to evaluate the long-term results of 24 patients undergoing laparoscopic adrenalectomy for pheochromocytoma.

## MATERIALS AND METHODS

From January 1995 to September 2006, we retrospectively reviewed the results of transperitoneal laparoscopic adrenalectomy performed in 24 patients with pheochromocytoma. This series consisted of 14 (58.3%) males and 10 (41.7%) females, with the mean age of 46 years (range 10 to 75 years, median 46.5).

The Body Mass Index (BMI) ranged from 19.4 to 33.5. Nine (37.5%) cases presented with overweight (BMI between 25 and 30) and one (4.2%) case with obesity (BMI 33.5).

Twenty (83.3%) of the twenty-four patients had arterial hypertension, half of them with severe hypertensive crisis and the other 10 patients with mild to moderate hypertension. The mean time between installation of hypertension and the diagnosis of pheochromocytoma was 3 years (3 months to 8 years). Four (16.7%) patients had normal blood pressure levels. Three were completely asymptomatic (incidental findings) and 1 had abdominal pain and recurrent anxiety crises.

The mean tumor size estimated by CT scan was 3.9 cm (1 to 12 cm, median 3.7 cm). In 14 (58.3%) patients the tumors were on the right side, 9 (37.5%) on the left, and only 1 (4.2%) was bilateral (Table-1).

The inclusion criteria of patients in this retrospective study were laparoscopic approach, unilateral or bilateral adrenal tumor, pathological diagnosis of pheochromocytoma and a minimum follow-up of 18 months.

The preoperative diagnosis of pheochromocytoma in the symptomatic patients was confirmed by the clinical presentation and the biochemical and radiographic findings. The vanilylmandelic acid level of a 24-hour urine sample and plasma norepinephrine and epinephrine levels were routinely tested before surgery and every six months after surgery. Abdominal CT scans were obtained in all cases, both in pre-operative as in the post-operative annually. 131I-MIBG was performed in 21 patients, 20 cases with clinical and laboratory suspicion of pheochromocytoma and one

case without any suspicion that presented an incidental finding. In all cases MIBG were repeated annually after surgery. MRI was performed in 7 patients in the pre-operative evaluation because of iodine allergy or inconclusive CT images.

Patients with hypertension and/or abnormally high catecholamine levels were given prazosin 2 to 20 mg/day during 14 to 21 days before surgery. In order to expand the blood volume, patients were infused with crystal liquids (2 to 3 liters) just prior to surgical intervention. All patients underwent general endotracheal anesthesia. The mean arterial pressure, central venous pressure, and vital signs were monitored during surgery. Sodium nitroprusside was administered to control the blood pressure when needed. Intraoperative hemodynamic changes resulting from the pneumoperitoneum and intraoperative manipulations were documented.

The surgical technique of transperitoneal laparoscopic adrenalectomy has been extensively described (2,5).

The follow-up of patients was done based on data review from medical records and telephone contacts. During the first year of follow-up, each patient was examined in at least four different occasions. Their blood pressure was measured and registered in their records. In the sixth and tenth months following the surgery, each patient was submitted to dosage of catecholamines in urine and serum. They were submitted to MIBG at the end of the first year after surgery. After the first year, each patient was examined at least once a year and submitted to laboratory exams and MIBG for at least five years. All the cases included in the study had a minimum follow-up of 18 months (18 to 150 months, mean 74 months).

## RESULTS

We successfully performed twenty-five laparoscopic adrenalectomies in twenty-four different patients. Twenty-three patients underwent unilateral LA and one patient underwent right total and left partial adrenalectomy for bilateral pheochromocytoma. This case was operated in two stages. Of the 25 interventions, 2 (8%) were converted to open surgery, one

## Laparoscopic Adrenalectomy for Pheochromocytoma

**Table 1 – Pre-operative data.**

Case	Age (years)	Gender	Clinical Presentation	Antecedent	Side	CT - Tumor Size (mm)
1	52	Male	Hypertensive crises	None	Left	55
2	55	Female	Hypertension	Familial pheochromocytoma	Left	20
3	10	Male	Hypertensive crises	None	Right	30
4	38	Male	Hypertensive crises	Familial pheochromocytoma	Right	13
5	22	Male	Hypertensive crises	None	Right	10
6	42	Female	Hypertension	Hysterectomy	Left	15
7	46	Male	Hypertensive crises	None	Right	80
8	57	Male	Hypertension	Kidney transplantation	Left	10
9	65	Female	Incidentally discovered	Depression	Left	41
10	62	Male	Hypertension	Radical prostatectomy	Right	35
11	47	Male	Hypertensive crises	Cholecystectomy	Right	45
12	61	Male	Hypertensive crises	None	Right	15
13	41	Female	Hypertension	None	Left	20
14	15	Male	Abdominal pain Anxiety crises Without hypertension	None	Right	45
15	44	Male	Hypertensive crises	Medullary thyroid cancer Familial pheochromocytoma	Bilateral	40/25
16	40	Male	Hypertension	None	Right	60
17	45	Male	Hypertensive crises	None	Left	30
18	61	Female	Hypertensive crises	None	Right	30
19	41	Female	Hypertension	None	Right	50
20	47	Female	Hypertension	None	Right	40
21	54	Female	Incidentally discovered	Hysterectomy	Left	55
22	48	Male	Incidentally discovered	None	Right	5
23	75	Female	Incidentally discovered Hypertension	Bilateral lumbar sympathectomy	Left	120
24	36	Female	Incidentally discovered	None	Right	50

due to a major venous bleeding and the other due to difficulty in freeing the gland, located almost entirely behind the inferior vena cava.

The mean operative time, excluding the two converted cases, was 126 minutes (60 to 215 min.).

Intra-operative complications occurred in 4 (16.7%) patients (Table-2).

In one case, during specimen withdrawal, the extractor bag ruptured and the specimen was not found by laparoscopic inspection. It was necessary to make

a small incision in the abdomen to remove the gland. In another case, we had a small vena cava injury that was sutured by laparoscopy without any difficulty. A 10-year-old patient suffered an injury in anomalous right adrenal vein. The subsequent bleeding required conversion to open surgery. The oldest patient in this series, a 75-year-old woman with a 12 cm left adrenal tumor, there was an injury of the splenic artery during dissection. The arterial injury could not be repaired and a laparoscopic splenectomy was performed.

## Laparoscopic Adrenalectomy for Pheochromocytoma

**Table 2 – Intra-operative (IO) occurrences.**

Case	IO Complication	Conduct	Operative Time (minutes)	Transfusion
1	Extractor bag rupture	Minilaparotomy	150	None
2	None		135	None
3	Venous injury	Conversion	Conversion	5 units IO
4	None		140	None
5	None		120	None
6	None		80	None
7	None		150	None
8	None		70	None
9	None		150	None
10	Vena cava injury	Laparoscopic suture	215	None
11	None	Conversion	Conversion	None
12	None		75	None
13	None		90/100 bilateral	None
14	None		160	None
15	None		150	None
16	None		90	None
17	None		75	None
18	None		125	None
19	None		60	None
20	None		90	None
21	None		120	None
22	None		190	None
23	Splenic artery injury	Laparoscopic splenectomy	180	2 units PO
24	None		190	None

PO = postoperative

No cases of severe hemodynamic instability were observed throughout the duration of anesthesia, but most of the patients had transient elevation of blood pressure during the manipulation of the gland, before adrenal vein ligation. These elevations were in general controlled with sodium nitroprusside.

Two (8.3%) patients had postoperative complications (Table-2). In one of the converted procedures, the patient developed an acute renal failure, postoperative ileum and subcutaneous infection. He left the hospital in a good condition on the 7<sup>th</sup> postoperative day. Another patient developed an abdominal and lumbar ecchymosis after hospital discharge with spontaneous resolution.

Two patients (8.3%) received a blood transfusion (Table-2), one of them in the operating room and the other during the first postoperative day.

All patients resumed oral nutrition and ambulation 1 to 2 days after the surgery.

The mean postoperative hospital stay was 3.8 days (1 to 11 days).

All the tumors were pathologically identified as pheochromocytomas. There was no evidence of malignancy such as local invasion or metastasis. The largest specimen removed measured 12 cm and weighed 200g (case 23).

Of the twenty patients who had symptomatic hypertension, 18 (90%) returned to normal blood

## Laparoscopic Adrenalectomy for Pheochromocytoma

**Table 3 – Postoperative (PO) results.**

Case	PO Complication	Long-term Follow-up	Follow-up (months)	Final Diagnosis
1	None	Cure	150	Pheochromocytoma
2	None	Cure	144	Familial pheochromocytoma
3	None	Cure	43	Pheochromocytoma
4	None	Cure	140	Familial pheochromocytoma
5	None	Hypertensive crises	118	Pheochromocytoma
6	None	Cure	100	Pheochromocytoma
7	None	Cure	116	Pheochromocytoma
8	None	Cure	111	Pheochromocytoma
9	None	Cure	110	Non-secretory pheo
10	None	Cure	58	Pheochromocytoma
11	Renal failure, post-operative ileum, SC infection	Cure	108	Pheochromocytoma
12	None	Cure	19	Pheochromocytoma
13	None	Mild hypertension	87	Pheochromocytoma
14	None	Cure	84	Pheochromocytoma
15	None	Cure (death due to a heart attack after 18 months)	18	Familial pheochromocytoma
16	None	Cure	19	Pheochromocytoma
17	None	Cure	61	Pheochromocytoma
18	None	Cure	63	Pheochromocytoma
19	None	Cure	63	Pheochromocytoma
20	None	Cure	56	Dopamine-secretory pheo
21	None	Cure	18	Pheochromocytoma
22	None	Cure	48	Pheochromocytoma
23	None	Cure	24	Pheochromocytoma
24	Ecchymosis	Cure	18	Non-secretory pheo

pressure immediately after the surgery, during the hospital stay. In one of the patients the blood pressure level remained unchanged (hypertensive crises). Another patient persisted with mild hypertension, controlled with a single antihypertensive drug. These results remained unchanged during the follow-up.

In one of four normotensive patients, the blood pressure had a peak during the anesthetic induction but was easily controlled with sodium nitroprusside. Another normotensive patient complained of abdominal pain and anxiety. His symptoms

disappeared after surgery (case 14). All these 4 cases remained normotensive in the late postoperative period (Table-3).

During a mean follow-up of 74 months, no tumor recurrence or metastasis was observed.

One patient died 18 months after surgery because of myocardial infarction. This patient underwent bilateral surgery, with right total and left partial adrenalectomy. He became normotensive and the postoperative adrenal function remained normal, without the use of glucocorticoids or mineralocorticoids (case 15).

## COMMENTS

Since the first report of laparoscopic adrenalectomy by Gagner et al. in 1992, this procedure has become the preferred surgical management of benign adrenal tumors due to its numerous advantages (6). Comparative studies between open and laparoscopic surgery have shown that laparoscopic intervention should be considered the gold-standard procedure for adrenal surgery (7,8).

To date no relevant prospective and randomized series comparing laparoscopic adrenalectomy versus conventional surgery for pheochromocytoma, to our knowledge, has been published in the literature. Nevertheless, the accumulated international experience is significant and suggests that laparoscopic approach is better than open surgery regarding morbidity, bleeding, length of hospitalization, convalescence, postoperative pain and aesthetic sequels (7-9).

Pheochromocytoma was initially considered a contraindication to LA because it was reported by Meurisse et al. that pneumoperitoneum could promote an acute release of catecholamines (10). However, several authors have shown that when there is an adequate preoperative preparation these changes are discrete and well-tolerated by patients (11-13).

In a recent study, Sood et al. showed that the maintenance of a lower intraabdominal pressure (8-10 mmHg) reduces the release of catecholamines and helps prevent hemodynamic instability (14).

There are four possible laparoscopic approaches to the adrenal gland, mainly transperitoneal, lateral retroperitoneal, posterior retroperitoneal and trans-thoracic trans-diaphragmatic (15,16). The transperitoneal access is often preferred by many surgeons because of its broader working space and familiar anatomy. Nonetheless, retroperitoneal laparoscopic adrenalectomy has gained popularity because it provides direct access to the adrenal gland and avoids bowel handling and potential intraabdominal viscera injury. Rubinstein et al. published a randomized trial with 56 patients at the Cleveland Clinic, showing that operative parameters, perioperative morbidity and pathological characteristics of the intact extracted specimen were similar between both approaches (17). The choice of laparoscopic

approach for adrenalectomy varies according to personal experience and preference of the laparoscopic surgeon.

In our experience, the small incidence of complications, the short convalescence period and the long-term satisfactory results, have enabled us to establish the laparoscopic adrenalectomy as the procedure of choice in pheochromocytoma management.

With the introduction of robotic surgery, adrenalectomy using robotic endoscopic surgical devices (Da Vinci system) has recently been proposed. Morino et al., published a prospective randomized trial with 20 patients, comparing the outcomes of robotic (RA) versus lateral transperitoneal laparoscopic procedures. This study showed that RA is associated with a longer operative time, increased cost and a higher morbidity when compared to lateral transperitoneal LA (18). However, further studies are needed to define the role of robotic-assisted adrenalectomy (19).

Perioperative management of patients with pheochromocytoma requires detailed knowledge of the potential complications. Intraoperatively, hypertensive crisis and tachyarrhythmia may occur resulting from massive catecholamine release. Thus, in agreement with other authors we consider preoperative treatment with the alpha-antagonist phenoxybenzamine obligatory (20).

Most research published on laparoscopic adrenalectomy refer to tumors smaller than 6 cm without pre-operative characteristics suggesting malignancy. Despite some reports of surgeries performed in large tumors with identified malignancy potential in pre-operative assessment, these procedures should be left to academic centers with extensive experience in laparoscopic surgery of the adrenal gland.

## CONCLUSIONS

Our results have confirmed that laparoscopic adrenalectomy for pheochromocytoma is a safe and effective procedure, providing the benefits of a minimally invasive approach. In our experience, the initial positive results obtained in the treatment of 24 patients were confirmed after a median follow-up of 74 months.

**CONFLICT OF INTEREST**

None declared.

**REFERENCES**

1. Karagiannis A, Mikhailidis DP, Athyros VG, Harsoulis F: Pheochromocytoma: an update on genetics and management. *Endocr Relat Cancer*. 2007; 14: 935-56.
2. Mittendorf EA, Evans DB, Lee JE, Perrier ND: Pheochromocytoma: advances in genetics, diagnosis, localization, and treatment. *Hematol Oncol Clin North Am*. 2007; 21: 509-25.
3. Castilho LN, Medeiros PJ: O tratamento laparoscópico do feocromocitoma. *Rev Cienc Med*. 2003; 12:63-7.
4. Kasturi S, Kutikov A, Guzzo TJ, Smith AL, Wein AJ: Modern management of pheochromocytoma. *Nat Clin Pract Urol*. 2007; 4: 630-3.
5. Castilho LN: Suprarrenalectomia. In: Castilho LN (ed.), *Laparoscopia Urológica*. Campinas, LPC Comunicações. 2000; pp. 365-77.
6. Gagner M, Lacroix A, Bolté E: Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. *N Engl J Med*. 1992; 327: 1033.
7. Castilho LN, Liang LS, Ferreira U, Fregonesi A, Saade RD, Netto Jr, NR: Cirurgia do tumor benigno de supra-renal por videolaparoscopia. *J Bras Urol*. 1996; 22:33-6.
8. Castilho LN, Medeiros PJ, Mitre AI, Dénes FT, Lucon AM, Arap S: Pheochromocytoma treated by laparoscopic surgery. *Rev Hosp Clin Fac Med Sao Paulo*. 2000; 55: 93-100.
9. Janetschek G, Altarac S, Finkenstedt G, Gasser R, Bartsch G: Technique and results of laparoscopic adrenalectomy. *Eur Urol*. 1996; 30: 475-9.
10. Meurisse M, Joris J, Hamoir E, Hubert B, Charlier C: Laparoscopic removal of pheochromocytoma. Why? When? and Who? (reflections on one case report). *Surg Endosc*. 1995; 9: 431-6.
11. Fernández-Cruz L, Sáenz A, Taurá P, Sabater L, Astudillo E, Fontanals J: Helium and carbon dioxide pneumoperitoneum in patients with pheochromocytoma undergoing laparoscopic adrenalectomy. *World J Surg*. 1998; 22: 1250-5.
12. Chigot JP, Movschin M, el Bardissi M, Fercocq O, Paraskevas A: Comparative study between laparoscopic and conventional adrenalectomy for pheochromocytomas. *Ann Chir*. 1998; 52: 346-9.
13. Col V, de Cannière L, Collard E, Michel L, Donckier J: Laparoscopic adrenalectomy for phaeochromocytoma: endocrinological and surgical aspects of a new therapeutic approach. *Clin Endocrinol (Oxf)*. 1999; 50: 121-5.
14. Sood J, Jayaraman L, Kumra VP, Chowbey PK: Laparoscopic approach to pheochromocytoma: is a lower intraabdominal pressure helpful? *Anesth Analg*. 2006; 102: 637-41.
15. Gill IS: Laparoscopic Adrenal Surgery. In: 95th Annual Meeting, Atlanta; 2000. *Laparoscopic Organ Ablative Urology – Postgraduate Course*. Houston: AUA Office of Education; 2000. p.1-4.
16. Subramaniam R, Pandit B, Sadhasivam S, Sridevi KB, Kaul HL: Retroperitoneoscopic excision of phaeochromocytoma--haemodynamic events, complications and outcome. *Anaesth Intensive Care*. 2000; 28: 49-53.
17. Rubinstein M, Gill IS, Aron M, Kilciler M, Meraney AM, Finelli A, et al.: Prospective, randomized comparison of transperitoneal versus retroperitoneal laparoscopic adrenalectomy. *J Urol*. 2005; 174: 442-5; discussion 445.
18. Morino M, Benincà G, Giraud G, Del Genio GM, Rebecchi F, Garrone C: Robot-assisted vs laparoscopic adrenalectomy: a prospective randomized controlled trial. *Surg Endosc*. 2004; 18: 1742-6.
19. Brunaud L, Bresler L, Ayav A, Zarnegar R, Raphoz AL, Levan T, et al.: Robotic-assisted adrenalectomy: what advantages compared to lateral transperitoneal laparoscopic adrenalectomy? *Am J Surg*. 2008; 195: 433-8.
20. Knüttgen D, Wappler F: Anaesthesia for patients with phaeochromocytoma - specifics, potential complications and drug strategies. *Anesthesiol Intensivmed Notfallmed Schmerzther*. 2008; 43: 20-7.

---

*Accepted after revision:  
September 1, 2008*

**Correspondence address:**

Dr. Lísias Nogueira Castilho  
Av. Princesa D'Oeste, 1144 / 171  
Campinas, SP, 13100-040, Brazil  
E-mail: lisias@dglnet.com.br

## EDITORIAL COMMENT

Surgical cure of pheochromocytomas is a real challenge and must be considered a model when multidisciplinary approach is essential to achieve the best results. The endocrinologist, cardiologist, the anesthesiologist as well as the surgeon must work together to avoid the devastating effects of non-programmatic surgical approach that in the past had high mortality (1).

Pheochromocytomas often secrete catecholamine that causes vasoconstriction and hypertension as the main symptom. The complications of the adequate treatment are mild, and mortality is more related to the patient's condition than to the surgical technique (2).

The variations on the blood pressure are the biggest problem during the anesthetic procedure. Endocrine and cardiologic preparations before the operation are the first steps to reduce complications. Alpha-blocking agents in the pre operative period are obligatory in the majority of patients for at least 15 days before the procedure. Beta blocking can be associated in cases of excessive tachycardia or arrhythmias. Fluid intake prior to the procedure is also mandatory (3). Echocardiogram defines selected patients with excessive compromises of left ventriculum when cardio tonics can show some benefits (4). After surgical resection, hypotension or left ventriculum failure may occur and vasopressors must be infused (3). Particularly when considering cure of hypertension after surgery, cardiac failure can be considered a confounding factor for the immediate evaluation.

As regards the surgical technique, in the past ten years laparoscopic surgery has become the gold standard for tumors smaller than 6 cm (5). At the beginning of the laparoscopic experience, it has been thought that pneumoperitoneum could affect the blood pressure during surgery (6).

Some contemporary reports have shown that the variation in blood pressure occurred independently conventional surgery or laparoscopic approach (7,8). Additionally, some authors have defended that beyond the vantages of lower bleeding and faster recovery, the delicate manipulation on laparoscopic technique would be an additional for minimum invasive procedure (8-11).

Into pheochromocytoma surgery, it is important to have an early stage control of the main adrenal vein with the intention of reducing the blood pressure decompensation, yet it has been a questionable paradigm these days (9). Some studies have proposed that the early control of the vein could be done only via the transperitoneal technique, Salomon et al. described the feasibility of doing this through extra peritoneal approach (10).

In our experience the control of the vein is not only bilateral feasibly but seems easier on the right side (where the adrenal vein is shorter and frequently retrocaval), than through transperitoneal approach, specially, when it is a large tumor (11).

Another important issue is the treatment of the malignant disease that occurs in approximately 10 % (12). Some initial series suggest that it is possible to offer laparoscopic treatment with good results, but there are some cases of tumor recurrence and portal implants (13).

The benefit of the laparoscopic procedure in the case of malignant pheochromocytoma at a locally confined stage still remains unclear and requires prospective, randomized studies.

## REFERENCES

1. Gagner M, Pomp A, Heniford BT, Pharand D, Lacroix A: Laparoscopic adrenalectomy: lessons learned from 100 consecutive procedures. *Ann Surg.* 1997; 226: 238-46; discussion 246-7.
2. Gil-Cárdenas A, Córdón C, Gamino R, Rull JA, Gómez-Pérez F, Pantoja JP, et al.: Laparoscopic adrenalectomy: lessons learned from an initial series of 100 patients. *Surg Endosc.* 2008; 22: 991-4.
3. Adams HA, Hempelmann G: Anesthesia for patients with pheochromocytoma. Our own results and a review. *Anesthesiol Intensivmed Notfallmed Schmerzther.* 1993; 28: 500-9.
4. Meune C, Bertherat J, Dousset B, Jude N, Bertagna X, Duboc D, et al.: Reduced myocardial contractility assessed by tissue Doppler echocardiography is associated with increased risk during adrenal surgery of patients with pheochromocytoma: report of a preliminary study. *J Am Soc Echocardiogr.* 2006; 19: 1466-70.

5. Guazzoni G, Cestari A, Montorsi F, Bellinzoni P, Centemero A, Naspro R, et al.: Laparoscopic treatment of adrenal diseases: 10 years on. *BJU Int.* 2004; 93: 221-7.
6. Mittendorf EA, Evans DB, Lee JE, Perrier ND: Pheochromocytoma: advances in genetics, diagnosis, localization, and treatment. *Hematol Oncol Clin North Am.* 2007; 21: 509-25.
7. Pugliese R, Boniardi M, Sansonna F, Maggioni D, De Carli S, Costanzi A, et al.: Outcomes of laparoscopic adrenalectomy. Clinical experience with 68 patients. *Surg Oncol.* 2008; 17: 49-57.
8. Tobias-Machado M, Rincón Ríos F, Tulio Lasmar M, Tristão R, Hermínio Forseto P Jr, Vaz Juliano R, et al.: Laparoscopic retroperitoneal adrenalectomy as a minimally invasive option for the treatment of adrenal tumors. *Arch Esp Urol.* 2006; 59: 49-54.
9. Lang B, Fu B, OuYang JZ, Wang BJ, Zhang GX, Xu K, et al.: Retrospective comparison of retroperitoneoscopic versus open adrenalectomy for pheochromocytoma. *J Urol.* 2008; 179: 57-60; discussion 60.
10. Salomon L, Rabii R, Soulie M, Mouly P, Hoznek A, Cicco A, et al.: Experience with retroperitoneal laparoscopic adrenalectomy for pheochromocytoma. *J Urol.* 2001; 165: 1871-4.
11. Tobias-Machado M, Lasmar MT, Zambon JP, Tristão R, Forseto PH Jr, Juliano RV, et al.: Laparoscopic adrenalectomy: a prospective study comparing transperitoneal and retroperitoneal approaches. *Rev Assoc Med Bras.* 2006; 52: 208-13.
12. Strong VE, Kennedy T, Al-Ahmadie H, Tang L, Coleman J, Fong Y, et al.: Prognostic indicators of malignancy in adrenal pheochromocytomas: clinical, histopathologic, and cell cycle/apoptosis gene expression analysis. *Surgery.* 2008; 143: 759-68.
13. Tobias-Machado M, Tristão RA, Silva MNR, Wroclawski ER: Laparoscopic adrenalectomy for malignant disease: Technical feasibility and oncological results. *Einstein.* 2007; 5: 44-47.

**Dr. Marcos Tobias-Machado &  
Dr. Maria Claudia Bicudo**

*Section of Urology  
ABC Medical School  
São Paulo, SP, Brazil*

*E-mail: tobias-machado@uol.com.br*

## EDITORIAL COMMENT

The surgical management of patients with pheochromocytoma is potentially curative and it has always been a question of debate because of the clinical complexity of such patients with potential high-risk peri-operative morbid-mortality.

When laparoscopic surgery was introduced as an alternative approach for open surgery the tension rose among traditional surgeons, used to the common problems associated with patients with pheochromocytoma, that were mainly concerned with the safety of the laparoscopic approach.

As the experience among laparoscopists grew, it became clear that this approach was not only a matter of better cosmesis, whereas on the contrary, several reports revealed the benefits of treating patients with pheochromocytoma preferentially via laparoscopy

over the conventional open approach, such as less catecholamines release (1), less bleeding (1,2), less UCI length of stay (2), less hospital stay (1,2), shorter convalescence (1) and mainly revealing to be as safe as open surgery (1,2).

Castilho and colleagues, in this issue of the *Int Braz J Urol* reported on the long-term follow-up of 24 patients who underwent laparoscopic adrenalectomy for pheochromocytoma over an 11-year period with a mean follow up of 74 months. Castilho's study found that only one patient was not totally cured in the period studied (1 out of 24 - 4.2%); this single patient continued to have an hypertensive crisis and another patient continued with mild hypertension under control. No tumor recurrence was observed. The Castilho et al. report is very important to demonstrate the long-term

safety of laparoscopic approach as a means of cure and tumor recurrence, in addition to the safety also reported during the peri-operative time.

Treatment of patients with pheochromocytoma requires a committed multidisciplinary team of urologist, endocrinologist, anesthesiologist, radiologist and all staff in a well equipped hospital and aware of all potential needs of such patients. Laparoscopic surgery performed by an experienced surgical group along a knowledgeable committed multidisciplinary team in a prepared hospital have proven efficacy and safety. It should be kept in mind that laparoscopy is only one of the advances now applied to patients with pheochromocytoma.

Nevertheless, laparoscopic surgery may not yet have eliminated open surgery. At our institution, 4 patients with pheochromocytoma out of 51 (8%) that

were operated on from 2000 to 2008 (non-published data) still required open conventional approach either because of major vessel involvement or tumor size greater than 10 cm or adjacent organ concomitant removal.

Further studies are encouraged to continue to improve our surgical results on such complex patients with a complex disease.

## REFERENCES

1. Gill IS: The case for laparoscopic adrenalectomy. *J Urol.* 2001; 166: 429-36.
2. Faria EF, Andreoni C, Krebs RK, Nascimento H, Goldman SM, Kater C, et al.: Advances in pheochromocytoma management in the era of laparoscopy. *J Endourol.* 2007; 21: 1303-7.

**Dr. Cassio Andreoni**

*Section of Urology*

*Federal University of Sao Paulo, UNIFESP*

*Sao Paulo, SP, Brazil*

*E-mail: cassio.andreoni@globocom*

## EDITORIAL COMMENT

Pheochromocytomas are relatively uncommon tumors whose operative resection has clear medical and technical challenges.

While the safety and efficacy of laparoscopic adrenalectomy are relatively well documented, few studies with extended follow-up have been conducted to measure the success of the procedure for the most challenging of the adrenal tumors. In addition, several reports have questioned the applicability of a minimally invasive approach for pheochromocytomas larger than 6 cm in diameter. This paper from Castilho et al. evaluated long term results of laparoscopic adrenalectomy in patients with pheochromocytoma (diameter ranging from 10 to 120 mm) and authors have to be commended for this interesting work. As other series of laparoscopic resection for pheochromocytoma, this paper shows that despite appropriate perioperative medical management, intraoperative hypertensive remains a valid concern especially during intra-abdominal insufflation and tumor manipulation (1). In

addition, it emphasizes that laparoscopic approach to these tumors has traditionally been associated with higher complication rates than adrenalectomy for other indications. Lesions larger than 6 cm are associated with longer operative times and may be more difficult to safely resect laparoscopically. Extreme care must be taken to avoid intraoperative capsular disruptions and lifetime follow-up is an important aspect of the postoperative care of the pheochromocytoma patient (1). Recently, robotic technology has been introduced providing a 3-dimensional display that enhances depth perception, enabling the surgeon to operate in a comfortable seated position in which the eye, hand, and target are in line, and the instruments contain a "wrist" joint to improve dexterity. These advantages could theoretically improve laparoscopic adrenalectomy procedure and then subsequently lead to improved perioperative and postoperative outcomes. We recently reported 24 patients with pheochromocytoma who underwent unilateral robotic-assisted

adrenalectomy (2). Conversion rate was 8.3% and tumor capsule was ruptured in 1 patient with a right 7.5 cm cystic pheochromocytoma (cyst rupture).

Moreover, per-operative hemodynamic modifications seem to be similar during robotic and conventional adrenalectomy for pheochromocytoma (unpublished data). This emphasizes that robotic approach can not be considered de facto as precluding all difficulties that can be observed during conventional laparoscopic adrenalectomy for pheochromocytoma. Laparoscopic excisions of pheochromocytomas with or without robotic system remain challenging surgical procedures because of intraoperative catecholamine release and tumor vascularization. Extensive experience in minimally invasive techniques, as well as in endocrine surgery are two key elements for surgeons performing laparoscopic adrenalectomy for pheochromocytoma.

#### REFERENCES

1. Kercher KW, Novitsky YW, Park A, Matthews BD, Litwin DE, Heniford BT: Laparoscopic curative resection of pheochromocytomas. *Ann Surg.* 2005; 241: 919-26; discussion 926-8.
2. Brunaud L, Ayav A, Zarnegar R, Rouers A, Klein M, Boissel P, Bresler L: Prospective evaluation of 100 robotic-assisted unilateral adrenalectomies. *Surgery.* 2008; 144: 995-1001.

***Dr. M Fau &***

***Dr. Laurent Brunaud***

*Department of General and Endocrine Surgery*

*CHU Nancy, Hopital Brabois Adultes*

*School of Medicine, University of Nancy*

*Nancy, France*

*E-mail: l.brunaud@chu-nancy.fr*

# Impact of Obesity on Ureteroscopic Laser Lithotripsy of Urinary Tract Calculi

Ricardo Natalin, Keith Xavier, Zephaniah Okeke, Mantu Gupta

*Department of Urology, Columbia University, College of Physicians and Surgeons, New York, NY, USA*

---

## ABSTRACT

*Purpose:* The treatment of urinary tract stones in obese patients may differ from the treatment of non-obese patients and their success rate varies. Our objective was to compare ureteroscopic treatment outcomes of ureteral and renal stones, stratified for stone size and location, between overweight, obese and non-obese patients.

*Materials and Methods:* Charts were reviewed for 500 consecutive patients presenting at our institution for renal and ureteral stones. A total of 107 patients underwent flexible or semi-rigid ureteroscopy with Ho:YAG laser lithotripsy and met criteria for review and analysis.

*Results:* Overall, initial stone-free rates were 91%, 97%, and 94% in normal, overweight and obese individuals respectively. When compared to non-obese patients, there were no significant differences ( $p$  value = 0.26; 0.50). For renal and proximal ureteral stones, the stone-free rate in overweight and obese individuals was 94% in both groups; and a stone-free rate of 100% was found for distal stones, also in both groups.

*Conclusions:* Ureteroscopic treatment of stones in obese and overweight patients is an acceptable treatment modality, with success rates similar to non-obese patients.

**Key words:** *ureter; calculi; ureteroscopy; Ho-YAG Laser; obesity*

**Int Braz J Urol. 2009; 35: 36-42**

---

## INTRODUCTION

Obesity has become a major health problem in the United States and the world and represents a chronic disease mediated by genetics, environment, metabolism, psychosocial causes, cultural, and physiologic variables (1). The prevalence of obesity in the United States has increased by approximately 30% from 1980 to 1994 (2). The most common method of defining obesity is the Body Mass Index (BMI). BMI measures the height to weight ratio by taking weight in kilograms and dividing it by height in squared meters ( $\text{kg}/\text{m}^2$ ). According to the World Health Organization

guidelines, a BMI of 18.5 to 25  $\text{kg}/\text{m}^2$  is considered normal, overweight is a BMI of 25 to 29.9, obese is a BMI  $\geq 30$ , and morbidly obese is a BMI  $\geq 40$  (3).

Various lithogenic risk factors are known to be associated with obesity and increase the chance of stone formation in these patients as hyperinsulinemia, increased BMI, hyperoxaluria, high sodium intake, low urinary volume and hypercalciuria. Duffey et al. found that 98% of obese patients had at least one lithogenic risk factor in a 24-hour urine sample and 80% of them had 3 or more factors (4).

Extracorporeal shock wave lithotripsy (ESWL) has emerged as the primary treatment of

choice for renal calculi less than 1.5-2 cm (5). ESWL has been recommended as first-line treatment of ureteral calculi less than 1 cm, resulting in up to a 92.6% stone free rate for proximal stones and 97.5% for mid and distal ones (6). However, obese patients are fraught with difficulties in treating calculi by ESWL and may not have these same high success rates as in non-obese patients. Delakas et al. reported an increased chance of ESWL failure in obese patients of 1.9 fold when BMI was > 30, and Muñoz et al. found a 72% stone free rate after ESWL for these patients (7,8). In these obese patients, a frequent factor limiting the success of ESWL is positioning the patient so the stone can be located at the focal point of the lithotripter. Most lithotripters have a maximum skin to stone distance of 12-14 cm for their focal point, which can restrict the depth in which stone fragmentation can be accomplished (9). For this reason, ESWL for obese patients may be a sub-optimal treatment.

PCNL as a potential treatment for renal calculi in obese patients can also be difficult. This is due to an increased distance that needs to be traversed in order to obtain the correct access into a calyx, making percutaneous access more difficult. Also, even if access is obtained, normal size instruments may not be able to be used and longer instruments including nephroscope and access sheath may be required in an obese patient. Another potential problem during PCNL in an obese patient is the increased anesthetic complication risk that can ensue from the patient being in the prone position for a long period of time.

For these previously mentioned reasons, rigid and flexible ureteroscopy is most likely the treatment of choice for urinary calculi in obese patients. The development of small caliber ureteroscopes and advances in intracorporeal lithotripsy, such as ultrasound, electrohydraulic waves, laser, and most recently the holmium: yttrium-aluminum-garnet (Ho:YAG) laser, have permitted more successful and safer endoscopic manipulation of ureteral calculi (10). In order to ascertain whether ureteroscopy is more effective in obese patients, we compared outcomes data, stratified for stone size and location, in overweight, obese, morbidly obese and normal weight patients as defined by BMI.

## MATERIALS AND METHODS

Charts were reviewed for 500 consecutive patients treated for renal and/or ureteral calculi at our institution over a five-year period. Inclusion criteria for the study included all patients with radio-opaque calculi who were treated ureteroscopically, in combination with Ho:YAG laser lithotripsy, as primary therapy. Indications for treatment were calculi that did not pass spontaneously or required earlier intervention because of recurrent colic or obstruction of the upper urinary tract. Patients who had contraindications such as pregnancy, urinary tract infection, coagulation disorders, or previous ureteral reimplantation were excluded from the study. After a thorough review, 107 patients met the criteria for this review.

Ureteroscopy was performed in combination with Ho:YAG laser lithotripsy by the same surgeon (M.G.) using a small caliber (6F) semi-rigid or flexible ureteroscope.

Distal stones were treated via a Wolf semi-rigid ureteroscope with a 6F self-dilating tip and for proximal ureteral stones we used the flexible ureteroscope Storz Flex-X or ACMI DUR-8 or DUR-8 Elite, depending on availability. No dilation of the ureteral orifice was necessary because of self-dilating tip ureteroscope (for distal stones). For proximal stones, ureteral access sheath was placed underneath the stone (Cook Flexor, 35 cm), with size varying from 9 to 11F when using Storz Flex-X and from 12 to 14F when using ACMI ureteroscope.

Our standard technique for ureteroscopic treatment of ureteral calculi includes cystoscopy with retrograde pyelogram, placement of a 0.038-inch floppy-tipped guide wire past the stone (glidewire when necessary) to maintain access, placement of a safety wire for flexible ureteroscopy, and ureteroscopy with Ho:YAG laser lithotripsy. Continuous irrigation and/or intermittent manual pumping of irrigant to obtain a clear ureteroscopic view were used where appropriate. For ureteroscopic laser lithotripsy, a Ho:YAG laser (Trimeddyne, Inc., Irvine, CA) was employed. The Ho:YAG laser operates at a wavelength of 2100-nm and the laser frequency was usually set between 5-10 Hz and a power of 5-10 W. Higher settings were used to treat harder calculi. The vast majority of the patients were treated with a 200 uH

quartz fiber. Basket retrieval of stone fragments was employed when necessary. Patients received general anesthesia at the beginning of the procedure.

A preoperative x-ray of the kidneys, ureters, and bladder were done in all patients, and excretory urogram (IVP), non-contrast helical computer tomography, or sonogram were done when indicated to document the size and location of the stone. Patients were postoperatively imaged with radiographs, non-contrast helical computer tomography, and/or IVP until they were stone-free or received additional treatment (0 to 3 months). A patient was considered stone free when post operative imaging revealed fragments of 2 mm or less. Characteristics of patient age, sex, stone size and location, operative time, and treatment outcome were recorded and tabulated. Average patient age and mean stone size were similar for all groups (Table-1).

Treatment outcomes were defined as radiographic evidence of fragmentation or complete disappearance of the stone. Retreatment and additional procedures were also registered. All procedures were performed on an outpatient basis.

For each of the treatment groups, 95% confidence intervals were calculated for the overall treatment success rates. Statistical comparison of two independent percentages was done by means of the Fisher's exact test (2-sided,  $p = 0.05$ ). If the result-

ing p value was  $< 0.05$ , the difference in the sample percentages was considered statistically significant.

## RESULTS

The average patient age and mean stone size were similar for all groups (Table-2). Mean operating time was 70.37 minutes for normal weight individuals, 88.78 minutes for overweight persons, 78.23 minutes for obese patients. These differences were not statistically significant between groups (Table-1).

Indications for the procedure were due to persistent pain despite analgesic medication in 51 patients, obstruction with ultrasound revealing hydronephrosis in 24 and persistent pain associated with evidence of obstruction in 32.

The initial stone-free rate for ureteral calculi 1 cm or greater following treatment with ureteroscopy with Ho:YAG laser lithotripsy was 93%. For ureteral calculi less than 1 cm, the initial stone-free rate was 100%.

Stratified for location (Table-1), the initial stone free rates for renal/ proximal ureteral stones ranged from 93% to 100% for all weight categories. The small numbers of patients (7 patients in total, 1 failure) with mid-ureteral stones had stone free rates that varied from 67% to 100%. For distal ureteral

**Table 1 – Outcomes.**

	Normal	Overweight	Obese
Operation time (minutes)	70.37	88.78	78.23
Range	30-170	30-159	30-156
p Value		0.16	0.36
Stone free (N)	31	38	32
Failure	3	1	2
p Value		0.26	0.5
Stone free (%)	91%	97%	94%
Location			
Renal / Proximal ureter	93%	94%	94%
Mid ureter	100%	100%	67%
Distal ureter	90%	100%	100%

*Table 2 – Patient characteristics.*

	Normal	Overweight	Obese
N	34	39	34
Age	46.93	51.26	53.32
Gender			
Male	9	20	21
Female	25	19	13
BMI	22.74	27.32	33.6
Range	17.82-24.85	25.10-29.75	30.13-45.55
Laterality			
Right	19	24	19
Left	15	15	15
Location			
Renal	1	0	6
Proximal ureter	11	15	14
Mid ureter	3	2	2
Distal ureter	17	21	12
Average size (cm)	0.9	0.8	0.81
< 1 cm	20	21	18
1 cm or greater	14	18	16

stones, the initial success rates ranged from 90% to 100%. Neither stone size nor location appeared to influence the efficacy of ureteroscopic treatment, since no significant difference was observed in the stone free rates between patients with ureteral calculi 1 cm or greater and those with calculi less than 1 cm.

Failures were due to proximal migration of stone with inability to retrieve all fragments from lower pole in 3 patients and to residual fragments left in the ureter that failed to spontaneously pass to the bladder in other 3 patients. No intraoperative or postoperative complications occurred in any of the groups.

## COMMENTS

When ESWL cannot be used or is not an appropriate treatment option in the obese patient, the next option is often ureteroscopy or percutaneous nephrolithotomy (PCNL). El-Assmy et al. showed that PCNL in obese patients was not only safe but that obese patients did not experience any difference in success,

operative time, or morbidity (11). Even though good results can be obtained PCNL in the obese patient it still presents many challenges to the urologist. The substantial amount of subcutaneous fat and increased mobility of the kidney secondary to excess fat in the retroperitoneum make instrument access more difficult. Also, sometimes standard PCNL equipment is not long enough and extra-long equipment (nephroscope, etc.) has to be used in the obese patient, making the procedure technically more difficult. Ureteroscopic laser lithotripsy and stone extraction has been shown to be an effective method for treating urolithiasis in morbidly obese patients who were too large for ESWL (12). Compared to in situ ESWL, ureteroscopic lithotripsy appears to be more effective in the treatment of proximal ureteral calculi 1 cm or greater.

Recent technological advances, especially in the field of optics, have allowed endoscopes to become smaller, more flexible, and easier to introduce. Prior to the development of small caliber ureteroscopes, the stone-free rates achieved with ureteroscopy for distal ureteral calculi using large diameter rigid ureteroscopes

(more than 10 F), ultrasonic lithotriptors, or electro hydraulic lithotriptors with probes larger than 3 F, was greater than 90% (12,13). However, for mid-ureteral calculi, it was in the range of 60%, and for proximal calculi, close to 50% (13). More recent contemporary series, using small diameter rigid and flexible endoscopes as well as laser lithotriptors, have reported success rates of greater than 90% for proximal ureteral calculi (13). In our experience, the initial overall stone-free rate after ureteroscopic laser lithotripsy of proximal ureteral calculi was 97%, with a stone-free rate of 93% for calculi 1 cm or greater, which is consistent with the success rates of other reported series.

The introduction of the Ho:YAG laser has improved ureteroscopy stone-free rates while decreasing the risk of complications, and thus has been employed for lithotripsy by many groups with encouraging results. The Ho:YAG laser can fragment all types of calculi, including hard calcium oxalate monohydrate and cystine stones, by delivering energy through small-diameter quartz fibers that can be used through the working channels of the smallest available ureteroscopes. It fragments stones with an ablative effect, removing portions of the stone as dust-like particles during the fragmentation procedure. This process allows for the treatment of large calculi within the upper urinary tract without the burdensome process of fragment removal. The safety and efficacy of the Ho:YAG laser as an endoscopic lithotripter has been confirmed in other studies (14,15).

Our results show that it is possible to achieve stone-free status even in obese patients when treating them with ureteroscopy. Our results in fact showed higher stone-free rates in patients with a BMI of greater than 25, although the rates are virtually the same. One limitation of the study is the small number of patients in the morbidly obese group. Based on these results, ureteroscopy with laser lithotripsy should be given serious consideration in any obese patient with a stone smaller than 2 cm. With the continued improvement in technology and scopes, the potentially more difficult access to the ureter of obese patients, due to body habitus reasons, can be easier overcome and stone-free rates can approach or be equivalent to that of non-obese patients.

Long-term complication rates of ureteroscopy range from 0.5 to 10% for larger caliber instruments

(16). Complications are rare with small caliber instruments. Our low overall complication rate was consistent with those reported by other series. The majority of cases may be treated without ureteral dilation and have a lower likelihood of ureteral trauma. Thus, routine ureteral stenting following ureteroscopy and intracorporeal lithotripsy may not be necessary, thereby decreasing morbidity (17,18).

## CONCLUSIONS

Our study demonstrates that ureteroscopy is an acceptable treatment modality for all ureteral calculi and may be preferable to ESWL for obese patients. By using small caliber ureteroscopes and Ho:YAG laser lithotripsy, the target stone could be treated safely and effectively in our patients. In overweight and obese patients, results are comparable to non-obese patients. These results presented are independent of stone size and location.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Pasulka PS, Bistran BR, Benotti PN, Blackburn GL: The risks of surgery in obese patients. *Ann Intern Med.* 1986; 104: 540-6.
2. Willett WC, Dietz WH, Colditz GA: Guidelines for healthy weight. *N Engl J Med.* 1999; 341: 427-34.
3. Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL: The effect of age on the association between body-mass index and mortality. *N Engl J Med.* 1998; 338: 1-7.
4. Duffey BG, Pedro RN, Kriedberg C, Weiland D, Melquist J, Ikramuddin S, et al.: Lithogenic risk factors in the morbidly obese population. *J Urol.* 2008; 179: 1401-6.
5. Jamshaid A, Ather MH, Hussain G, Khawaja KB: Single center, single operator comparative study of the effectiveness of electrohydraulic and electromagnetic lithotripters in the management of 10- to 20-mm single upper urinary tract calculi. *Urology.* 2008; 72: 991-5.

6. Murota-Kawano A, Ohya K, Sekine H: Outpatient basis extracorporeal shock wave lithotripsy for ureter stones: efficacy of the third generation lithotripter as the first line treatment. *Int J Urol.* 2008; 15: 210-5.
7. Delakas D, Karyotis I, Daskalopoulos G, Lianos E, Mavromanolakis E: Independent predictors of failure of shockwave lithotripsy for ureteral stones employing a second-generation lithotripter. *J Endourol.* 2003; 17: 201-5.
8. Muñoz RD, Tirolien PP, Belhamou S, Desta M, Grimberg R, Dulys P, et al.: Treatment of reno-ureteral lithiasis with ESWL in obese patients. Apropos of 150 patients. *Arch Esp Urol.* 2003; 56: 933-8.
9. Calvert RC, Burgess NA: Urolithiasis and obesity: metabolic and technical considerations. *Curr Opin Urol.* 2005; 15: 113-7.
10. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck AC, Gallucci M, et al.: 2007 Guideline for the management of ureteral calculi. *Eur Urol.* 2007; 52: 1610-31.
11. El-Assmy AM, Shokeir AA, El-Nahas AR, Shoma AM, Eraky I, El-Kenawy MR, et al.: Outcome of percutaneous nephrolithotomy: effect of body mass index. *Eur Urol.* 2007; 52: 199-204.
12. Nguyen TA, Belis JA: Endoscopic management of urolithiasis in the morbidly obese patient. *J Endourol.* 1998; 12: 33-5.
13. Anderson KR, Keetch DW, Albala DM, Chandhoke PS, McClennan BL, Clayman RV: Optimal therapy for the distal ureteral stone: extracorporeal shock wave lithotripsy versus ureteroscopy. *J Urol.* 1994; 152: 62-5.
14. Jiang H, Wu Z, Ding Q: Ureteroscopy and holmium: YAG laser lithotripsy as emergency treatment for acute renal failure caused by impacted ureteral calculi. *Urology.* 2008; 72: 504-7.
15. Farkas A, Péteri L, Lorincz L, Salah MA, Flaskó T, Varga A, et al.: Holmium:YAG laser treatment of ureteral calculi: A 5-year experience. *Lasers Med Sci.* 2006; 21: 170-4.
16. Elashry OM, Elgamasy AK, Sabaa MA, Abo-Elenien M, Omar MA, Eltatawy HH, et al.: Ureteroscopic management of lower ureteric calculi: a 15-year single-centre experience. *BJU Int.* 2008; 102: 1010-7.
17. Ibrahim HM, Al-Kandari AM, Shaaban HS, Elshebini YH, Shokeir AA: Role of ureteral stenting after uncomplicated ureteroscopy for distal ureteral stones: a randomized, controlled trial. *J Urol.* 2008; 180: 961-5.
18. Cheung MC, Lee F, Yip SK, Tam PC: Outpatient holmium laser lithotripsy using semirigid ureteroscope. Is the treatment outcome affected by stone load? *Eur Urol.* 2001; 39: 702-8.

---

*Accepted after revision:  
November 10, 2008*

---

**Correspondence address:**

Dr. Mantu Gupta  
 Dept of Urology, Columbia University  
 Irving Pavilion, 11th Floor  
 161 Ft. Washington Avenue  
 New York, NY, 10032, USA  
 Fax: + 1 212 342-6870  
 E-mail: guptama@pol.net

**EDITORIAL COMMENT**

Obesity has become a major health problem in the world. Various lithogenic risk factors are associated with obesity, increasing the chance of stone formation in these patients.

The surgical treatment of kidney and ureteral stones in morbidly obese patients remains difficult because shockwave lithotripsy may be a sub-optimal treatment due to weight limitations and percutaneous

nephrolithotomy is associated with difficult access, anesthetic complications and a high rate of transfusion (1).

Dash et al. showed in a matched comparison (obese x normal) that ureteroscopic (URS) treatment of renal calculi when matched for location and size is as successful as and no more morbid in morbidly obese than in normal weight patients. URS treatment of renal calculi is a safe and effective first-line treatment for renal calculi in morbidly obese patients (2).

The authors study demonstrates that ureteroscopy is an acceptable treatment modality for all ureteral calculi and may be preferable to ESWL for obese patients.

The development of small caliber ureteroscopes and advances in intracorporeal lithotripsy have allowed for more successful and safer endoscopic manipulation of renal/ureteral calculi in overweight, obese, and morbidly obese patients.

#### REFERENCES

1. Andreoni C, Afane J, Olweny E, Clayman RV: Flexible ureteroscopic lithotripsy: first-line therapy for proximal ureteral and renal calculi in the morbidly obese and superobese patient. *J Endourol.* 2001; 15: 493-8.
2. Dash A, Schuster TG, Hollenbeck BK, Faerber GJ, Wolf JS Jr: Ureteroscopic treatment of renal calculi in morbidly obese patients: a stone-matched comparison. *Urology.* 2002; 60: 393-7; discussion 397.

**Dr. Mauricio Rubinstein**

*Federal Univ. of State of Rio de Janeiro*

*UNIRIO*

*Rio de Janeiro, RJ, Brazil*

*E-mail: mrubins@attglobal.net*

#### EDITORIAL COMMENT

The authors present their experience with ureteroscopic laser lithotripsy in obese and morbidly obese patients. The conclusion is that obesity is not a hindrance and results are similar with those obtained in non-obese patients.

Some articles have been published on the outcome of percutaneous nephrolithotomy in this group of patients and showed that results are comparable to those obtained in non-obese (1-3). This is the first article addressing specifically ureteroscopy in obese and results are encouraging. Since the results of extracorporeal shock wave lithotripsy in these patients are not as good as in non-obese, ureteroscopy could be considered the first line approach even in proximal ureteral stones. As obesity represents a worldwide public health problem owing to its relationship with urolithiasis, articles comparing the various forms of treating stones in obese are welcome.

#### REFERENCES

1. Bagrodia A, Gupta A, Ramon SD, Bensalah K, Pearle MS, Lotan Y: Impact of body mass index on cost and clinical outcome after percutaneous nephrostolithotomy. *Urology.* 2008; 29 (In press).
2. El-Assmy AM, Shokeir AA, El-Nahas AR, Shoma AM, Eraky I, El-Kenawy MR, et al.: Outcome of percutaneous nephrolithotomy: effect of body mass index. *Eur Urol.* 2007; 52: 199-204.
3. Nguyen TA, Belis JA: Endoscopic management of urolithiasis in the morbidly obese patient. *J Endourol.* 1998; 12: 33-5.

**Dr. Eduardo Mazzucchi**

*Division of Urology*

*University of Sao Paulo, USP*

*Sao Paulo, SP, Brazil*

*E-mail: mazucchi@terra.com.br*

# Critical Analysis of Salvage Radical Prostatectomy in the Management of Radioresistant Prostate Cancer

Daniel Seabra, Eliney Faria, Breno Dauster, Gunther Rodrigues, Gilberto Fava

Section of Urology, Pio XII Foundation, Barretos, Sao Paulo, Brazil

---

## ABSTRACT

*Purpose:* To critically evaluate salvage radical prostatectomy (SRP) in the treatment of patients with recurrent prostate cancer (PCa).

*Materials and Methods:* From January 2005 to June 2007, we assessed patients with recurrent localized PCa. Recurrence was suspected when there were three or more successive increases in prostate specific antigen (PSA) after nadir. After the routine imagery examinations, and once localized PCa was confirmed, patients were offered SRP. Following surgery, we evaluated bleeding, rectal injury, urinary incontinence or obstruction and impotence. PSA values were measured at 1, 3, 6, months and thereafter twice a year.

*Results:* Forty-two patients underwent SRP. The average age was 61 years. Following radiotherapy, the mean PSA nadir was 1.5 ng/mL (0.57-5.5). The mean prostate specific antigen doubling time (PSA-DT) was 14 months (6-20). Prior to SRP, the mean PSA was 5.7 ng/mL (2.9-18). The pathologic staging was pT2a: 13%; pT2b: 34%; pT2c: 27%; pT3a: 13%; and pT3b: 13%. Bleeding > 600 mL occurred in 14% of the cases; urethral stenosis in 50%; and urinary incontinence (two or more pads/day) in 72%. The mean follow-up post-SRP ranged from 6 to 30 months. The PSA level rose in 9, of which 6 had PSA-DT < 10 months.

*Conclusions:* SRP is a feasible method in the management of localized radioresistant PCa. PSA-DT has shown to be important for the selection and SRP should not be performed if PSA-DT > 10 months. Due to its increased morbidity, SRP should be only offered to the patients who are more concerned about survival rather than quality of life.

*Key words:* prostate cancer; radiotherapy; salvage therapy; prostatectomy

*Int Braz J Urol. 2009; 35: 43-8*

---

## INTRODUCTION

According to estimates for 2008 from the Brazilian National Cancer Institute (INCA) 49,530 new cases of prostate cancer (PCa) are expected in Brazil (1). Of these, more than 1,200 will be seen at our hospital. In the last decade, we have employed doses higher than 7,000 Gy in external beam radiation therapy (RT) to manage localized neoplasia. When localized recurrence is confirmed during follow-up of these patients, we recommend hormone blockade

via androgen ablation or salvage radical prostatectomy (SRP). The first treatment method is considered palliative and the second is definitive with the intention to cure. Furthermore, when begun early in the course of recurrent disease, SRP allows excellent disease control without the need of concomitant hormonal treatment (2,3).

Despite being employed for more than three decades, currently SRP is only offered to 25% of eligible patients who potentially are most likely to benefit from such therapy (4-6). The main reasons for

this low rate of use are the technical challenges during the procedure and the increased risk of complications, such as urinary incontinence or obstruction, erectile dysfunction, and rectal lesions (2,5). The aim of our study was to critically evaluate the role of radical prostatectomy in saving patients suffering from confirmed recurrence of prostate cancer restricted to the gland after treatment with conventional RT.

## MATERIALS AND METHODS

In our medical service, between January 2005 and June 2007, we carried out a prospective study in which we evaluated patients in whom recurrent PCa was proven following external RT with more than 7,000 cGy as early management with intention to cure for a localized cancer in clinical Stages I and II. Recurrence was suspected when there were three or more successive marker rises after PSA nadir, a criterion of the American Society for Therapeutic Radiology and Oncology (ASTRO). In these men, recurrence was ruled out by employing digital rectal exam to verify prostate status; pelvic magnetic resonance to study prostate and regional nodes; abdominal ultrasound to assess abdominal metastases; bone scintigraphy to rule out bone involvement; and thoracic radiography to rule out mediastinal or pulmonary disease. In the absence of dissemination, we performed a transrectal ultrasound-guided prostate rebiopsy (TRUS) to confirm prostate cancer. In this study, we only included patients with localized cancer, independently of PSA value. We excluded all men with negative rebiopsy and locally advanced or metastatic disease. Once recurrent localized tumor had been confirmed, all patients were proposed SRP. The procedure was fully explained and those who accepted the surgery were asked to sign the written informed consent for radical prostatectomy, which was adapted to be suitable for SRP. Following prostatectomy, the patients were evaluated for major complications inherent to the method: transoperative bleeding measured by aspirated blood; rectal lesions; urinary incontinence measured by numbers of pads used per day, considering incontinent patient that required 2 or more pads daily; urinary flow obstruction and erectile dysfunction. In the subsequent follow-up in order to control

for neoplasia, we measured PSA after 1,3, and 6 months, and thereafter twice a year. Additionally, we calculated the PSA doubling time (PSA-DT) before SRP and correlated it with postoperative outcomes. We preferred do not perform survival studies since the median follow-up time is very short.

## RESULTS

A total of 42 patients underwent SRP. The RT dose in 38 of these patients was 7,020 cGy, and 7,200 cGy in the remaining 4. The mean age was 61 years old (59-69). The mean PSA was 9.2 ng/mL (4.5-39.0). Mean post-RT PSA nadir was 1.5 (0.57-5.5). Mean time to achieve nadir was 12 months (5-24). Mean PSA-DT time was 14 months (6-20). Mean pre-SRP PSA was 5.7 ng/mL (2.9-18) (Table-1). Pre-RT clinical staging (TNM) was as follows: T1c: 27%; T2a: 27%; T2b: 37%; and T2c: 9%. Post-surgery pathological staging (pTNM) was as follows: pT2a: 13%; pT2b: 34%; pT2c: 27%; pT3a: 13%; and pT3b: 13% (Table-2). Pre-RT biopsy Gleason histological grading was 5 (3+2): 40%; 6 (3+3): 33%; 7 (4+3): 20%; and 8 (4+4): 7%. Post-SRP Gleason score was 5 (3+2): 20%; 6 (3+3): 20%; 7 (4+3): 46%; and 8 (4+4): 14%. SRP mean time was 80 minutes (50-160). Dissection of the seminal vesicles was our most difficult step. Table-3 lists the main complications. Median blood loss was 300 mL and bleeding greater than 600 mL occurred in 14% of the cases. Urinary flow obstruction by urethral stenosis or bladder neck sclerosis occurred in 21 patients (50%). These patients were submitted to internal urethrotomy and 5 (12%) of them had pro-

**Table 1** – PSA characteristics in 42 patients submitted to salvage radical prostatectomy (SRP).

PSA Characteristics	Values (range)
Pre-RT PSA (ng/mL)	9.2 (4.5 - 39.0)
PSA nadir (ng/mL)	1.5 (0.57 - 5.5)
Time to PSA nadir (months)	12 (5 - 24)
PSA - DT (months)	14 (6 - 20)
Pre SRP PSA (ng/mL)	5.7 (2.9 - 18)

**Table 2** – Pre-RT and post SRP staging (TNM - 2002) in 42 patients who underwent salvage radical prostatectomy (SRP).

Stage	%
Pre-RT (clinical)	
T1c	27
T2a	27
T2b	37
T2c	9
Post SRP (pathological)	
T2a	13
T2b	34
T2c	27
T3a	13
T3b	13

longed obstruction signs requiring further endoscopic surgery. A third additional urethrotomy was performed in 2 patients. At the end of the study, all 21 patients were stenosis free. In 72% of the cases, incontinent patients required two or more pads daily. Erectile dysfunction occurred in 74% of the cases. Two rectovesical fistulas developed. One was a high fistula in the supratrigonal area, which occurred 32 days after surgery. The cause was probably inflammatory through adherence of the sigmoid colon to the bladder apex. This patient was subsequently treated using segmental colectomy, colostomy, repair of vesical lesion and late reconstruction of intestinal transit. The other

**Table 3** – Main complications in 42 patients submitted to salvage radical prostatectomy (SRP).

Complications	Values
Blood loss (mL aspirated)	300 (50 - 1200)
Urinary flow obstruction	
1 urethrotomy	50%
2 urethrotomies	12%
3 urethrotomies	7%
Incontinence ( $\geq 2$ pads/day)	72%
Erectile dysfunction	74%
Rectovesical fistulas	4.8%

patient had a low fistula in the vesicourethral anastomosis region and the cause was probably ischemic. A successful late approach with simple suture through the anus was performed. Median postoperative follow-up time was 18 months (range 1 to 36 months). In the subsequent assessments, 9 patients (24%) had rising PSA. Of these, six had PSA-DT  $< 10$  months. In the remaining patients, the levels remained under 0.2 ng/mL.

## COMMENTS

In 2006, nearly half of the new patients with localized PCa in the United States elected RT as primary treatment (6). This choice hinges mainly on the concern of these men with quality of life, which in principle should be better than that of those who undergo radical surgery (7).

Factors influencing the success of RT can be patient treatment specific (8). Patient-specific factors can be stratified into 3 risk groups for relapse: the low risk group ( $\leq T2a$ , Gleason score  $\leq 6$  and PSA  $\leq 10$ ); the intermediary group (T2b, Gleason score of 7 and PSA  $\leq 20$ ); and the high risk group (T3-4, Gleason score  $\geq 8$  and PSA  $\geq 20$ ). The parameters related to treatment included the modality of RT used (namely conventional, three-dimensional or intensity modulated conformal), the escalation and the maximum permissible dose. These are independent predictive factor of success with a failure rate varying between 25% and 32% (9). Another important point in the RT outcomes is the fact that 93% of the failures occur at the apex, an area that can pose a greater management failure risk and is difficult to treat due to its location (6). Following therapy, patients are periodically monitored for at least 15 years, an interval considered today as a curative criterion. In this period, due to the apoptosis of prostatic cells induced by treatment, reduced PSA levels are observed until the nadir, or minimum, level is reached. Thereafter, if there are successive increases in the marker level, recurrent neoplasia is suspected, which can be local or distant. If recurrence is confirmed by post-RT follow-up, it can have a profound impact on the patient's quality of life and the news can even be worse than the initial information that the patient has cancer (2,8).

Currently there is no definitive predictor criterion of local recurrence after RT. There are more than 100 different types described, with prostate cancer biopsy standing out, which is mandatory after 18 to 24 months after the treatment. Other criteria are nadir; the time to achieve nadir; PSA doubling time (PSA-DT); the ASTRO criterion (three or more successive rises in PSA) and PSA nadir + 2 ("Houston" +2) (8).

The value of a positive biopsy after RT is controversial, with a false positive rate of 60% and a false negative rate of 20% (10). The "traditional" ideal PSA nadir value is  $< 0.5$  ng/mL. In clinical practice, when there is a local recurrence, the average PSA nadir is 1.1 ng/mL, and if there is a systemic recurrence, the PSA nadir is 2.2 ng/mL. On the other hand, 80% of the patients who have survived 10 years after radiation therapy have PSA values up to 1.0 ng/mL (10,11). Thus, this would discredit the nadir of 0.5 ng/mL as a cutoff point. The average PSA nadir of our patients after radiation therapy was 1.5 ng/mL.

The time to reach the nadir is important to understand the course of PCa after RT. Patients who achieve long-term disease control take longer to reach PSA nadir, an average of 24 months, while those who experience local recurrence had an average time to PSA nadir of 17 months and those with distant metastases attain PSA nadir in roughly 12 months (10,11).

In patients with local recurrence, PSA-DT is greater than 6 months and in those with systemic recurrence PSA-DT is less than 3 months (12). Moreover, if PSA-DT  $< 10$  months, the 7-year survival after radiation therapy is only 52% (13,14). The mean PSA-DT of our patients was 14 months.

According to ASTRO criterion, biochemical recurrence alone does not justify the beginning additional therapy, because it is not considered a clinical recurrence (15). It is suspected if there are three or more successive rises in PSA after the nadir. Despite its high specificity, there is a lack of sensitivity because patients with distant recurrence are also being included. In addition, by using the current ASTRO criterion, the relapse can be diagnosed late, up to five years after radiation therapy, which can minimize the chances of a definitive cure (16).

Patients with confirmed tumor recurrence, had individualized management consisting of obser-

vation without early treatment, brachytherapy, SRP, hormonal blockade, or even therapies considered to be experimental, such as cryosurgery and radiofrequency therapy (6,8). The goal of these experimental therapies is to cause maximum destruction of prostate tissue with minimal damage to critical surrounding structures such as the urethra, urinary sphincter and rectum. On the other hand, the preservation of these structures may result in incomplete management, since some regions of the prostate are closely adjacent or adherent to these structures (6).

The justification for employing some kind of treatment is that the time interval from PSA failure until the discovery of the metastases varies from 3 to 8 years, after which death from cancer generally occurs within the next 5 years (17). Thus, certain groups of patients, especially younger ones, would benefit from early institution of definitive treatment (16). For this purpose, SRP provides survival rates similar to those of primary radical prostatectomy (16). Open retropubic SRP has been employed for more than 30 years with intent to cure after RT failure (3). Because it is considered more difficult and contains a higher risk of complications than primary radical prostatectomy, it is only currently offered to 25% of eligible patients who potentially are most likely to benefit from such therapy (6). In contrast, it is a procedure that is being constantly improved and presently its complication rate is not as high as it was in the past (18). The "ideal" candidates for such a procedure are the same as those for primary radical surgery: those with life expectancy of 10 years or more, no co-morbidities, highly motivated, i.e., those who accept increased surgical morbidity, with pre-radiation PSA values 10 ng/mL, preoperative PSA less than 10 ng/mL, pre-radiation PSA-DT  $> 10$  months and with both pre-radiation and preoperative localized clinical stage (2).

The surgery is tactically and technically similar to primary radical retropubic prostatectomy (5,16). Also, laparoscopic salvage radical prostatectomy has been reported as a surgical approach (19). Pelvic lymphadenectomy should be extended because an extensive lymphatic involvement has been found in 7% to 11% of the cases (6,8). This surgical step is considered critical whereas there are adhesions between the bladder and iliac vessels reported in 27% of patients. Furthermore, it is difficult to dissect the

apex of the prostate and the seminal vesicles as a result of vasculitis, fibrosis and obliterations resulting from radiation therapy (8).

Contrary to what has been reported in the literature, where the mean blood loss reported was 900 mL, in our study blood loss superior to 600 mL occurred in only 14% of the patients. None of them required blood transfusion. There was a high rate of stenosis/sclerosis of the vesicourethral anastomosis: 50% in our series versus an average of 18% reported in the literature. The high obstruction rate can be explained by the decreased tissue vascularization that occurs after RT, with consequent healing difficulty (6). The urinary incontinence rate in our study, defined as two or more pads required daily was 72%, which is far above the 45% reported in the literature. Furthermore, we have not yet evaluate the response of the incontinent patients to urinary physiotherapy, to which all patients have been submitted, through Kegel exercises, biofeedback or electrostimulation. Nearly, 74% of the patients reported worse erectile function, but we did not evaluate how many patients already had erectile dysfunction prior to surgery, or their rate of improvement after the treatment was instituted. The intraoperative rectal injury rates were considered insignificant, since it occurred in only one case. The rate of rectal injury reported in the literature was between 0% and 19% (3-5,8).

PSA-DT calculation seemed important to us, since 6 out of 9 patients with persistent PSA rise following SRP had PSA-DT < 10 months.

This series could be considered limited in time, but not as regards the number of cases: in less than three years we were able to treat 42 patients. This can be a reflection of our concern to offer optimal care as well as the certainty that SRP remains one of the treatment modalities most capable of providing a definitive cure in these cases (6).

Nevertheless, given the shorter follow-up, we cannot yet show the relapse-free survival rates. Another important point to be taken into consideration is that we still need to study the prostate cancer patient's real concern regarding the quality versus quantity of life dichotomy.

It was interesting to observe that in the eligible candidates to SRP, after minute considerations regarding the outcome, both related to the discovery

of recurrence itself and to the possible consequences of surgical-associated morbidity, the greatest concern for each patient was survival, even if they would experience a worse quality of life.

## CONCLUSIONS

We consider that salvage radical prostatectomy should be offered with intention to cure following failure of external beam radiation therapy as a treatment method of localized prostate neoplasia. SPR, despite being more technically challenging than the primary radical surgery, is feasible. PSA-DT calculation has proven to be important in these patients' selection. As a result of postoperative complications, surgery should only be offered to those considered to be "ideal" candidates who are self motivated

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Estimativa 2008: incidência de câncer no Brasil. Rio de Janeiro, INCA. 2007; pp. 33-4. Disponível em: <http://www.inca.gov.br/estimativa/2008/versaofinal.pdf>
2. Sanderson KM, Penson DF, Cai J, Groshen S, Stein JP, Lieskovsky G, et al.: Salvage radical prostatectomy: quality of life outcomes and long-term oncological control of radiorecurrent prostate cancer. *J Urol.* 2006; 176: 2025-31; discussion 2031-2.
3. Mador DR, Huben RP, Wajzman Z, Pontes JE: Salvage surgery following radical radiotherapy for adenocarcinoma of the prostate. *J Urol.* 1985; 133: 58-60.
4. Ward JF, Sebo TJ, Blute ML, Zincke H: Salvage surgery for radiorecurrent prostate cancer: contemporary outcomes. *J Urol.* 2005; 173: 1156-60.
5. Dall'Oglio MF, Barreto F, Paranhos M, Nesrallah A, Nesrallah L, Srougi M: Salvage radical prostatectomy: an alternative treatment for local recurrence of radioresistant cancer. *Int Braz J Urol.* 2006; 32: 550-6.
6. Huang WC, Kuroiwa K, Serio AM, Bianco FJ Jr, Fine SW, Shayegan B, et al.: The anatomical and pathological characteristics of irradiated prostate cancers may

- influence the oncological efficacy of salvage ablative therapies. *J Urol.* 2007; 177: 1324-9.
7. Berry DL, Ellis WJ, Woods NF, Schwien C, Mullen KH, Yang C: Treatment decision-making by men with localized prostate cancer: the influence of personal factors. *Urol Oncol.* 2003; 21: 93-100.
  8. Touma NJ, Izawa JI, Chin JL: Current status of local salvage therapies following radiation failure for prostate cancer. *J Urol.* 2005; 173: 373-9.
  9. Zelefsky MJ, Fuks Z, Leibel SA: Intensity-modulated radiation therapy for prostate cancer. *Semin Radiat Oncol.* 2002; 12: 229-37.
  10. Crook J, Malone S, Perry G, Bahadur Y, Robertson S, Abdolell M: Postradiotherapy prostate biopsies: what do they really mean? Results for 498 patients. *Int J Radiat Oncol Biol Phys.* 2000; 48: 355-67.
  11. Zietman AL, Tibbs MK, Dallow KC, Smith CT, Althausen AF, Zlotecki RA, et al.: Use of PSA nadir to predict subsequent biochemical outcome following external beam radiation therapy for T1-2 adenocarcinoma of the prostate. *Radiother Oncol.* 1996; 40: 159-62.
  12. Sartor CI, Strawderman MH, Lin XH, Kish KE, McLaughlin PW, Sandler HM: Rate of PSA rise predicts metastatic versus local recurrence after definitive radiotherapy. *Int J Radiat Oncol Biol Phys.* 1997; 38: 941-7.
  13. Lee WR, Hanks GE, Hanlon A: Increasing prostate-specific antigen profile following definitive radiation therapy for localized prostate cancer: clinical observations. *J Clin Oncol.* 1997; 15: 230-8.
  14. Lee AK, D'Amico AV: Utility of prostate-specific antigen kinetics in addition to clinical factors in the selection of patients for salvage local therapy. *J Clin Oncol.* 2005; 23: 8192-7.
  15. [No authors listed] Consensus statement: guidelines for PSA following radiation therapy. American Society for Therapeutic Radiology and Oncology Consensus Panel. *Int J Radiat Oncol Biol Phys.* 1997; 37: 1035-41.
  16. Stephenson AJ, Eastham JA: Role of salvage radical prostatectomy for recurrent prostate cancer after radiation therapy. *J Clin Oncol.* 2005; 23: 8198-203.
  17. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC: Natural history of progression after PSA elevation following radical prostatectomy. *JAMA.* 1999; 281: 1591-7.
  18. Vaidya A, Soloway MS: Salvage radical prostatectomy for radiorecurrent prostate cancer: morbidity revisited. *J Urol.* 2000; 164: 1998-2001.
  19. Vallancien G, Gupta R, Cathelineau X, Baumert H, Rozet F: Initial results of salvage laparoscopic radical prostatectomy after radiation failure. *J Urol.* 2003; 170: 1838-40.

---

*Accepted after revision:  
September 30, 2008*

---

**Correspondence address:**

Dr. Daniel Seabra  
Rua Brasil, 1500  
Barretos, SP, 14783-180, Brazil  
E-mail: daniel.seabra@terra.com.br

## Corporoplasty Using Bovine Pericardium Grafts in Complex Penile Prosthesis Implantation Surgery

Eduardo J. A. Lopes, Andre Y. Kuwano, Andreia N. Guimaraes, Jesuino P. Flores, Modesto A. O. Jacobino

*Section of Urology, School of Medicine, Federal University of Bahia, Salvador, Bahia, Brazil*

---

### ABSTRACT

*Purpose:* This paper is the first, to our knowledge, to propose the use of a bovine pericardium graft in corporoplasty for penile prosthesis implantation. The advantages of bovine pericardium graft have been demonstrated by its use in cardiac surgery, including low cost, biocompatibility, impermeability, resistance to dilatation, flexibility, low likelihood of retraction, absence of antigenic reaction and natural absorption of the tissue. In this paper, we propose the use of this heterologous material graft in corporoplasty for penile prosthesis implantation.

*Materials and Methods:* Five patients with a history of erosion, infection and fibrosis, mean time of follow-up 32 months (range 9-48 months). Bovine pericardium was used to cover large areas of implanted penile prostheses when use of the tunica albuginea was unfeasible.

*Results:* The surgical procedure resulted in no complications in all patients.

*Conclusions:* Bovine pericardium may substitute synthetic and autologous material with the additional advantages of lower cost and greater availability.

*Key words:* penile prosthesis; infection; penile fibrosis; graft; bovine pericardium  
*Int Braz J Urol. 2009; 35: 49-55*

---

### INTRODUCTION

Many materials, both natural and synthetic, have been used to substitute part of the tunica albuginea during corporoplasty and also as material for grafts in penile prosthesis implantation (1). Various series have reported the use of synthetic products such as Gore-Tex, Marlex, Dacron and Silicone (2-4). However, the complication rate following penile grafts of these synthetic materials is high and includes high infection rates, greater risk of fibrosis and absence of elasticity (2-4). Biological materials such as dermis, vein, fascia temporalis, tunica vaginalis and even part of the albuginea of the corpora cavernosa have been used to recompose defects in the penis (5-

12). Although they are not immunogenic and have a lower probability of rejection, biological materials are far from being the ideal substitutes for the tunica albuginea, in most cases due to their low tensile strength. The need for an additional incision increases the duration of surgery, the cost and the possibility of complications in patients who are already debilitated due to the presence of degenerative diseases (6-8,12). Disadvantages of the use of cadaveric pericardium include the high cost and poor availability of this material (9-11). This paper reports the first use of bovine pericardium grafts in penile prosthesis implantation in a small series of cases of extreme complexity in which there was insufficient space for implantation of the prosthesis due to intense fibrosis (13-16).

## MATERIAL AND METHODS

Five patients with a previous medical history of erosion, infection and fibrosis were submitted to implantation of penile prosthesis lined by bovine pericardium. The opening space for implantation by simple cavernotomy and corporotomy was not enough to insert the thinner prosthesis.

The mean age of patients was 38.4 years. The mean number of previous surgeries to which these patients had been submitted was 1.8 and the mean time of follow-up was 32 months (range 9-48 months).

Patient #1 presented one of the cylinders of the prosthesis extruding from the urethra (Figure-1). During surgery for reimplantation, the existence of a single space was found in the corpora cavernosa. In view of the infection and the urethral lesion, a conservative treatment was chosen. Reimplantation of a single unit was performed 60 days after resolution of the infectious process.

Patients #2, #3 and #5 had fibrosis of corpus cavernosum after several events of priapism caused by sickle-cell anemia. All of the patients had priapism



*Figure 1 – Prosthesis extruding from the urethra.*

episodes during more than 72 hours, without receiving appropriate medical assistance. Patient #5 also had type 1 diabetes mellitus.

Patient #4 had prostate cancer and was treated by radical prostatectomy; however, he developed erectile dysfunction and underwent an implantation of flexible penile prosthesis. An infection developed, and the patient had the prosthesis removed. Six months later, a new prosthetic implant was performed. Due to the intense fibrosis and the small space within the corpus cavernosum, the pair of implanted prosthesis was lined with 10 cm segment of bovine pericardium sutured to the albuginea.

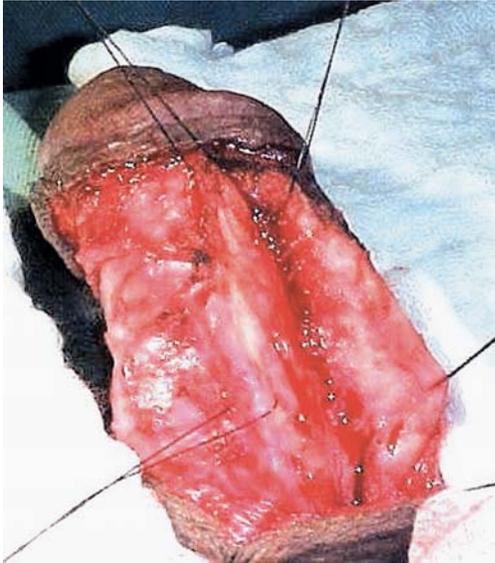
All five patients underwent surgery, which was performed by the same surgeon between January 2003 and December 2006.

## SURGICAL TECHNIQUE

All patients started to receive prophylactic antibiotic therapy two hours prior to surgery and maintained for 7 days following the surgical procedure. The drug of choice was ceftriaxone. Gentamicin diluted in 0.9% saline solution was used to repeatedly clean the surgical field. Spinal (epidural) anesthesia was used. Malleable prostheses were implanted in all cases. The incision adopted was penoscrotal in 4 cases and circular subcoronal degloving incision in one case.

In case #1, the tunica albuginea was thickened and the spongy tissue had been replaced by fibrosis (Figure-2). Only a single space was found; hence, it was only possible to implant one single unit of the penile prosthesis. Since there was small space and the albuginea could not be used to cover the prosthesis, a 10 cm segment of thin bovine pericardium was sutured to the remaining tunica albuginea using continuous polyglactac acid 2-0 sutures.

Due to the intense fibrosis in the corpora cavernosa of patients #2, #3, #4 and #5, it was not practical to implant even the thinnest penile prosthesis available. In these cases, 8-10 cm segments of bovine pericardium were used to complement the tunica albuginea lining the cylinders. Medium-thick bovine pericardium grafts were fixed to the albuginea using continuous polyglactac acid 2-0 sutures (Figure-3).



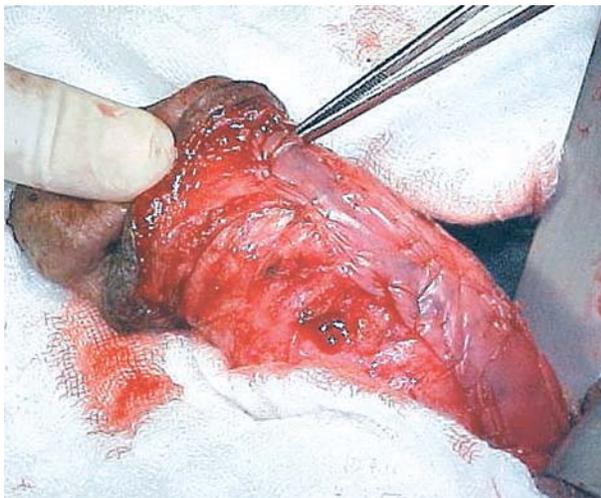
**Figure 2** – *Fibrous corpora cavernosa.*

In all 4 cases, the two cylinders of the penile prosthesis were successfully implanted.

The patients were advised to wait at least 8 weeks after prosthesis implantation and albuginea reconstruction before having sexual intercourse.

## RESULTS

There were no complications observed in the immediate postoperative period. After 8 weeks, all



**Figure 3** – *Bovine pericardium lining the prosthesis.*

patients maintained sexual intercourse. None of the patients complained of pain or difficulty to penetrate the vagina of the partner. The average follow-up was 32 months (ranging from 9 to 48 months). All patients were satisfied with the results.

## COMMENT

Extrusion of the penile prosthesis through the tunica albuginea is an uncommon complication following surgical implantation of a penile prosthesis when either synthetic or natural materials are used for reconstruction. Removal of the prosthesis due to infection is one of the major complications of penile prosthesis implantation (Figure-1). Rescue reimplantation procedures are considered extreme measures and have been defended in few reported series (17). Late reimplantation may constitute a complex surgical procedure when the spongy tissue of the corpora cavernosa has been overtaken by fibrosis.

Patients with sickle-cell anemia are relatively common in this geographical region, in which 80% of the population is of African descent. Many of these patients develop stuttering priapism, which is treated with topical therapies. The formation of fibrosis inside the corpora cavernosa makes implantation of even the thinnest prosthesis impracticable without the use of complementary grafts sutured to the tunica albuginea, covering the prosthesis.

Here, for the first time, to our knowledge, we report the use of bovine pericardium to cover large areas of implanted penile prostheses when use of the tunica albuginea is unfeasible (13-16). Although bovine pericardium is a heterologous material, it has been used in heart valve prostheses and vascular grafts for more than 18 years with exceptional results and no rejection or retraction (18). It has been extensively used in the treatment of urological pathologies such as congenital penile curvature and Peyronie's disease (19-22). Moreover, its biocompatibility and resistance have previously been tested in organs in which the circulatory and functional dynamics demand good tensile strength. Its use eliminates the need for a second incision, thereby reducing the time of surgery, risks and the cost for the patient.

Bovine pericardium is an inert material with a low probability of retraction. It has a lower cost than cadaveric pericardium, being, therefore, accessible to any hospital unit. It is available in segments measuring 4.0 x 5.5 cm, 7.6 x 11 cm and 10 x 12.5 cm, and in three different thicknesses (thin, medium and thick) at a cost of 60-90 dollars. It is an heterologous material treated with glutaraldehyde and has no antigenic reaction. It is conserved in a solution of formaldehyde or glycerin and packaged in sterile containers. It is flexible, impermeable and resistant to sutures. Moreover, it does not tear when the suture needle is inserted and is resistant to the traction necessary for a good suture. It is very resistant to tension and may be used to cover large defects without bulging. Bovine pericardium grafts are not subject to rejection, and provoke only a mild inflammatory reaction, if any. It also serves as a framework for the growth of the tunica albuginea along its extension. The remodeling process is long and may take several months.

## CONCLUSIONS

Despite the small number of patients, our results with the use of bovine pericardium as a substitute for the tunica albuginea were optimal. Bovine pericardium is inexpensive, widely available, impermeable, resistant and flexible. Moreover, it has a low probability of retraction, no antigenic reaction and is easily incorporated into the structure of the tissue. Bovine pericardium may substitute synthetic and autologous material with the further advantages of lower cost and greater availability. The processes of sterilization and storage are simple and permit its conservation for long periods of time with no damage to its properties. These advantages make bovine pericardium an accessible material for any patient who requires penile prosthesis implantation in situations of greater complexity.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Fishman IJ: Corporeal reconstruction procedures for complicated penile implants. *Urol Clin North Am.* 1989; 16: 73-90.
2. Smith CP, Kraus SR, Boone TB: Management of impending penile prosthesis erosion with a polytetrafluoroethylene distal wind sock graft. *J Urol.* 1998; 160: 2037-40.
3. Blumenfrucht M, Bhattacharya S, Brunner R, Wise GJ: Penile corporoplasty with polytetrafluoroethylene (PTFE) grafts. *Urology.* 1983; 22: 46-8.
4. Herschorn S, Ordorica RC: Penile prosthesis insertion with corporeal reconstruction with synthetic vascular graft material. *J Urol.* 1995; 154: 80-4.
5. Melman A, Holland TF: Evaluation of the dermal graft inlay technique for the surgical treatment of Peyronie's disease. *J Urol.* 1978; 120: 421-2.
6. Kadioglu A, Tefekli A, Usta M, Demirel S, Tellaloglu S: Surgical treatment of Peyronie's disease with incision and venous patch technique. *Int J Impot Res.* 1999; 11: 75-81.
7. Burnett AL: Fascia lata in penile reconstructive surgery: a reappraisal of the fascia lata graft. *Plast Reconstr Surg.* 1997; 99: 1061-7.
8. Alter GJ, Greisman J, Werthman PE, Seid AS, Joseph BJ: Use of a prefabricated tunica vaginalis fascia flap to reconstruct the tunica albuginea after recurrent penile prosthesis extrusion. *J Urol.* 1998; 159: 128-32.
9. Landman J, Bar-Chama N: Initial experience with processed human cadaveric allograft skin for reconstruction of the corpus cavernosum in repair of distal extrusion of a penile prosthesis. *Urology.* 1999; 53: 1222-4.
10. Hellstrom WJ, Reddy S: Application of pericardial graft in the surgical management of Peyronie's disease. *J Urol.* 2000; 163: 1445-7.
11. Leungwattanakij S, Bivalacqua TJ, Reddy S, Hellstrom WJ: Long-term follow-up on use of pericardial graft in the surgical management of Peyronie's disease. *Int J Impot Res.* 2001; 13: 183-6.
12. Teloken C, Grazziotin T, Rhoden E, Da Ros C, Fornari A, Soares FC, et al.: Penile straightening with crural graft of the corpus cavernosum. *J Urol.* 2000; 164: 107-8.
13. Lopes EJ, Oliveira VS, Lacerda S, Jacobino M: Use of bovine pericardium in penile prosthesis reimplantation. *Official Bulletin of the Brazilian Association for Sexual Inadequacy (ABEIS).* 2003; vol. VII, p. 6-6. [in Portuguese]

14. Lopes EJ, Oliveira VS, Lacerda S, Jacobino M: Penile prosthesis replantation by using bovine pericardium. *Int Braz J Urol.* 2005; 29 (Suppl.): p. 239. (Abst P-030). [in Portuguese]
15. Lopes EJ, Santos TC, Santos DSN, Carrera H: Penile prosthesis implation in neo penis. *Int Braz J Urol.* 2005; 30 (Suppl.): p. 89. (Abst PO-55). [in Portuguese]
16. Lopes EJ, Santos TC, Jacobino M: Bovine pericardium in penile prosthesis reimplantation. *Int Braz J Urol.* 2007; 33: 74-6.
17. Mulcahy JJ, Brant MD, Ludlow JK: Management of infected penile implants. *Tech Urol.* 1995; 1: 115-9.
18. Pomerantzeff PM, Zerbini EJ, Verginelli G, Jatene AD: Valve replacement in the Heart Institute, University of Sao Paulo, Brazil. *Ann Thorac Surg.* 1989; 48 (Suppl. 3): S41-4.
19. Lopes EJ, Oliveira VS, Lacerda S, Jacobino M, Lima DMO: Congenital penile curvature. *Int Braz J Urol.* 2005; 29 (Suppl.): p. 243. (Abst P-045). [in Portuguese]
20. Lopes EJ, Santos TC, Flores JP, Santos DSN: Correction of penile curvature using bovine pericardium. *Int Braz J Urol.* 2005; 30 (Suppl. ): p. 91. (Abst PO-62). [in Portuguese]
21. Lopes EJ, Santos TC, Flores JP, Jacobino M, Carrera H: Peyronie's disease. Elongation of short side with interposition of bovine pericardium. *Int Braz J Urol.* 2005; 30 (Suppl.): p. 63. (Abst TL-275). [in Portuguese]
22. Egydio PH, Lucon AM, Arap S: Treatment of Peyronie's disease by incomplete circumferential incision of the tunica albuginea and plaque with bovine pericardium graft. *Urology.* 2002; 59: 570-4.

---

*Accepted after revision:  
November 10, 2008*

---

**Correspondence address:**

Dr. Eduardo J. A. Lopes  
 Rua Altino Seberto de Barros, 241/405  
 Salvador, BA, 41850-010, Brazil  
 Fax: + 55 71 3351-7424  
 E-mail: ejalopes@oi.com.br

**EDITORIAL COMMENT**

Burnett and Palese in 2001 (1) first described the use of cadaveric human pericardium graft in complex penile prosthesis surgery. Hellstrom and Reddy (2) described the application of cadaveric human pericardium for tunica albuginea expansion to correct penile curvature associated or not with penile prosthesis implantation and no postoperative evidence of tissue rejection or infection was observed.

Egydio and co-workers (3-5) used the cadaveric bovine pericardium graft applying geometrical principles for the precise placement of tunica incision aiming to expand the cavernous space to allow the penile prosthesis implantation for maximum penile length and girth gain, limited by the length of the dissected neurovascular bundle.

The authors in the present study in fact corroborate with the use of cadaveric bovine pericardium, as a graft, to expand the cavernous space, even in cases associated with cavernous tissue fibrosis.

**REFERENCES**

1. Palese MA, Burnett AL: Corporoplasty using pericardium allograft (tutoplast) with complex penile prosthesis surgery. *Urology.* 2001; 58: 1049-52.
2. Hellstrom WJ, Reddy S: Application of pericardial graft in the surgical management of Peyronie's disease. *J Urol.* 2000; 163: 1445-7.
3. Egydio PH, Lucon AM, Arap S: A single relaxing incision to correct different types of penile curvature:

- surgical technique based on geometrical principles. BJU Int. 2004; 94: 1147-57.
4. Egydio PH: Surgical treatment of Peyronie's disease: choosing the best approach to improve patient satisfaction. Asian J Androl. 2008; 10: 158-66.
  5. Egydio PH, Perovic SV, Sansalone S: Surgical treatment of severe Peyronie's disease for maximum penile length and girth gain. J Urol. 2008; 179: 256(Suppl), Abst #733.

**Dr. Paulo H. Egydio**

*Center for Peyronie's Disease*

*São Paulo, SP, Brazil*

*E-mail: phegydio@peyronie.com.br*

## EDITORIAL COMMENT

This is a very interesting paper of heterologous substitution with bovine pericardium for extreme fibrosis and defects of the corporal bodies. Revision-surgery of penile prosthesis, although rather rare, is difficult and challenging. Homologous materials (vein grafts, tunica vaginalis, dermal grafts) are a possibility but an additional operation field is needed. These grafts are routinely used in corporoplasty for Peyronie's disease but are not used in revision-surgery for the covering of a penile prosthesis (1). I personally consider synthetic products such as Gore-Tex and Dacron as obsolete in penile prosthesis surgery due to

the risk of damaging the prosthesis caused by friction with the foreign material. This paper has splendid results but the report only concerns a limited group of patients with median-term follow-up. Larger groups of patients with longer follow-up are needed before considering this treatment as a standard treatment for this difficult type of patients.

## REFERENCE

1. Backhaus BO, Muller SC, Albers P: Corporoplasty for advanced Peyronie's disease using venous and/or dermis patch grafting: new surgical technique and long-term patient satisfaction. J Urol. 2003; 169: 981-4.

**Dr. Nicolaas C. Lumen**

*Department of Urology*

*Ghent University Hospital*

*Ghent, Belgium*

*E-mail: lumennicolaas@hotmail.com*

## REPLY BY THE AUTHORS

The present paper was not on the use of small grafts implantation for rectifying curved penile as in Peyronie's disease, associated or not with penile prosthesis implantation. We presented the partial substitution of tunica albuginea with bovine pericardium for harvesting the implanted prosthesis in cases

of extreme fibrosis and defects of corpora cavernosa (1-3). We performed the same procedure as other authors using different materials (4-7), however, we used bovine pericardium by the first time (1,2). For clarification, pioneering studies have been presented at various congresses (1,2), previously to the cited

publication in 2004 by Dr. Egydio (8), which dealt with penile curvature and not with fibrosis and corpora cavernosa defects. Also, our material was not human cadaveric pericardium as used by Palese and Burnett (7), but bovine pericardium (heterologous material). This graft is routinely used in corporoplasty for Peyronie's disease but is not used in revision-surgery for covering penile prostheses (9).

In 2007, we published the report of the first patient operated on 2000 (1). In the present paper published here, we present our small series of five patients. We agree with Dr. Lumen that it is necessary to include more patients and long-term follow-up for considering this kind of treatment as the gold standard for cases of extreme complexity.

#### REFERENCES

1. Lopes EJ, Oliveira VS, Lacerda S, Jacobino M: Use of bovine pericardium in penile prosthesis reimplantation. Official Bulletin of the Brazilian Association for Sexual Inadequacy (ABEIS). 2003; 7: p. 6-6. [in Portuguese]
2. Lopes EJ, Flores JP, Jacobino M: Reimplantation of penile prosthesis using bovine pericardium. Int Braz J Urol (Suppl.). 2003; 29: p. 33. [in Portuguese]
3. Lopes EJ, Santos T, Jacobino M: Bovine pericardium in penile prosthesis reimplantation. International Braz J Urol, 2007; 33: 74-76.
4. Backhaus BO, Muller SC, Albers P: Corporoplasty for advanced Peyronie's disease using venous and/or dermis patch grafting: new surgical technique and long-term patient satisfaction. J Urol. 2003; 169: 981-4.
5. Palese MA, Burnett AL: Corporoplasty using pericardium allograft (tutoplast) with complex penile prosthesis surgery. Urology. 2001; 58: 1049-52.
6. Hellstrom WJ, Reddy S: Application of pericardial graft in the surgical management of Peyronie's disease. J Urol. 2000; 163: 1445-7.
7. Palese MA, Burnett AL: Corporoplasty using pericardium allograft (tutoplast) with complex penile prosthesis surgery. Urology. 2001; 58: 1049-52.
8. Egydio PH, Lucon AM, Arap S: A single relaxing incision to correct different types of penile curvature: surgical technique based on geometrical principles. BJU Int. 2004; 94: 1147-57.
9. Backhaus BO, Muller SC, Albers P: Corporoplasty for advanced Peyronie's disease using venous and/or dermis patch grafting: new surgical technique and long-term patient satisfaction. J Urol. 2003; 169: 981-4.

*The Authors*

# Penile Torsion Correction by Diagonal Corporal Plication Sutures

**Brent W. Snow**

*Division of Urology, University of Utah, Salt Lake City, Utah, USA*

---

## ABSTRACT

Penile torsion is commonly encountered. It can be caused by skin and dartos adherence or Buck's fascia attachments. The authors suggest a new surgical approach to solve both problems. If Buck's fascia involvement is demonstrated by artificial erection then a new diagonal corporal plication suture is described to effectively solve this problem.

**Key words:** *penis; sutures; male urologic surgical procedure*  
*Int Braz J Urol. 2009; 35: 56-9*

---

## INTRODUCTION

Penile torsion in childhood is usually in the counterclockwise direction, if the physician is facing the patient. If the penile torsion is less than 20-30 degrees, surgical correction is not considered. The etiology of torsion of the penis has been thought to be due to skin and dartos attachments and yet others suggest involvement of Buck's fascia. When penile torsion correction is appropriate, various repairs have been considered: 1) penile shaft skin rotation (1); 2) suturing the tunica albuginea to the periosteum of the pubis (2) or 3) dorsal dartos flap rotation (3); 4) Nesbit plication (4) or u-shaped plicating sutures (5). A new technique is presented to correct penile torsion that is persistent after the skin had been completely degloved and an artificial erection has demonstrated persistence of the torsion.

## SURGICAL TECHNIQUE

The skin of the penis is degloved to the base of the penis and an artificial erection is performed.

If the penile torsion is resolved with degloving of the shaft skin, the skin is over-rotated to allow the penis to be straight in the flaccid state to complete the repair.

If the artificial erection shows persistence of the penile torsion, an inverted permanent braided 4-0 diagonal plicating suture is taken parallel to the neurovascular bundle on the right corporal cavernous body and the opposite half of the suture is taken parallel to the neurovascular bundle more proximally on the left corporal cavernous body (Figure-1) (presuming the normal counterclockwise rotation of the penis). When this diagonal plicating suture is tied protecting the neurovascular bundle, the artificial erection is repeated and this is usually sufficient to correct the penile torsion. If the torsion persists, additional diagonal plicating sutures may be used. The permanent sutures will last long enough for scarring to take place before the sutures will lose their tension. An incision in the tunica albuginea on each corpus beside the plicating sutures can be used to allow fresh cut edges to permanently heal the plication if desired.



**Figure 1** – Shows the diagonal corporal plication suture, which is more distal on the right corpora and more proximal on the left corpora to correct the most common direction of penile torsion. Once the suture is tied, the artificial erection will be repeated to make certain that the torsion has been entirely corrected.

## COMMENTS

With this recommended technique of degloving first and performing an artificial erection if only skin and dartos are involved with the torsion, the common over-rotation of the skin can be used to complete the penile detorsion procedure. If the erections demonstrate persistent penile torsion, this

diagonal corporal plication suture is much easier to perform than suturing the corpora to the periosteum of the pubis, which requires much more dissection, and has been very effective.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Bar-Yosef Y, Binyamini J, Matzkin H, Ben-Chaim J: Degloving and realignment--simple repair of isolated penile torsion. *Urology*. 2007; 69: 369-71.
2. Zhou L, Mei H, Hwang AH, Xie HW, Hardy BE: Penile torsion repair by suturing tunica albuginea to the pubic periosteum. *J Pediatr Surg*. 2006; 41: e7-9.
3. Fisher C, Park M: Penile torsion repair using dorsal dartos flap rotation. *J Urol*. 2004; 171: 1903-4.
4. Slawin KM, Nagler HM: Treatment of congenital penile curvature with penile torsion: a new twist. *J Urol*. 1992; 147: 152-4.
5. Hsieh JT, Wong WY, Chen J, Chang HJ, Liu SP: Congenital isolated penile torsion in adults: untwist with plication. *Urology*. 2002; 59: 438-40.

*Accepted after revision:  
October 30, 2008*

## Correspondence address:

Dr. Brent W. Snow  
Division of Urology, University of Utah  
100 N Mario Capecchi Drive, Ste. 2200  
Salt Lake City, Utah, 84113-1100, USA  
E-mail: brent.snow@hsc.utah.edu

## EDITORIAL COMMENT

Although penile torsion is not frequent in childhood, it is not so rare. Each individual urologist will face a few cases of torsion during the life of their practice. Despite the most common technique used

to repair this defect is the modified Nesbit plication. I believe in everyday practice we all perform this procedure as mentioned by the authors. On the other hand, because young men can present very strong

erections I in fact prefer to use an inverted permanent braided 2-0 suture.

It is worth remembering that a simple procedure as described in this article can really help a

number of young men who have often their quality of life severely affected by penile torsion.

**Dr. Joaquim A. Claro**

*Division of Urology*

*University of Sao Paulo, USP*

*Sao Paulo, Brazil*

*E-mail: joaquimclaro@hotmail.com*

### EDITORIAL COMMENT

This is another reliable technique for correction of penile torsion. I am concerned that the sutures are tied over the neurovascular bundle with the consequent strangulation. A procedure around this is the mobilization of the bundle at the desired site of plication and placing the suture beneath the bundle. In addition, diagonal sutures at different vertical levels across the midline may result in shortening especially in cases of severe torsion requiring multiple sutures. In this context, it is my opinion that the “diagonal corporal placation sutures” should be the last resort

if other shortening-free techniques prove short of full correction, not merely skin over-rotation (a step within the author’s procedure) but also dorsal dartos flaps.

**Dr. O. Shaer**

*Department of Andrology*

*Faculty of Medicine, Cairo University*

*Cairo, Egypt*

*E-mail: dr-osama@link.net*

### EDITORIAL COMMENT

The true incidence of penile torsion, which is not a very common deformity, is not known. Penile torsion can be encountered independently or in association with other penile and urethral malformations, such as chordee and hypospadias (1). Several relatively old techniques have been described in the literature for correcting penile torsion, including degloving the penis and reattaching the skin (2) incising the base of the penis (3) and removing angular ellipses of corporeal tissue with subsequent plication, in addition to the techniques described in the literature of the current paper. However, these procedures have not been very effective in severe penile torsion cases

or associated with significant operative morbidity. In the current report author described a novel technique to correct penile torsion that is persistent after the skin had been completely degloved and an artificial erection has demonstrated persistence of the torsion. The author has demonstrated that diagonal corporal plication suture is much easier to be performed than suturing the corpora to the periosteum of the pubis, which requires much more dissection, and has been very effective. Although the current technique is promising and has some potential, however long term data on a larger number of patients is required to popularize this technique.

**REFERENCES**

1. Redman JF, Bissada NK: One-stage correction of chordee and 180-degree penile torsion. *Urology*. 1976; 7: 632-3.
2. Azmy A, Eckstein HB: Surgical correction of torsion of the penis. *Br J Urol*. 1981; 53: 378-9.
3. Culp OS: Struggles and triumphs with hypospadias and associated anomalies: review of 400 cases. *J Urol*. 1966; 96: 339-51.

***Dr. Ahmed I. El-Sakka***  
*Andrology Clinic, Diabetic Centre*  
*Al-Noor Specialist Hospital, PO Box 6251*  
*Makkah, Saudi Arabia*  
*E-mail: aielsakka@yahoo.com*

# Clinical and Quality-of-Life Outcomes after Autologous Fascial Sling and Tension-Free Vaginal Tape: A Prospective Randomized Trial

Joao L. Amaro, Hamilto Yamamoto, Paulo R. Kawano, Guilherme Barros, Monica O. O. Gameiro, Aparecido D. Agostinho

*Department of Urology (JLA, HY, PRK, ADA), Department of Anesthesia (GB) and Section of Physiotherapy (MOOG), School of Medicine, UNESP, Botucatu, Sao Paulo, Brazil*

---

## ABSTRACT

*Purpose:* Evaluate the impact autologous fascial sling (AFS) and tension-free vaginal tape (TVT) procedures on quality-of-life in incontinent women.

*Materials and Methods:* Forty-one women were randomly distributed into two groups. Group G1 (n = 21), underwent AFS and group G2 (n = 20) TVT implant. The clinical follow up was performed at 1, 6, 12 and 36 months.

*Results:* TVT operative time was significantly shorter than AFS. Cure rates were 71% at 1 month, 57% at 6 and 12 months in G1. In G2, cure rates were 75% at 1 month, 70% at 6 months and 65% at 12 months; there was no significant difference between groups. As regards the satisfaction rate, there was no statistical difference between groups. Analysis of quality of life at 36 months revealed that there was no significant difference between groups.

*Conclusion:* Similar results between AFS and TVT, except for operative time were shorter in TVT.

*Key words:* urinary incontinence, stress; suburethral slings; tensionless vaginal tape; random allocation

*Int Braz J Urol. 2009; 35: 60-7*

---

## INTRODUCTION

Urinary incontinence (UI) can have a severe impact on quality of life (QoL). Thus, assessing the effect of interventions is of relevance. QoL is a multidimensional concept reflecting an individual's experience of physical, emotional and social well being, as well as perceptions of health status (1). In general, UI has been shown to affect the psychological occupational, domestic and sexual lives of 15% to 30% of women at all ages (2). QoL is an abstract and highly subjective concept influenced by personal and cultural values, beliefs, self concepts, goals, age and life expectancy. It is usually measured using structured

questionnaires containing a variable number of fields. There are two major types of QoL questionnaire, generic and disease specific. Unfortunately, the generic forms are often used inappropriately in incontinent women (3) and it is necessary to use a disease or condition-specific quality of life measure, e.g. the King's Health Questionnaire (KHQ) (4).

Sling procedures have been used for treatment of urinary incontinence in women since the beginning of the 20<sup>th</sup> century (5). Indications for biologic grafts include patients with a history of poor vaginal healing, pelvic bone trauma, pelvic radiation therapy, or urethral reconstruction or are based on surgeon's preference (6). Success rates of autologous graft used

for mid-urethral slings range from 70-91 % at 33-52 months (7).

Tension-free vaginal tape (TVT) has been introduced as a minimal invasive sling procedure for treatment of stress urinary incontinence (SUI) with a high success rate (8).

The aim of this study was to evaluate the impact of autologous fascial sling (AFS) and TVT procedures on QoL in incontinent women.

## MATERIALS AND METHODS

Between January 2001 and March 2002, 41 women, from the Urogynecology Outpatient Clinic of Botucatu Medical School - UNESP, with a principal complaint of stress urinary incontinence were studied in a prospective trial. These patients were randomly distributed into two groups. Group G1 (n = 21) was submitted to AFS and Group G2 (n = 20) to TVT implant. The randomization followed a blind raffle where the procedures (TVT and Sling) were written on small pieces of paper, folded and placed into a closed box. It was opened just before the surgery when the medical team found out which procedure would be performed. Mean age in G1 was 49 years (range 26-69), and in G2, 52 years (range 26-79). All surgical procedures were performed by the same surgeon. This study was approved by the Bioethics Committee of Botucatu Medical School - UNESP.

Before surgery, stress urinary incontinence was urodynamically confirmed (Dynograph R.611 recorder) in all study participants. The following parameters were investigated: free maximum urinary flow ( $Q_{max}$ ), maximum detrusor pressure ( $P_{det,max}$ ) and maximum urinary flow ( $Q_{max}$ ) during voiding. Valsalva leak-point pressure (VLPP) was obtained when the patient, in lithotomy position, reported the desire to void due to maximum bladder capacity. Detrusor overactivity was defined as the presence of spontaneous or provoked involuntary detrusor contractions during vesical filling phase, whether partially suppressed or not (9). Bladder outlet obstruction was considered when  $P_{det}/Q_{max}$  exceeded 20 cm H<sub>2</sub>O with maximum flow rate ( $Q_{max}$ ) below 12 mL per second (10). Patients with involuntary detrusor contractions or preexisting bladder outlet obstruction during urodynamic analysis were excluded.

The clinical follow-up was performed and subjective success rate was evaluated in a transversal cut off at 1, 6, and 12 months and then annually after hospital discharge. A questionnaire was used to obtain personal data, obstetric, gynecologic, family medical history, and subjective analysis of urine loss. Cure was defined as complete dryness with no usage of pads as reported by the patient.

De novo urgency was defined as the postoperative development of symptoms of urgency, which were not present before surgery and persisted for more than 1 month. These symptoms were based on clinical evaluation.

Cure rate, long-term patients' satisfaction and impact on QoL were performed at 36 months after surgery. For QoL evaluation, a validated questionnaire (11) (King's Health Questionnaire) and personal interviews were conducted. The questionnaire consists of 4 sections, the first contains 2 domains that measure female perception of general health and the impact of urinary symptoms on life. The second section contains 14 questions that allow women to rate the impact of urinary symptoms on 5 other QoL fields, namely role limitations, physical/social limitations, personal relationships, emotions and sleep and energy. The third section assesses the severity of measures associated with urinary incontinence. The fourth section consists of a separate scale for rating different urinary symptoms, including stress incontinence. Scores in each domain range between zero and 100, a higher score indicating a greater impairment of QoL (4). Follow-up ranged from 36 to 54 months (median: 44 months) as surgeries were performed at the different dates.

Body mass index (BMI) was calculated and classified according to Garrow (12).

All patients underwent physical examination including stress test. The degree of pelvic organ prolapse was assessed and graded according to Baden et al. (13).

Basal laboratory investigations (serum creatinine, complete blood count, chemical and microscopic urinalysis, urine culture) were all routinely performed. In exceptional cases (history of lithiasis, urinary infection) renal ultrasound and plain X-ray of the kidney, ureters and bladder were carried out.

In the immediate postoperative, intravenous tramadol ( $10 \text{ mg/mL}^{-1}$ ) was used in a patient-controlled analgesia (PCA) pump. After an i.v. loading dose of  $0.07 \text{ mL/Kg}^{-1}$  (administered over a period of 30 min), a continuous background i.v. infusion was set at  $1.5 \text{ mL/h}^{-1}$  and a demand bolus injection was set at  $0.2 \text{ mL}$  (lock out interval of 30 min.). Data of PCA demand, dose delivered and total analgesic consumption were retrieved from the PCA computer data bank.

### Operative Technique

Autologous fascial sling was carried-out as previously described with some modifications (14). A transverse suprapubic incision for withdrawal of the rectus fascia strip ( $10 \times 2 \text{ cm}$ ) and aponeurosis closure was done with 1-vicryl thread. The strip was prepared and both its edges were tied with 0-prolene, which was left long. A Foley catheter was used to empty the bladder. A submucosal saline injection was performed on the anterior vaginal wall and a longitudinal incision was performed 2 cm from the urethral orifice. Dissection of the vaginal mucosa was done until identification of the retropubic space. Then the strip of rectus fascia was positioned with the aid of Stamey needle around the middle urethra maintaining the strip without tension. The wires were approximated in the midline and the sling was fixed to the underlying peri-urethral fascia using 4-0 catgut sutures at the 6 and 12 o'clock positions. The vaginal mucosa and the suprapubic skin incision were then closed. Cystoscopy was performed in all patients submitted to autologous sling.

The TVT procedure was performed as described by Ulmsten et al., except that the operation was carried out under spinal anesthesia (8). Cystoscopy was performed in all patients.

Foley catheter was left indwelling for 1 day in all patients after anti-incontinence surgery. The following parameters were postoperatively evaluated: operative-room time, objective postoperative pain, complications, length of hospital stay, postoperative catheterization, and time to return to normal activities.

The analysis of clinical and urodynamic characteristics were performed using the Mann-Whitney non-parametric test for quantitative variables (15) and the Godman test as regards the categorical ones (16).

Differences were considered significant for  $p$  value  $< 0.05$ .

### RESULTS

No statistically significant difference in the demographic data and urodynamic parameters were preoperatively observed between groups (Table-1). Operative time was significantly shorter than TVT than with AFS. There was no statistical difference between groups in bladder injuries, hospitalization time, post-operative catheterization and return to normal activities (Table-2). There was neither prolonged urine retention nor other complications in both groups.

Cure rates were 71% at 1 month, 57% at 6 and 12 months, and 55% at 36 months in G1, whereas in G2 they were 75% at 1 month, 70% at 6 months, 65% at 12 months and 63% at 36 months, with no significant difference between groups.

Although 2 patients, one from each group, died from other diseases within the 36-month following period, the post-operative satisfaction rate was 80% in G1 and 58% in G2, with no statistical difference between groups (Table-3). However, in AFS group, the satisfaction rate was 62.5 to 97.5%, while in TVT group it was between 36 to 80%. A 95% confidence interval was used for satisfaction assessment.

De novo urgency symptoms were observed in 40% of the patients in G1 and in 42% of those in G2 at 36 months with no difference between groups.

Condition-specific QoL postoperatively assessed by the King's Health Questionnaire (KHQ) did not significantly differ between groups (Table-4).

The comparison between satisfaction rate and condition-specific QoL contained in the KHQ showed a significant correlation between these variables demonstrating that unsatisfied patients had higher scores in all different fields, except in perception of general health.

### COMMENTS

In our study, the initial demographic and urodynamic data demonstrated homogeneity between the groups.

**Autologous Fascial Sling and Tension-Free Vaginal Tape**

**Table 1** – Preoperative clinical and urodynamics characteristics of the patients submitted to autologous fascial sling (AFS) (n = 21) and tension-free vaginal tape (TVT) (n = 20).

Variables	Group		Statistics
	AFS	TVT	
Mean age (range)	49 (26-69)	52 (26-79)	0.38 (p > 0.05)
Mean of body mass index (k/m <sup>2</sup> )(range)	30.2 (22-34)	28.2 (24-42)	1.37 (p > 0.05)
Mean of parity (range)	4 (1-9)	4 (1-12)	0.48 (p > 0.05)
Mean vaginal deliveries (range)	4 (1-8)	4 (0-11)	0.12 (p > 0.05)
Previous incontinence surgery	4 (19%)	6 (30%)	0.82 (p > 0.05)
Hysterectomy	1 (4.7%)	4 (20%)	1.51 (p > 0.05)
Abdominal leak point pressure (cm H <sub>2</sub> O) (range)	99 (50-154)	95.5 (64-157)	0.34 (p > 0.05)
Mean free maximum urinary flow (mL/s) (range)	30 (17-57)	33 (13-65)	0.86 (p > 0.05)
Mean of maximum detrusor pressure (cm H <sub>2</sub> O) (range)	29 (14-48)	25 (13-37)	1.08 (p > 0.05)
Mean of maximum volume (mL) (range)	398 (285-700)	406 (200-678)	0.21 (p > 0.05)

In the immediate postoperative period, there were no differences between the groups, except for operating time, which was significantly shorter in

the TVT group. Similar outcomes were observed in relation to this parameter; however, no additional risk associated with this finding was observed (17).

**Table 2** – Outcome of autologous fascial sling (AFS) and tension-free vaginal tape (TVT).

Variables	Group		Statistics
	AFS	TVT	
Mean operative time (min) (range)	70 (45-105)	33 (25-70)	4.80 (p < 0.05)
Mean dosage of analgesics (mg) (range)	142 (50-473)	85 (15-269)	1.78 (p > 0.05)
Bladder injuries	1 (4.8%)	2 (10%)	0.64 (p > 0.05)
Mean of hospitalization time (h) (range)	24 (24-48)	24 (24-48)	0.63 (p > 0.05)
Mean of postoperative catheterization (h) (range)	24 (12-48)	24 (12-72)	0.16 (p > 0.05)
Mean days to return to normal activities (range)	30 (3-90)	30 (4-90)	0.16 (p > 0.05)

**Table 3** – Satisfaction rate of autologous fascial sling (AFS) and tension-free vaginal tape (TVT) at 36-month follow up.

Group	Satisfaction Rate		Statistics
	Unsatisfied (%)	Satisfied (%)	
AFS	20	80	2.24 (p > 0.05)
TVT	42	58	

Song et al. (18) observed a shorter operating time and quicker recovery in TVT group. Despite this, in the postoperative analgesia using PCA pump did not statistically differ between groups in this study, showing that there was no additional discomfort associated to the techniques used.

In general, cure rate may be based on a great variety of parameters, some of them seem to be very lenient whereas others are relatively subjective. Therefore, it may be more appropriate to report each selected variable separately in order to accurately convey true outcomes. In our series, cure rate was considered as complete dryness with no usage of pads, and similar results were observed in both groups. Applying the same cure criteria in a prospective randomized study, Wadie et al. (17) observed short-term success rates with AFS and TVT

(92%) which were higher than those encountered in this study.

Urgency incontinence is usually more bothersome for women than stress urinary incontinence. Women with de novo urgency are significantly older, have higher BMI, and higher parity than those without it (19). Damage to bladder autonomic denervation has been suggested as one of the causes of de novo urgency, which could be due to extensive bladder dissection for pubovaginal sling in contrast with TVT procedure that required little dissection (20). However, incidence of de novo urgency was similar both groups studied here. Nonetheless, given that de novo urgency is more bothersome, this fact might have similarly interfered with the quality of life of patients in both groups. Some authors observed 4% of de novo detrusor overactivity with AFS and no cases

**Table 4** – Postoperative evaluation of condition-specific quality of life King's Health Questionnaire (KHQ) of the patients submitted to autologous fascial sling (AFS) and tension-free vaginal tape (TVT) at 36-month evaluation.

Domain of KHQ	Group		Statistics
	AFS	TVT	
Median of score general health (range)	50.00 (0-100)	50.00 (0-75)	0.39 (p > 0.05)
Median of score incontinence Impact (range)	33.34 (0-100)	0.00 (0-100)	0.19 (p > 0.05)
Median of score role limitations (range)	0.00 (0-83.33)	0.00 (0-100)	0.93 (p > 0.05)
Median of score physical limitations (range)	0.00 (0-100)	0.00 (0-100)	0.96 (p > 0.05)
Median of score social limitations (range)	5.56 (0-100)	0.00 (0-66.67)	0.81 (p > 0.05)
Median of score personal relationships (range)	0.00 (0-100)	0.00 (0-100)	0.69 (p > 0.05)
Median of score emotions (range)	0.00 (0-100)	0.00 (0-100)	0.87 (p > 0.05)
Median of score sleep (range)	25.00 (0-100)	0.00 (0-100)	0.34 (p > 0.05)
Median of score severity perception of UI (range)	16.67 (0-86.67)	26.57 (0-100)	0.94 (p > 0.05)

with TVT implant (20). It is noteworthy that in this study the diagnosis of de novo urgency was based on clinical rather than urodynamic criteria, and this might explain the higher incidence observed.

Long-term satisfaction rate did not statistically differ between groups. Despite the higher satisfaction rate observed in the AFS group (80% versus 58%,  $p > 0.05$ ), even if more samples were included in this study, the results would likely show significantly higher satisfaction rate in AFS group.

In long-term evaluation of QoL no statistical difference was observed between groups. This study assessed the effect of AFS versus TVT on QoL in the surgical treatment of UI in women. The measurement of QoL is particularly important in the field of urinary incontinence, given that it is largely a symptom-defined condition. The disease-specific QoL (KHQ) a version validated in Portuguese, classified as recommended, was used (11). The present findings showed that AFS and TVT produced similar improvements in QoL at 36-month study. Morgan et al. (21), using a mailed questionnaire validated to QoL (HRQoL), also observed no significant differences in patients who had undergone AFS or TVT.

The analysis between satisfaction rate and QoL evaluation showed that unsatisfied women presented a higher score in the different fields, except in general health; this demonstrated the importance of using disease-specific QoL when evaluating outcomes in anti incontinence procedures.

## CONCLUSION

In this study, AFS and TVT yielded similar results, except for operating time which was shorter in TVT. This finding is very relevant for developing countries where synthetic slings are often costly. However, further control studies are warranted considering AFS is associated with lower cost and rate of disease transmissions, as well as no rejections when compared with synthetic techniques.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Lose G, Fantl JA, Victor A, Walter S, Wells TL, Wyman J, et al.: Outcome measures for research in adult women with symptoms of lower urinary tract dysfunction. *Neurourol Urodyn.* 1998; 17: 255-62.
2. Diokno AC, Brock BM, Brown MB, Herzog AR: Prevalence of urinary incontinence and other urological symptoms in the noninstitutionalized elderly. *J Urol.* 1986; 136: 1022-5.
3. Gill TM, Feinstein AR: A critical appraisal of the quality of quality-of-life measurements. *JAMA.* 1994; 272: 619-26.
4. Kelleher CJ, Cardozo LD, Khullar V, Salvatore S: A new questionnaire to assess the quality of life of urinary incontinent women. *Br J Obstet Gynaecol.* 1997; 104: 1374-9.
5. Bidmead J, Cardozo L: Sling techniques in the treatment of genuine stress incontinence. *BJOG* 2000; 107: 147-56.
6. Amrute KV, Badlani GH: Female incontinence: a review of biomaterials and minimally invasive techniques. *Curr Opin Urol.* 2006; 16: 54-9.
7. McBride AW, Ellerkmann RM, Bent AE, Melick CF: Comparison of long-term outcomes of autologous fascia lata slings with Suspend Tutoplast fascia lata allograft slings for stress incontinence. *Am J Obstet Gynecol.* 2005; 192: 1677-81.
8. Ulmsten U, Johnson P, Rezapour M: A three-year follow up of tension free vaginal tape for surgical treatment of female stress urinary incontinence. *Br J Obstet Gynaecol.* 1999; 106: 345-50.
9. Elbadawi A, Yalla SV, Resnick NM: Structural basis of geriatric voiding dysfunction. III. Detrusor overactivity. *J Urol.* 1993; 150: 1668-80.
10. Axelrod SL, Blaivas JG: Bladder neck obstruction in women. *J Urol.* 1987; 137: 497-9.
11. Tamanini JT, D'Ancona CA, Botega NJ, Rodrigues Netto N Jr: Validation of the Portuguese version of the King's Health Questionnaire for urinary incontinent women. *Rev Saude Publica.* 2003; 37: 203-11.
12. Garrow JS: Treatment of obesity: *Lancet.* 1992; 340: 409-13.
13. Baden WF, Walker TA, Lindsey JH: The vaginal profile. *Tex Med.* 1968; 64: 56-8.
14. Blaivas JG, Jacobs BZ: Pubovaginal fascial sling for the treatment of complicated stress urinary incontinence. *J Urol.* 1991; 145: 1214-8.
15. Zar JH: Biostatistical analysis. New Jersey, Prentice-Hall. Prentice-Hall. 1999; vol.1; p.122-60.

16. Goodman LA: Simultaneous confidence intervals for contrast among multinomial populations. *Annals of Mathematical Statistics*. 1964; 35: 716-25.
17. Wadie BS, Edwan A, Nabeeh AM: Autologous fascial sling vs polypropylene tape at short-term followup: a prospective randomized study. *J Urol*. 2005; 174: 990-3.
18. Song YF, Huang HJ, Xu B, Hao L: Comparative study of tension-free vaginal tape and fascia lata for stress urinary incontinence. *Zhonghua Fu Chan Ke Za Zhi*. 2004; 39: 658-61.
19. Holmgren C, Nilsson S, Lanner L, Hellberg D: Frequency of de novo urgency in 463 women who had undergone the tension-free vaginal tape (TVT) procedure for genuine stress urinary incontinence--a long-term follow-up. *Eur J Obstet Gynecol Reprod Biol*. 2007; 132: 121-5.
20. Kershen RT, Appell RA: De novo urge syndrome and detrusor instability after anti-incontinence surgery: current concepts, evaluation, and treatment. *Curr Urol Rep*. 2002; 3: 345-53.
21. Morgan DM, Dunn RL, Fenner DE, Faerber G, DeLancey JO, McGuire EJ, et al.: Comparative analysis of urinary incontinence severity after autologous fascia pubovaginal sling, pubovaginal sling and tension-free vaginal tape. *J Urol*. 2007; 177: 604-8; discussion 608-9.

---

*Accepted after revision:  
September 9, 2008*

---

**Correspondence address:**

Dr. João Luiz Amaro  
Departamento de Urologia  
Faculdade de Medicina de Botucatu  
Botucatu, SP, 18618-970, Brazil  
Fax: + 55 14 3811-6271  
E-mail: jamaro@fmb.unesp.br

## EDITORIAL COMMENT

The authors present a randomized study, with mid-term follow-up, comparing autologous versus synthetic retropubic sling to treat patients with urodynamic stress urinary incontinence. It is a very important study, since it compares the use of an autologous fascia, which has some morbidity related to the harvesting process, and a synthetic material, which may have the inconvenience of being a foreign body. The main questions regarding these two approaches are related to cure rate, morbidity, complications and costs. There is a lack of well-designed randomized series to clearly answer those questions. The use of synthetic material has great acceptance for the physicians, since it decreases the surgery time, avoids the harvesting process and seems to have similar cure rates as fascial slings. On the other hand, the fascial

slings have passed the test of time and may have lower cost. The procedure cost is a very important subject. In the present article, the authors have demonstrated that both procedures have similar outcome, with cure rates at 36 months of 55% on fascial sling group and 63% on TVT group. However, the surgical time was double in the sling procedure. Thus, other similar studies should be designed to compare the final cost for extra time in the operative room and the cost of using synthetic sling.

In the present study, the authors performed a good quality randomization that is illustrated by the similarity on demographics. However, the urinary incontinence impact on quality of life (QoL) was not evaluated pre-operatively. Since we do not have this information, it creates a bias in the results. Thus, we

do not know if patients had similar scores at baseline and we do not know how much they improve after surgery regarding their QoL.

The authors determined that pain was similar in both groups. Usually, patients who undergo fascia harvesting have significant pain in the surgical site. The authors evaluate the postoperative pain by the dosage of analgesics delivered, which was almost double in the fascial sling group. The sample size may be a reason why the authors did not find any statistical difference in the analgesic use. Furthermore, the fact that patient did not ask for medication did not exclude the fact that they were experiencing pain. Thus, to draw any conclusion regard pain, it would be necessary to additionally apply a pain visual analogical scale and include more patients in the analysis.

It is interesting to note that 40% of patients who underwent TVT procedure were unsatisfied, while on the fascial sling group only 20% were unsatisfied.

This is very concerning. The authors more likely did not find a significant statistical difference between groups because of the small sample size ( $n = 20$ ). The difference may be associated with those patients that were not “dry” but had significant improvement ( $> 50\%$ ) on the symptoms, since most of those patients with significant improvement did not need or want alternative treatment and, usually, had an improvement in QOL. Unfortunately, it this not described in the article. Interestingly, when we examine the King’s Health Questionnaire to evaluate the quality of life at 36 months post operatively, the median is zero in the majority of fields, which suggests that the majority of the patients are completely satisfied.

There are several questions to be addressed regarding surgical stress urinary incontinence treatment. Similar randomized studies should be done to clearly determine which procedure has the best cost-efficiency with greater safety and lower morbidity.

***Dr. Fernando G. Almeida***

*Section of Urology*

*Federal University of Sao Paulo*

*Sao Paulo, SP, Brazil*

*E-mail: fernandourologia@hotmail.com*

# Outcomes Following Mid-Urethral Sling Placement in Patients with Intrinsic Sphincteric Deficiency: Comparison of Sparc and Monarc Slings

David E. Rapp, Fred E. Govier, Kathleen C. Kobashi

*The Continence Center at Virginia Mason Medical Center, Seattle, Washington, USA*

---

## ABSTRACT

*Purpose:* The treatment of patients with intrinsic sphincteric deficiency (ISD) remains difficult. It is theorized that differing vectors of support provided by retropubic versus transobturator mid-urethral sling routes may affect outcomes. We sought to compare outcomes of patients undergoing SPARC versus MONARC sling types in patients with Valsalva leak point pressures (VLPPs) below 60 cm H<sub>2</sub>O.

*Materials and Methods:* A retrospective review of female patients with stress urinary incontinence undergoing SPARC™ (n = 97) or MONARC™ (n = 39) placement following urodynamic diagnosis of ISD was performed, with minimum 12-month follow-up required. Outcomes were assessed using a questionnaire comprising validated incontinence questionnaires (UDI-6, IIQ-7) and additional items addressing satisfaction.

*Results:* Success rates of 76% and 77% were observed in the SPARC (mean follow-up 36 months) and MONARC (mean follow-up 32 months) cohorts, respectively ( $p > 0.05$ ). Superior UDI scores were demonstrated in the MONARC cohort (3.8 vs. 5.3,  $p = 0.04$ ), in contrast to similar IIQ scores across both groups (3.7 vs. 3.1,  $p > 0.05$ ). A deterioration in success rates was seen in both cohorts with more extended follow-up and with lower VLPPs. However, this finding was limited by low patient numbers in these cohorts. A complication rate of 7% and 3% was noted in SPARC and MONARC cohorts ( $p > 0.05$ ).

*Conclusions:* We observed no significant differences in subjective outcomes when comparing patients undergoing SPARC versus MONARC sling placement in the treatment of SUI with VLPP < 60 cm H<sub>2</sub>O. A deterioration in continence rates was seen with extended follow-up. These data may be affected by low patient numbers and related study power, in particular with more extended follow-up.

**Key words:** urinary incontinence; suburethral sling; treatment outcome; sphincteric deficiency

*Int Braz J Urol. 2009; 35: 68-75*

---

## INTRODUCTION

The emergence of the integral theory and the mid-urethral sling (MUS) has resulted in an evolution of the understanding and treatment of stress urinary incontinence (SUI) (1). Multiple MUS types exist, with long-term outcomes supporting their use as a safe

and efficacious treatment for SUI. Despite this success, a paucity of data exists to define the efficacy of these sling types in the specific treatment of intrinsic sphincteric deficiency (ISD).

As initially described, the MUS served to recreate a physiologic backboard beneath the urethra to prevent hypermobility and SUI. However, the non-

obstructing support specific to MUS may not be ideal in patients with a fixed urethra and/or intrinsic sphincteric deficiency. In these cases, alternative sling types may be preferable. Indeed, it can be argued that the pubovaginal sling (PVS) is the gold standard in such cases, exhibiting important differences from MUS, such as immediate and secure sling fixation, a greater mesh width, and a bladder neck position. Supporting evidence has been reported in meta-analysis by Muller et al., demonstrating that in patients undergoing a TVT sling (Ethicon, Somerville, NJ), urethral hypermobility is associated with increased efficacy in contrast to women with a fixed urethra who are at significant risk for procedure failure (2).

Despite such findings, a widespread acceptance of the MUS has been seen and such slings are commonly used in patients with not only type I SUI, but types II and III as well. With this in mind, research focusing on MUS outcomes in patients with ISD becomes increasingly important. Whereas some investigation has identified inferior cure rates following MUS in patients with Valsalva leak point pressures (VLPP) < 60 cm H<sub>2</sub>O, other investigators have found that pre-operative VLPP may not be predictive of outcome (3,4).

Central to the issue of MUS outcomes in the treatment of ISD is the theoretical effect that sling vector may have on efficacy. Accordingly, it may be postulated that the more horizontal sling vector of the transobturator (TOT) sling approach may not provide equivalent obstruction and/or support when compared to retropubic (RP) sling types. Despite evidence suggesting that transobturator and retropubic MUS are associated with similar outcomes in a general population (5), it is unknown whether the differences in support vectors will be clinically significant in a focused population of patients with ISD. The purpose of this investigation was to assess for differences in patient-reported outcomes (PRO) following SPARC versus MONARC placement in a focused population of patients with VLPP < 60 cm H<sub>2</sub>O.

## MATERIALS AND METHODS

A retrospective review of patients undergoing SPARC™ (American Medical Systems, Minnetonka,

MN) or MONARC™ (American Medical Systems, Minnetonka, MN) mid-urethral sling placement following urodynamic diagnosis of ISD was performed. Review was performed using the prospectively collected Continence Center database at Virginia Mason Medical Center. All patients undergoing SPARC/MONARC placement with a minimum follow-up of 12 months were included for data analysis; no other specific inclusion or exclusion criteria were used for patient identification.

As part of patient work-up for incontinence and database inclusion, all patients undergo standard history, general and focused urogynecologic physical examination, and videourodynamic (URD) evaluation. URD procedure and related terminology is performed in accordance with International Continence Society guidelines (6). VLPP measurement is performed in the standing position at cystometric bladder capacity. Gradual increases in abdominal straining are performed by patients with concurrent monitoring for urinary leakage via fluoroscopic visualization. VLPP is identified as the lowest intravesical pressure at the time of urinary leakage and is calculated as a differential value from baseline intravesical pressure.

Subjective satisfaction was assessed using a mailed questionnaire comprising separate validated incontinence and quality of life questionnaires (UDI-6, IIQ-7), as well as additional items addressing global satisfaction and patient-perceived improvement. Outcome measures used for data analysis are detailed in Appendix-1. The primary study outcome assessed was dry rate by questionnaire response (Appendix-1, Question-1). Given the documented and significant effect that choice of outcome measure has on “success” rate, we also assessed a variety of related PRO. Accordingly, additional outcomes assessed included patients achieving < 1 incontinence episode weekly, validated symptom score levels, overall patient satisfaction, and subjective percent improvement. Patient satisfaction and percent improvement are questionnaire items measured on a Likert scale. Overall outcomes were also presented using our previously described definition of success, which attempts to account for such known discrepancies in outcomes when measuring semi-objective variables such as incontinence episodes as compared to degrees of subjective patient-reported improvement. Therefore,

we define success as < 1 SUI episode per week or > 70% subjective improvement in those patients with > 1 SUI episode per week. Additional focus was placed on assessing for differences in the rate and type of surgical complications.

Our technique for SPARC placement is previously described (7). MONARC sling placement is performed using standard technique, as originally described by Delorme (8). Surgical procedures were performed by one of two surgeons (FG, KK). Procedures were performed under general or spinal anesthesia per patient preference. Given the referral pattern characteristic of our institution, patients are admitted overnight to allow for observation and avoid lengthy travel in the immediate post-operative hours. As part of this protocol, both patients undergoing sling with and without concurrent pelvic organ prolapse (POP) repair receive IV antibiotics and vaginal packing. The Foley catheter and vaginal packing are removed on the following morning prior to discharge. The study was approved by the Virginia Mason Medical Center Institutional Review Board. Z-test for proportions was used to compare outcome rates. Student’s “t” test was used for comparative data. Each analysis was structured as a two-tailed test at the  $\alpha = 0.05$  level.

**RESULTS**

Retrospective review identified 107 (SPARC) and 43 (MONARC) patients achieving 12-month minimum follow-up. Of this population, 97 (91%) and 39 (91%) of patients completed follow-up questionnaires and were included for per-protocol data analysis.

A complete list of patient demographics and characteristics is provided in Table-1. Mean follow-up was significantly longer in the SPARC cohort (36 versus 32 months) ( $p = 0.03$ ). In addition, mean VLPP was lower in the SPARC cohort (43 versus 49 cm H<sub>2</sub>O) ( $p < 0.01$ ). No other significant differences were identified in comparison of baseline cohort characteristics.

Subjective outcomes following MUS placement are detailed in Tables 2-3. Dry rates of 29% and 41% were observed in the SPARC and MONARC cohorts, respectively. An additional 39% and 28% of patients reported incontinence episodes < 1/weekly, respectively. Based on the previously described definition of success, 76% and 77% of procedures were considered successful in these cohorts, respectively. Comparison of each of these outcomes revealed no

**Table 1 – Patient demographics and characteristics.**

	Sparc (N = 97)	Monarc (N = 39)	p Value
Age (y ± SD)	64 ± 11	61 ± 12	NS
Follow-up (y ± SD)	2.9 ± 0.9	1.8 ± 0.8	0.03
VLPP (cm H <sub>2</sub> O ± SD)	43 ± 11	49 ± 14	< 0.01
Parity (n ± SD)	2.5 ± 1.4	2.5 ± 1.2	NS
Previous surgeries (N)			
Hysterectomy	42 (43%)	15 (38%)	NS
Anti-incontinence	17 (18%)	6 (15%)	NS
Prolapse repair	7 (7%)	5 (13%)	NS
Concurrent surgeries (N)			
Anterior colporrhaphy	26 (27%)	14 (36%)	NS
Posterior colporrhaphy	21 (22%)	6 (15%)	NS
Vault suspension	2 (2%)	2 (5%)	NS
Complications (N)	5 (7%)	1 (3%)	NS

NS = not significant ( $p > 0.05$ ). VLPP = Valsalva leak point pressure, Student’s “t” test was used for analysis of comparative data (age, follow-up, VLPP, parity); Z-test for proportions was used for remaining comparisons (surgeries, complications).

Comparison of Sparc and Monarc Slings for ISD

**Table 2 – Outcomes following mid-urethral sling placement.**

Outcome	Sparc (n = 97)	Monarc (n = 39)	p Value
Incontinence frequency			
Dry (no leakage)	28 (29%)	16 (41%)	NS
< 1 episode/week	38 (39%)	11 (28%)	NS
% Improvement (≥ 70%)	66 (68%)	26 (67%)	NS
Success	74 (76%)	30 (77%)	NS
Satisfaction (≥ 7)	63 (65%)	26 (67%)	NS
Recommend (Yes)	65 (67%)	28 (72%)	NS
Repeat (Yes)	69 (71%)	30 (77%)	NS
UDI-6*	5.3 (3.9)	3.8 (3.5)	0.04
IIQ-7*	3.7 (3.6)	3.1 (4.6)	NS

\* Figures are listed as mean score (standard deviation). NS = not significant ( $p > 0.05$ ). Student's *t* test was used for analysis of comparative data (UDI/IIQ); Z-test for proportions used for remaining comparisons. UDI-6 = validated incontinence questionnaire; IIQ-7 = quality of life questionnaire.

statistically significant differences. Intention to treat analysis of continence and success rates was carried out assuming all questionnaire non-responders to be failures. In this analysis, dry rates of 26% versus 37% and success rates of 69% versus 70% were seen in the SPARC and MONARC cohorts, respectively. Again, these comparisons revealed no statistically significant differences.

As described, significant differences in mean VLPP and mean follow-up were identified in the

comparison of SPARC and MONARC cohorts. Accordingly, cohorts were further stratified by VLPP and follow-up length in an attempt to assess for outcome differences influenced by these baseline differences (Table-3). No significant differences in continence rates were identified in comparing MUS types across these stratification points. However, a deterioration in success rates was observed in both cohorts with more extended follow-up and with lower VLPPs. This finding was limited by low patient numbers in these cohorts.

**Table 3 – Incontinence rates following mid-urethral sling placement.**

VLPP (cm H <sub>2</sub> O)	Sparc (N = 97)				Monarc (N = 39)				p Value
	N of Pts	Never	< 1/week	Success	N of Pts	Never	< 1/week	Success	
50-59	36	12	14	31 (86)	26	14	7	22 (85)	NS
40-49	29	10	11	21 (72)	6	2	1	4 (66)	NS
30-39	19	4	7	12 (63)	5	0	2	3 (60)	NS
< 30	13	2	6	12 (50)	2	0	1	1 (50)	NS
Follow-up (years)									
1-2	17	3	9	13 (76)	25	13	5	20 (80)	NS
2-3	34	10	14	25 (74)	10	2	5	8 (80)	NS
3-4	38	13	14	33 (87)	3	1	1	2 (67)	NS
4+	8	2	1	3 (40)	1	0	0	0 (40)	NS

Data represents number of patients (percentage of total). NS = non-significant ( $p > 0.05$ ); Pts = patients; Z-test for proportions used for comparisons. VLPP = Valsalva leak point pressure.

Comparison of UDI-6 and IIQ-7 questionnaire scores was also performed. UDI scores were superior in the MONARC cohort ( $p = 0.04$ ), whereas IIQ scores did not demonstrate significant differences when comparing MUS types. Finally, an overall complication rate of 7% (7/97) and 3% (1/39) was observed in the SPARC and MONARC cohorts, respectively. Vaginal mesh extrusion ( $n = 2$ , SPARC;  $n = 0$  MONARC) and blood loss requiring transfusion ( $n = 2$ , SPARC;  $n = 1$  MONARC) were the most common complications. Vaginal extrusions were each treated with operative reclosure under sedation. Additional complications in the SPARC cohort included persistent granulation tissue/suture granuloma requiring local excision. This complication was considered to be associated with concomitant POP repair, although it is reported to completely present our data. No trends in complication incidence were noted in this comparison.

## COMMENTS

The primary finding of this study is the demonstration of similar subjective outcomes in SPARC and MONARC cohorts with baseline VLPP  $< 60$  cm H<sub>2</sub>O. In the comparison of multiple PRO measures, findings were similar between the two cohorts. Interestingly, a superior patient-reported dry rate was associated with MONARC placement, although this finding failed to achieve statistical significance. Given the limited study population, we cannot associate any clinical difference with this finding. In addition, superiority of UDI scores was seen in the MONARC cohort, although this finding was not reproduced in comparison of IIQ scores.

Given the variety of MUS types currently in use, more recent research focus has been placed on assessing for potential clinical differences in comparative outcomes. In comparison of RP and TOT sling types in a generalized SUI population, significant randomized investigation would suggest comparable subjective and objective outcomes with short-term follow-up (5,9,10). Despite these findings, the treatment of ISD may represent a more complex undertaking. Indeed, non-comparative investigation has demonstrated that patients with

maximum urethral closing pressure (MUCP) less than 40 cm H<sub>2</sub>O are associated with a higher failure rate following TOT as compared to that found with higher closing pressures (11). In a similar fashion, lower VLPPs are associated with inferior outcomes following TOT (3). However, other investigation focusing only on RP sling types suggests that VLPP may not predict for outcome following MUS surgery (4,12,13). Therefore, it becomes crucial that the urologic community assess whether differing sling approaches (e.g. TOT versus RP) are equally efficacious in ISD cohorts.

Theoretically, it is possible that the differing sling vectors of RP and TOT types will be associated with clinical differences that are only evident in patients with more severe incontinence as characteristic of ISD. Anatomic study supports the concept of differing vectors, with a more vertical, U-shaped vector characteristic of the RP slings, in contrast to the more horizontal, hammock-shaped vector of the TOT types (14). Additional anatomical differences are suggested by sonographic study demonstrating a more proximal position of the TOT slings at both rest and Valsalva, in comparison to RP types (15). Accordingly, a more circumferential compression of the urethra may be afforded through RP slings. In contrast, the lateral vector of TOT slings may not allow for equivalent suburethral tensioning (16). Clinical evidence supports this theory, in which progressive intra-operative tensioning of TOT slings was unable to stop cough test induced urinary leakage (17). In contrast, a negative cough test was achieved following immediate removal of the TOT slings and subsequent replacement by a RP sling in a “tensionless” fashion.

Limited clinical investigation has specifically focused on comparison of success rates in RP versus TOT cohorts with documented ISD. Miller et al. demonstrated that patients with a MUCP  $\leq 42$  cm H<sub>2</sub>O had a relative risk for procedure failure of 5.89 following MONARC, as compared to a similar cohort of patients undergoing TVT (18).

A paucity of additional directed investigation exists. However, further indirect evidence supporting the clinical importance of vector differences between RP and TOT slings is gleaned through analysis of persistent and de novo urge urinary incontinence (UII)

and voiding dysfunction following MUS placement. Accordingly, Botros et al. demonstrated a reduced rate of de novo UUI, as well as an increased chance of resolution of pre-operative UUI with TOT versus RP sling types (16). Concurrently, Dietz and colleagues identified a lower incidence of voiding dysfunction symptomatology with MONARC (versus TVT), concluding that the MONARC sling may be less obstructive when compared to RP types (15). Although such data cannot be extrapolated to continence outcomes, they serve to further suggest that vector (and associated tensioning or positional) differences may exist between RP and TOT slings and that these differences may have clinical implications.

The authors acknowledge certain weaknesses in our study. First, the retrospective nature is a limitation to our study design. Second, the difference in observed follow-up length may bias outcomes, as MONARC patients may be associated with an increased failure rate given longer follow-up. It should be emphasized, however, that the previously described deterioration in outcomes following transobturator sling reported by other groups occurred with far shorter follow-up than that presented in our investigation (18,19). Further, several PRO measures reported are not empirically validated. Nonetheless, our data are strengthened by the use of a comprehensive collection of PRO measures commonly used in incontinence research.

Notably, the higher baseline VLPP observed in the MONARC cohort may bias results in favor of these patients. While such differences may be within error characteristic of UDY VLPP measurement and may not be clinically meaningful, we believe this difference is important to detail. Certainly, this difference reflects a selection bias, as surgeons were not blinded to pre-operative VLPP and favored a retropubic approach in patients with more severe ISD. Subset analysis attempting to control for VLPP and follow-up differences found no differences. Most importantly, however, these and other conclusions are limited by a small study population that is particularly notable with extended follow-up. Despite these limitations, we believe that our data most importantly serve to suggest that prospective randomized study is needed, given the limited and conflicting data that exists, and the significant popularity of the MUS in the current treatment algorithm for SUI.

A secondary finding to our study is a deterioration in continence rates observed irrespective of sling type in ISD cohorts with extended follow-up. Certainly, the widespread use of MUS is accompanied by mid- and long-term data suggesting good continence outcomes. In such reports, cure rates range from 80%-95% across all MUS types and include follow-up extending to 83 months (20). We have previously suggested that strict long-term continence rates may not consistently approach these rates, with a strict dry rate of 34% being identified in our experience following SPARC with long-term follow-up (minimum 24 months, mean 36 months) (7). Both the present data and additional series would again suggest that dry and success rates may experience significant deterioration with long-term follow-up and may be particularly problematic in patients with ISD (19). Foremost, this finding would underscore the need to critically assess long-term dry rates in patients following MUS placement and to further focus such investigation on outcomes in a defined population with ISD. Indeed, it may be possible that both RP and TOT sling types are not optimal for patients with low VLPP and that consideration of other sling types (e.g. PVS) in this complex cohort should be revisited.

## CONCLUSION

We identified no significant differences in subjective outcomes when comparing patients undergoing SPARC versus MONARC sling placement in the treatment of SUI with VLPP < 60 cm H<sub>2</sub>O. A deterioration in continence rates was seen with extended follow-up. These data may be affected by low patient numbers and related study power, in particular with more extended follow-up. Foremost, this investigation would highlight the importance for future prospective and randomized study assessing retropubic and transobturator MUS outcomes in patients with ISD is important.

## CONFLICT OF INTEREST

None declared.

*Appendix - Selected outcomes measures from incontinence questionnaire.*

**1. Do you leak when you cough, sneeze, or perform physical activities? [Incontinence Frequency]**

*A) never B) < 1/week C) once/day D) always E) not sure*

**2. How much improved is your urinary leakage now compared to before the surgery? [% Improvement]**

*100% better, 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10% better, the same, worse*

**3. Overall, how satisfied are you with the results of your sling surgery? [Satisfaction]**

*0 (not satisfied), 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 (very satisfied)*

**4. Knowing what you know now, would you have the sling surgery again? [Repeat]**

*A) yes B) no C) not sure*

**5. Would you recommend the sling surgery to a friend? [Recommend]**

*A) yes B) no, C) not sure*

[ ] Indicate outcome measure assessed by question

**REFERENCES**

1. Petros PE, Ulmsten UI: An integral theory and its method for the diagnosis and management of female urinary incontinence. *Scand J Urol Nephrol Suppl.* 1993; 153: 1-93.
2. Muller M, Koebele A, Deval B: Determinants of success and recurrence after suburethral free tape procedure for female urinary incontinence. *J Gynecol Obstet Biol Reprod (Paris).* 2007; 36: 19-29.
3. O'Connor RC, Nanigian DK, Lyon MB, Ellison LM, Bales GT, Stone AR: Early outcomes of mid-urethral slings for female stress urinary incontinence stratified by valsalva leak point pressure. *Neurourol Urodyn.* 2006; 25: 685-8.
4. Cetinel B, Demirkesen O, Onal B, Akkus E, Alan C, Can G: Are there any factors predicting the cure and complication rates of tension-free vaginal tape? *Int Urogynecol J Pelvic Floor Dysfunct.* 2004; 15: 188-93.
5. Tseng LH, Wang AC, Lin YH, Li SJ, Ko YJ: Randomized comparison of the suprapubic arc sling procedure vs tension-free vaginal taping for stress incontinent women. *Int Urogynecol J Pelvic Floor Dysfunct.* 2005; 16: 230-5.
6. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al.: The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn.* 2002; 21: 167-78.
7. Nazemi TM, Yamada B, Govier FE, Kuznetsov DD, Kodama K, Kobashi KC: Minimum 24-month followup of the sling for the treatment of stress urinary incontinence. *J Urol.* 2008; 179: 596-9.
8. Delorme E, Droupy S, de Tayrac R, Delmas V: Transobturator tape (Uratape): a new minimally-invasive procedure to treat female urinary incontinence. *Eur Urol.* 2004; 45: 203-7.
9. Liapis A, Bakas P, Creatsas G: Monarc vs TVT-O for the treatment of primary stress incontinence: a randomized study. *Int Urogynecol J Pelvic Floor Dysfunct.* 2008; 19: 185-90.
10. Barry C, Lim YN, Muller R, Hitchins S, Corstiaans A, Foote A, et al.: A multi-centre, randomised clinical control trial comparing the retropubic (RP) approach versus the transobturator approach (TO) for tension-free, suburethral sling treatment of urodynamic stress incontinence: the TORP study. *Int Urogynecol J Pelvic Floor Dysfunct.* 2008; 19: 171-8.
11. Guerette NL, Bena JF, Davila G: Transobturator slings for stress incontinence: using urodynamic parameters to predict outcomes. *Int Urogynecol J Pelvic Floor Dysfunct.* 2008; 19: 97-102.
12. Rodríguez LV, de Almeida F, Dorey F, Raz S: Does Valsalva leak point pressure predict outcome after the distal urethral polypropylene sling? Role of urodynamics in the sling era. *J Urol.* 2004; 172: 210-4.

13. Abdel-Hady el-S, Constantine G: Outcome of the use of tension-free vaginal tape in women with mixed urinary incontinence, previous failed surgery, or low valsalva pressure. *J Obstet Gynaecol Res.* 2005; 31: 38-42.
14. Whiteside JL, Walters MD: Anatomy of the obturator region: relations to a trans-obturator sling. *Int Urogynecol J Pelvic Floor Dysfunct.* 2004; 15: 223-6.
15. Dietz HP, Barry C, Lim Y, Rane A: TVT vs Monarc: a comparative study. *Int Urogynecol J Pelvic Floor Dysfunct.* 2006; 17: 566-9.
16. Botros SM, Miller JJ, Goldberg RP, Gandhi S, Akl M, Beaumont JL, et al.: Detrusor overactivity and urge urinary incontinence following trans obturator versus midurethral slings. *Neurourol Urodyn.* 2007; 26: 42-5.
17. Mukai M, Aboujaoude R, Culligan PJ: Two cases illustrating a potential difference between transobturator and retropubic slings. *Int Urogynecol J Pelvic Floor Dysfunct.* 2007; 18: 967-9.
18. Miller JJ, Botros SM, Akl MN, Aschkenazi SO, Beaumont JL, Goldberg RP, et al.: Is transobturator tape as effective as tension-free vaginal tape in patients with borderline maximum urethral closure pressure? *Am J Obstet Gynecol.* 2006; 195: 1799-804.
19. Jeon MJ, Jung HJ, Chung SM, Kim SK, Bai SW: Comparison of the treatment outcome of pubovaginal sling, tension-free vaginal tape, and transobturator tape for stress urinary incontinence with intrinsic sphincter deficiency. *Am J Obstet Gynecol.* 2008; 199: 76-7.
20. Rapp DE, Kobashi KC: The evolution of midurethral slings. *Nat Clin Pract Urol.* 2008; 5: 194-201.

---

*Accepted after revision:  
October 2, 2008*

---

**Correspondence address:**

Dr. David E. Rapp  
Virginia Mason Medical Center  
1100 9th AVE C-7 URO  
Seattle, WA, 98111, USA  
Fax: + 1 206 223-7650  
E-mail: derapp@yahoo.com

## EDITORIAL COMMENT

This is an interesting paper comparing suprapubic versus transobturator slings for the treatment of females with stress urinary incontinence (SUI) due to intrinsic sphincter deficiency (ISD). Even though this is a retrospective study it allows some interesting conclusions. Few studies in the literature compared the Monarc and Sparc slings for the treatment of females with SUI due to ISD. In particular, few studies compared the present type of material. The majority compares TVT and TVTO. Therefore, this study is important because shows that the transobturator approach has the same efficacy of the suprapubic approach even in women with ISD. This also has been

demonstrated with the TVTO. On the other hand, the complication rates are also very similar showing the two approaches seems to be equivalent.

It would be very useful to have a randomized controlled trial comparing these two approaches to treat female SUI.

**Dr. Flavio Trigo Rocha**  
Division of Urology  
University of Sao Paulo, USP  
Sao Paulo, SP, Brazil  
E-mail: flaviotrigo@uol.com.br

# Investigations into the Presence of Functional $\beta_1$ , $\beta_2$ and $\beta_3$ -Adrenoceptors in Urothelium and Detrusor of Human Bladder

Pradeep Tyagi, Catherine A. Thomas, Naoki Yoshimura, Michael B. Chancellor

Department of Urology (CAT, NY, PT), University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA, and Department of Urology (MBC), William Beaumont Hospital, Royal Oak, Michigan, USA

---

## ABSTRACT

*Purpose:* We investigated the presence of functional  $\beta_1$ ,  $\beta_2$  and  $\beta_3$ -adrenoceptor in urothelium and detrusor muscle of human bladder through in vitro pharmacology of selective  $\beta_3$  adrenoceptor agonist solabegron.

*Materials and Methods:* Expression of these adrenoceptors in surgically separated human urothelium and detrusor muscle were investigated using RT-PCR. The effects of activating these receptors were studied by determining the relaxation produced by  $\beta$ -adrenoceptors agonist in pre-contracted human detrusor strips.

*Results:* The results confirmed the presence of mRNA for  $\beta_1$ ,  $\beta_2$  and  $\beta_3$ -adrenoceptor in both human urothelium and detrusor. In an in vitro functional bladder assay, Solabegron and other agonists for  $\beta$ -adrenoceptors such as procaterol and isoproterenol evoked potent concentration-dependent relaxation of isolated human bladder strips with  $pD_2$  values of  $8.73 \pm 0.19$ ,  $5.08 \pm 0.48$  and  $6.28 \pm 0.54$ , respectively.

*Conclusions:* Selective  $\beta_3$ -adrenoceptor agonist may be a potential new treatment for the overactive bladder OAB syndrome. Existence of  $\beta_3$ -adrenoceptor mRNA exists in the urothelium in addition to the detrusor muscle suggest multiple site of actions for the  $\beta_3$ -adrenoceptor in the lower urinary tract.

*Key words:* bladder; urothelium; detrusor; adrenoceptors

*Int Braz J Urol. 2009; 35: 76-83*

---

## INTRODUCTION

The overactive bladder (OAB) syndrome affects more than 17 million people in the United States. Muscarinic receptor antagonists are the most common form of pharmacologic treatment therapy prescribed for treating OAB, but are associated with mechanistic side effects related to effect of these agents on muscarinic receptors at other sites (1). Muscarinic receptor antagonists act to block nerve evoked bladder contraction and alternative approach may be to develop drugs acting on the storage phase of micturition (2). It is also commonly accepted that the muscarinic receptor antagonists act during the

storage phase (3). Towards that goal, it seems logical that bladder relaxation mediated by  $\beta$ -adrenoceptors will be a viable target, because increased relaxation of the detrusor smooth muscle will lengthen the duration of storage phase in micturition cycle and thereby alleviate the symptoms of OAB (4).

Studies have shown that bladder relaxation evoked by  $\beta$ -adrenoceptor agonists is mainly mediated by  $\beta_3$ -adrenoceptor in most species (5).  $\beta_3$ -adrenoceptor agonist are said to stimulate the G protein (Gs) and activate adenyle cyclase (AC) to increase the intracellular level of adenosine 3',5'-cyclic mo-

nophosphate and causes relaxation of smooth muscle in the bladder (5). Other mechanisms involved in  $\beta$ -adrenoceptor induced relaxation of bladder are also not ruled out (5). Studies have shown that at least 95% of the adrenoceptor transcripts in human bladder are represented by  $\beta$ 3-adrenoceptor subtype (6). Selective  $\beta$ 3-adrenoceptor agonists have been shown to cause significant relaxation of human bladder strips as compared with  $\beta$ 1 and  $\beta$ 2-adrenoceptor agonists, and this was observed in normal and neurogenic bladders (7).  $\beta$ 3-adrenoceptor agonists are expected to be clinically useful agents in the treatment of the OAB syndrome.

Although expression of  $\beta$ -adrenoceptors in human bladder has been previously reported using receptor-binding studies, but the anatomical distribution of the expression and which subtype(s) of  $\beta$ -adrenoceptor are expressed in the urothelium has only recently been indicated (8). Expression of  $\beta$ -adrenoceptors in urothelium is favored by the mounting evidence in support of a important role played by bladder epithelial cells in modulating bladder activity in response to local chemical and mechanical stimuli (9). Thus, in this study, we aimed to investigate the presence of  $\beta$ 1-,  $\beta$ 2- and  $\beta$ 3-adrenoceptor in separate tissue of urothelium and detrusor muscle from human bladder. Functional significance of  $\beta$ 3-adrenoceptors was investigated by studying the effects of GW427353 or Solabegron®, a selective  $\beta$ 3-adrenoceptor agonist in human detrusor muscle.

## MATERIALS AND METHODS

**Human bladders** - The human bladders were obtained via Institutional Review Board approved informed consent from the next of kin of the six organ donors using an honest broker system from the Health Sciences Tissue Bank at University of Pittsburgh Medical Center. The organ donors were 4 males and 2 females aged between 18-69 years. The health and disease status of organ donors was not available to the study investigators.

**Isolated bladder strips** - The mucosa and adventitia was removed and longitudinal detrusor strips of approximately 10x5x3 mm were obtained. Fine silk sutures were tied to each end of the strips, and tissues

were lowered into the myobath multi-channel tissue bath system (World Precision Instruments, Sarasota, Florida, USA). The changes in muscle tension were digitally recorded by PowerLab Software (Charts 5, ADInstruments, Colorado Springs, CO, USA). Each tissue sample was suspended in a 7 mL organ bath containing oxygenated Krebs solution (NaCl, 118 mmol/l; KCl, 5.6 mmol/l; NaHCO<sub>3</sub>, 25 mmol/l; KH<sub>2</sub>PO<sub>4</sub>, 1.2 mmol/l; CaCl<sub>2</sub>, 2.5 mmol/l; MgSO<sub>4</sub>, 1.2 mmol/l; glucose 6.1 mmol/l; pH 7.4; aerated with 95% O<sub>2</sub> / 5% CO<sub>2</sub>) and maintained at 37°C and constantly aerated with 95% oxygen and 5% carbon dioxide. The tissues were subjected to a resting tension of 1-2 grams and allowed to equilibrate for 60 min, during this time the tissue was washed every 15 min and resting tension was adjusted. After obtaining basal tension of 1-2 grams, muscle contractions were induced using 30 mM KCl bath application. For electrical field stimulation (EFS) studies, the equilibrated strips were given EFS using following parameters (5-40 Hz, 0.1 ms pulses, 1s train duration, 80V SIU). Bladder strips were incubated for 15 min with  $\beta$ 3-adrenoceptor agonist prior to testing EFS responses and with a 10 min wash after each stimulus.

**Chemicals** - KCl, procaterol, isoproterenol and papaverine were obtained from Tocris bioscience Catalog (Ellisville, Missouri, USA). GW427353 or solabegron (a selective  $\beta$ 3-adrenoceptor agonist) was provided by GlaxoSmithKline Pharmaceutical Company (King of Prussia, PA, USA). All solutions were freshly prepared daily. Drugs were dissolved in deionized distilled water. Further dilutions were carried out in Krebs solution. The concentrations are expressed as the final molar concentration in the tissue chamber.

**RT-PCR studies** - Total RNA extraction was performed with TRIzol® reagent using manufacturer instructions (Invitrogen™) from surgically separated urothelium and detrusor tissues. Reverse transcription with 3  $\mu$ g of RNA was followed by PCR with primers specific for the cDNA coding for human  $\beta$ 1,  $\beta$ 2, and  $\beta$ 3 receptor subtypes (Table-1). Reactions were performed under certain conditions, including 95°C for 10 minutes, 40 cycles at 95°C for 30 seconds, 55°C for 1 minute and 72°C for 1 minute. Good separation of the bladder layers was evaluated by H&E staining.

**Table 1** – Primer sequences.

Primer	Sequence	PCR Product
β1	Forward: TCGTGTGCACCGTGTGGGCC Reverse: AGGAAACGGCGCTCGCAGCTGTCC	265bp
β2	Forward: GCCTGCTGACCAAGAATAAGGCC Reverse: CCCATCCTGCTCCACCTTGG	329bp
β3	Forward: GCTCCGTGGGCCTCACGAGAACAGC Reverse: CCCAACGGCCAGTGGCCAGTCAGC	314bp

Immunostaining - Separated tissues of urothelium and detrusor were snap frozen in liquid nitrogen immediately after dissection and embedded in OCT freezing medium. Cryosections 10 μM thick were used for Hematoxylin & Eosin staining.

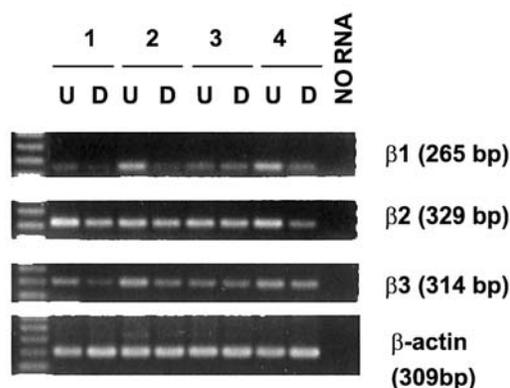
Statistical evaluation - Results are expressed as means ± SEM of measurements in strips obtained from at least 6 different human bladders, and a maximum of three strips per bladder were used. Contractile responses are expressed as absolute values (M) or as percentage of the relaxation induced by 10<sup>-3</sup> M papaverine. Concentration-response data of KCl were evaluated by sigmoid curve fitting and -logEC<sub>50</sub> values (pD<sub>2</sub>) were calculated by non-linear regression analysis using GraphPad Prism. Differences between mean values were statistically analyzed using an unpaired student t-test. A probability value of p < 0.05 was regarded to be significant. All analyses were performed using GraphPad Prism software (version 4.0; Graphpad Software Inc., San Diego, CA).

**RESULTS**

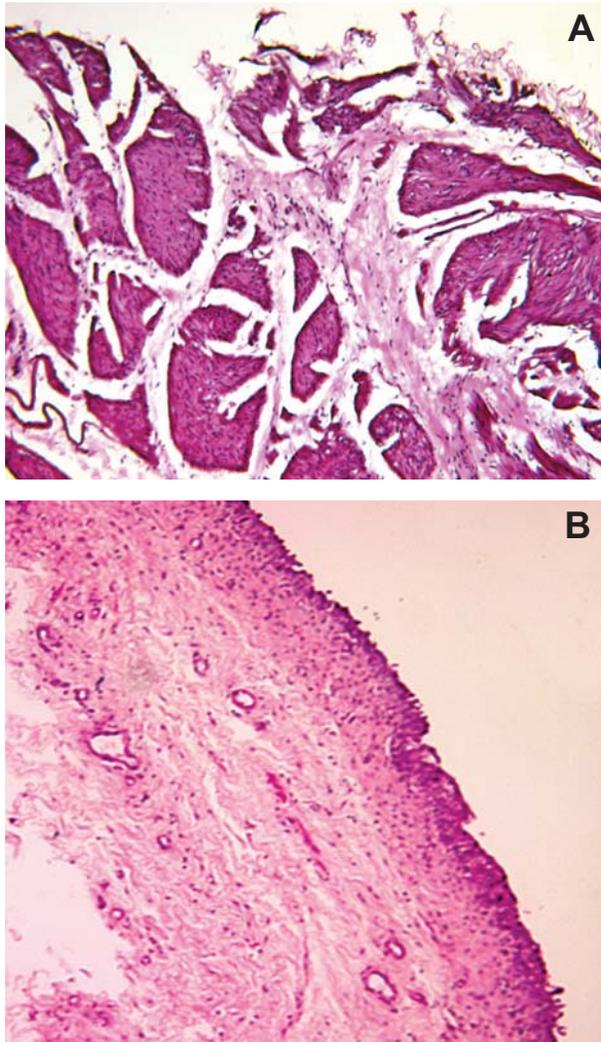
Presence of transcripts for β1-, β2-, and β3-adrenoceptors was determined by PCR amplification of cDNA obtained from surgically separated detrusor and urothelium tissue of human bladder. Specific primers for the β1-, β2-, and β3-adrenoceptor gene produced a single PCR product of expected size in all sets when separated on ethidium bromide stained 1.5% agarose gels (Figure-1). Separation of urothelium and detrusor was demonstrated by lack of any smooth muscle tissue stain in H&E staining

(Figure-2). The lack of contamination from detrusor tissue in the separated urothelium was further verified by lack of immunoreactivity for nonvascular smooth muscle specific protein desmin in urothelium (data not shown). The detrusor tissue showed strong stain for desmin compared to a faint stain in urothelium.

Functional significance of these receptors was tested by relaxation of human bladder strips by β3-adrenoceptor agonist Solabegron. Responses of drugs were expressed as a percentage of the 10<sup>-3</sup> M papaverine induced relaxation of tension produced



**Figure 1** – Expression β-adrenoceptors in human urothelium and detrusor. The representative ethidium bromide stained agarose gel of RT-PCR products for β1, β2 and β3-adrenoceptors show their mRNA expression in separated detrusor and urothelium tissue from 4 bladder specimens marked 1-4 on top. Lane from urothelium tissue of each bladder specimen is marked by U and lane for detrusor tissue is marked by D. Left lane is 100 bp DNA ladder in all gels and products of expected size are shown by bands for β1, β2 and β3-adrenoceptors in gels from top to bottom. Right most lane representative control with no template.



**Figure 2** – H & E staining of surgically separated tissue of detrusor (Panel A) and urothelium (Panel B). Absence of any smooth muscle cells in urothelium section verify lack of contamination from detrusor in the expression studies demonstrated in Figure-1.

by KCl. Cumulative addition of Solabegron into the myobath evoked concentration-dependent relaxation of KCl precontracted human bladder strips and attained a significant effect at nanomolar concentration range. Solabegron relaxed the human bladder strips that were pre-contracted with 30 mM KCl with a  $pD_2$  value of  $8.73 \pm 0.19$  (Figure-3).

Isoproterenol (a non-selective  $\beta$ -adrenoceptor agonist) produced significant relaxation of pre-contracted muscle strips at  $>10^{-6}$  M, whereas, solabegron

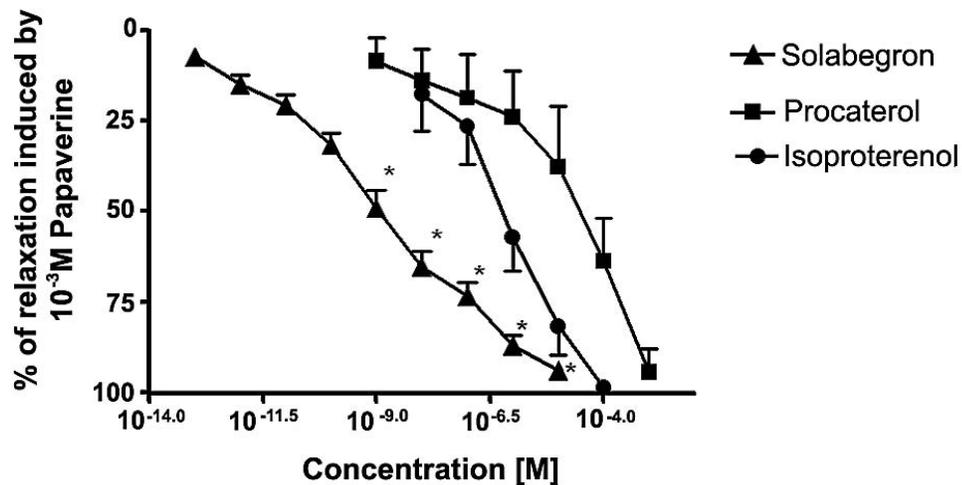
produced significant relaxation at  $>10^{-9}$  M (Figure-3). When compared with procaterol (a selective  $\beta_2$  agonist), solabegron produced a significant ( $p < 0.05$ ) relaxation (Figure-3). The  $pD_2$  values were calculated from the concentration-relaxation curve were  $5.08 \pm 0.48$ ,  $6.28 \pm 0.54$  and  $8.73 \pm 0.19$  for procaterol, isoproterenol and solabegron, respectively.

In other experiments, efficacy of solabegron to relax human bladder contraction in response to electrical field stimulation EFS at the lower frequencies (5, 10 and 15 Hz) was compared against isoproterenol. Drugs were incubated for 20 min. in the myobath prior to testing their effect on EFS (Figure-4). There was a significant inhibition of detrusor contraction at 10 Hz by solabegron and isoproterenol at  $10^{-4}$  M (Figure-4) and the detrusor response was reduced at all frequencies. However, maximum suppression was observed at EFS induced contractions of lower frequencies as 5 Hz. The force-frequency curve was shifted to the right by both solabegron and isoproterenol, at  $10^{-4}$  M (the percentage effect become similar for frequencies of 10-15 Hz). Efficacy of solabegron was slightly better than isoproterenol in suppressing EFS evoked contraction, but not statistically significant.

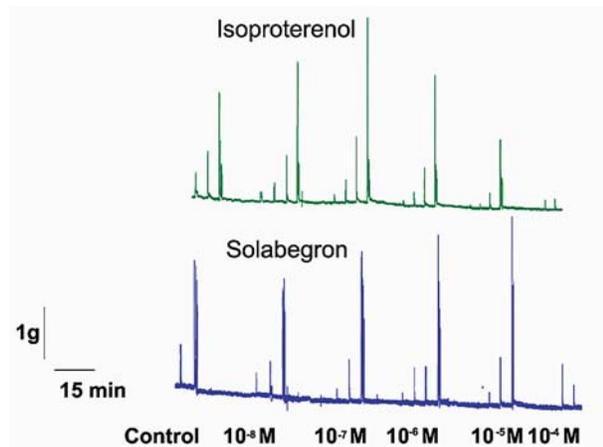
## COMMENTS

A previous study by Yamaguchi has determined the relative abundance of  $\beta_1$ -,  $\beta_2$ -, and  $\beta_3$ -adrenoceptor in the human bladder, but the anatomical distribution of expression in bladder in terms of urothelium and detrusor has not been determined (6). In our study, we demonstrated expression of all three  $\beta$ -adrenoceptors mRNAs urothelium as well as in detrusor muscles of the human bladder. The functional importance of  $\beta$ -adrenoceptors expressed in urothelium remains to be completely investigated. It is interesting to note that effect of  $\beta$ -adrenoceptors agonists on micturition is mediated principally by these receptors (10).

The effect of Solabegron on human bladder strips was recently reported (11). Our results on the effect of same drug Solabegron on human bladder generally agree with the earlier study showing relaxation of human detrusor strip pre-contracted with carbachol (11). However, the few notable



**Figure 3** – Concentration dependent relaxation of the KCl-induced tone of human detrusor strips by Solabegron, Procaterol and Isoproterenol. Relaxation evoked by drugs in muscle strips pre-contracted with 30nM KCl is expressed as percentage of the relaxation induced by 10<sup>-3</sup> M papaverine. Values are expressed as the mean (SEM) and significant difference from control was considered at \**p* < 0.05. Dose response curve were evaluated by sigmoid curve fitting and -logEC<sub>50</sub> values (pD<sub>50</sub>) were calculated by non-linear regression analysis using Graph Pad Prism.



**Figure 4** – A representative trace for the response of a human detrusor strip to EFS (5, 10, 15 Hz) in the presence of oxygenated Krebs' solution, and after 20 min incubation in Solabegron and Isoproterenol (10<sup>-8</sup>-10<sup>-4</sup> M). Both the drugs suppressed EFS evoked detrusor contraction at 10<sup>-4</sup> M concentration. The maximum suppression was observed at EFS induced contractions of lower frequencies as 5 Hz.

differences are the use of different stimuli of KCl to evoke contraction prior to the addition of solabegron in this study. The significant relaxation of KCl pre-contracted muscle strips were produced at much

lower concentration of 10<sup>-9</sup> M, as against 10<sup>-7</sup> M reported for relaxation of carbachol tone (11). Another major difference between the two studies on human bladder was the lack of difference observed in this study with respect to the suppression of EFS induced detrusor contraction. Biers et al. reported that only solabegron was able to suppress EFS contraction at 10<sup>-4</sup> M, whereas we observed that isoproterenol was equipotent in suppressing the EFS induced contraction of human detrusor (Figure-4). It is possible that different experimental methodology followed in the two studies will explain the differences reported here. On other hand, the EFS response on tissue strips was measured prior to testing of drugs and no drugs were added to myobath before EFS was done. Whereas the previous study (11), the tissue strips were subjected to carbachol 10<sup>-5</sup> M contraction prior to EFS response. In addition to different experimental methodology to explain different results, there could be differences in the sensitivities of bladder specimens used in the two studies to drugs and electrical stimulation.

Evidence suggests that β-adrenoceptor activation by isoproterenol in rat urothelial cells can trigger production and release of NO due to an increase

in intracellular  $\text{Ca}^{2+}$  following activation of the adenylate cyclase pathway in the urothelial cells (12). It has been reported that intravesical administration of NO scavenger decreased bladder capacity inducing bladder contractions (13) and that an intravesically applied NO donor decreased bladder overactivity induced by a chemical irritant, cyclophosphamide in rats (14). Considering the minimal relaxing effects of NO on rat bladder smooth muscles (15); it is believed that effect of NO on reflex bladder activity is much better explained by suppression of excitability of and/or the release of transmitters from bladder afferent nerves (16). Thus, it seems reasonable to assume that information about  $\beta$ -adrenoceptors expressed in the human urothelium might be involved in the regulation of bladder sensory functions.

Studies have shown that stimulation of  $\beta$ 2- and  $\beta$ 3-adrenergic receptors existing in the human detrusor can produce direct relaxation of the detrusor smooth muscle without blocking voiding induced bladder contraction (2,6). This  $\beta$ -adrenergic-stimulated relaxation is mediated through the stimulation of adenylyl cyclase and the accumulation of cyclic AMP (17). The involvement of  $\beta$ 3-adrenoceptor activation in mediating the relaxation of human detrusor by  **$\beta$ 3-adrenoceptor agonists was demonstrated by lack of suppression of its effect by selective  $\beta$ 1 and/or  $\beta$ 2-adrenoceptor antagonists such as dobutamine and procaterol (6).** The role of  $\beta$ 3-adrenoceptor is further verified by the blockade of Solabegron evoked relaxation by selective  **$\beta$ 3-adrenoceptor antagonists.**

Considering the role of  $\beta$ 3-adrenoceptors in modulating the control of bladder smooth muscle tone in humans; these results support the hypothesis that  **$\beta$ 3-AR agonists represent a useful clinical strategy for treating detrusor overactivity (18).**  **$\beta$ -adrenoceptor antagonists blockers** have also been advocated for stress urinary incontinence owing to inappropriate reflex urethral relaxation, because propranolol prevents the reduction in urethral pressure after sacral root stimulation (19). However,  **$\beta$ -adrenoceptor antagonists** are not particularly useful in treating bladder or urethral disorders (20). Currently therapy for the OAB syndrome, such as with antimuscarinic agents or direct acting smooth muscle relaxants, can produce the result of urinary retention and other mechanistic side-effects (21).

## CONCLUSIONS

The present study demonstrates that stimulation of  $\beta$ 3-receptor with Solabegron evokes human bladder relaxation, suggesting that selective  $\beta$ 3-adrenoceptor agonist may be a valuable new treatment for the OAB syndrome. The expression of  $\beta$ 1-,  $\beta$ 2- and  $\beta$ 3-adrenoceptors in urothelium apart from detrusor may suggest additional mechanism of action for the  $\beta$ 3-adrenoceptor in the lower urinary tract.

## CONFLICT OF INTEREST

This work was supported in part by GlaxoSmithKline.

## REFERENCES

1. Andersson KE: LUTS treatment: future treatment options. *Neurourol Urodyn.* 2007; 26: 934-47.
2. Takeda H, Yamazaki Y, Akahane M, Igawa Y, Ajisawa Y, Nishizawa O: Role of the beta(3)-adrenoceptor in urine storage in the rat: comparison between the selective beta(3)-adrenoceptor agonist, CL316, 243, and various smooth muscle relaxants. *J Pharmacol Exp Ther.* 2000; 293: 939-45.
3. Finney SM, Andersson KE, Gillespie JI, Stewart LH: Antimuscarinic drugs in detrusor overactivity and the overactive bladder syndrome: motor or sensory actions? *BJU Int.* 2006; 98: 503-7.
4. Yoshimura N, Kaiho Y, Miyazato M, Yunoki T, Tai C, Chancellor MB, et al.: Therapeutic receptor targets for lower urinary tract dysfunction. *Naunyn Schmiedeberg Arch Pharmacol.* 2008; 377: 437-48.
5. Frazier EP, Peters SL, Braverman AS, Ruggieri MR Sr, Michel MC: Signal transduction underlying the control of urinary bladder smooth muscle tone by muscarinic receptors and beta-adrenoceptors. *Naunyn Schmiedeberg Arch Pharmacol.* 2008; 377: 449-62.
6. Yamaguchi O: Beta3-adrenoceptors in human detrusor muscle. *Urology.* 2002; 59: 25-9.
7. Igawa Y, Yamazaki Y, Takeda H, Kaidoh K, Akahane M, Ajisawa Y, et al.: Relaxant effects of isoproterenol and selective beta3-adrenoceptor agonists on normal, low compliant and hyperreflexic human bladders. *J Urol.* 2001; 165: 240-4.
8. Otsuka A, Shinbo H, Matsumoto R, Kurita Y, Ozono S: Expression and functional role of beta-adrenocep-

- tors in the human urinary bladder urothelium. *Naunyn Schmiedeberg's Arch Pharmacol.* 2008; 377: 473-81.
9. Murakami S, Chapple CR, Akino H, Sellers DJ, Chess-Williams R: The role of the urothelium in mediating bladder responses to isoprenaline. *BJU Int.* 2007; 99: 669-73.
  10. Yamaguchi O, Chapple CR: Beta3-adrenoceptors in urinary bladder. *NeuroUrol Urodyn.* 2007; 26: 752-6.
  11. Biers SM, Reynard JM, Brading AF: The effects of a new selective beta3-adrenoceptor agonist (GW427353) on spontaneous activity and detrusor relaxation in human bladder. *BJU Int.* 2006; 98: 1310-4.
  12. Birder LA, Nealen ML, Kiss S, de Groat WC, Caterina MJ, Wang E, et al.: Beta-adrenoceptor agonists stimulate endothelial nitric oxide synthase in rat urinary bladder urothelial cells. *J Neurosci.* 2002; 22: 8063-70.
  13. Pandita RK, Rønn LC, Jensen BS, Andersson KE: Urodynamic effects of intravesical administration of the new small/intermediate conductance calcium activated potassium channel activator NS309 in freely moving, conscious rats. *J Urol.* 2006; 176: 1220-4.
  14. Ozawa H, Chancellor MB, Jung SY, Yokoyama T, Fraser MO, Yu Y, et al.: Effect of intravesical nitric oxide therapy on cyclophosphamide-induced cystitis. *J Urol.* 1999; 162: 2211-6.
  15. Andersson KE, Persson K: Nitric oxide synthase and the lower urinary tract: possible implications for physiology and pathophysiology. *Scand J Urol Nephrol Suppl.* 1995; 175: 43-53.
  16. Masuda H, Kim JH, Kihara K, Chancellor MB, de Groat WC, Yoshimura N: Inhibitory roles of peripheral nitrenergic mechanisms in capsaicin-induced detrusor overactivity in the rat. *BJU Int.* 2007; 100: 912-8.
  17. Harmon EB, Porter JM, Porter JE: Beta-adrenergic receptor activation in immortalized human urothelial cells stimulates inflammatory responses by PKA-independent mechanisms. *Cell Commun Signal.* 2005; 3: 10.
  18. Furuta A, Thomas CA, Higaki M, Chancellor MB, Yoshimura N, Yamaguchi O: The promise of beta3-adrenoceptor agonists to treat the overactive bladder. *Urol Clin North Am.* 2006; 33: 539-43.
  19. Kaisary AV: Beta adrenoceptor blockade in the treatment of female urinary stress incontinence. *J Urol (Paris).* 1984; 90: 351-3.
  20. Zinner NR, Koke SC, Viktrup L: Pharmacotherapy for stress urinary incontinence : present and future options. *Drugs.* 2004; 64: 1503-16.
  21. Reynard JM: Does anticholinergic medication have a role for men with lower urinary tract symptoms/benign prostatic hyperplasia either alone or in combination with other agents? *Curr Opin Urol.* 2004; 14: 13-6.

---

*Accepted after revision:  
November 17, 2008*

---

**Correspondence address:**

Dr. Pradeep Tyagi  
Beaumont Research Institute  
3811, w. 13 mile road,  
suite 160  
Royal Oak, Michigan, 48073, USA  
Fax: + 1 248 551-2615  
E-mail: pradeep.tyagi@beaumont.edu

**EDITORIAL COMMENT**

Recent interest of the bladder physiology has focused on urothelial/suburothelial cells of the urinary bladder. The present study demonstrates the presence of three subtypes of  $\beta$ -adrenoceptors on the urothelium and the detrusor of human bladder, and

would support recent findings that  $\beta$ -adrenoceptor subtypes are functionally expressed in the urinary bladder urothelium (1,2). Although many findings about the urothelial muscarinic receptor subtypes have been reported, little remains known as regards

the distribution and functional roles of urothelial  $\beta$ -adrenoceptor subtypes.

Multiple lines of evidence suggest that  $\beta_3$ -adrenoceptors are predominantly abundant in the human detrusor muscle of the urinary bladder, and play important roles in detrusor relaxation during urinary storage in humans. Besides, it is postulated that  $\beta_3$ -adrenoceptor agonists could be highly promising agents to treat overactive bladder by a clinical trial (3).

In the near future, I hope novel findings of mechanism of the urothelial/suburothelial  $\beta$ -adrenoceptor subtypes in the urinary bladder may shed light on the pathological conditions such as overactive bladder and interstitial cystitis.

## REFERENCES

1. Murakami S, Chapple CR, Akino H, Sellers DJ, Chess-Williams R: The role of the urothelium in mediating bladder responses to isoprenaline. *BJU Int.* 2007; 99: 669-73.
2. Otsuka A, Shinbo H, Matsumoto R, Kurita Y, Ozono S: Expression and functional role of beta-adrenoceptors in the human urinary bladder urothelium. *Naunyn Schmiedebergs Arch Pharmacol.* 2008; 377: 473-81.
3. Chapple CR, Yamaguchi O, Ridder A, Liehne J, Carl S, Mattiasson A, et al: Clinical proof of concept study (Blossom) shows novel  $\beta_3$  adrenoceptor agonist YM178 is effective and well tolerated in the treatment of symptoms of overactive bladder. *Eur Urol (Suppl).* 2008; 7: 239.

***Dr. Atsushi Otsuka***

*Department of Urology*

*Hamamatsu University School of Medicine*

*Shizuoka, Japan*

*E-mail: otsuka@hama-med.ac.jp*

# Urethral Catheter Insertion Forces: A Comparison of Experience and Training

Benjamin K. Canales, Derek Weiland, Scott Reardon, Manoj Monga

*Department of Urology (BKC), University of Florida, Gainesville, Florida, USA and Department of Urology (DW, SR, MM), University of Minnesota, Minneapolis, Minnesota, USA*

---

## ABSTRACT

*Purpose:* This study was undertaken to evaluate the insertion forces utilized during simulated placement of a urethral catheter by healthcare individuals with a variety of catheter experience.

*Materials and Methods:* A 21F urethral catheter was mounted to a metal spring. Participants were asked to press the tubing spring against a force gauge and stop when they met a level of resistance that would typically make them terminate a catheter placement. Simulated catheter insertion was repeated five times, and peak compression forces were recorded. Healthcare professionals were divided into six groups according to their title: urology staff, non-urology staff, urology resident/ fellow, non-urology resident/ fellow, medical student, and registered nurse.

*Results:* A total of fifty-seven healthcare professionals participated in the study. Urology staff (n = 6) had the lowest average insertion force for any group at  $6.8 \pm 2.0$  Newtons (N). Medical students (n = 10) had the least amount of experience ( $1 \pm 0$  years) and the highest average insertion force range of  $10.1 \pm 3.7$  N. Health care workers with greater than 25 years experience used significantly less force during catheter insertions ( $4.9 \pm 1.8$  N) compared to all groups ( $p < 0.01$ ).

*Conclusions:* We propose the maximum force that should be utilized during urethral catheter insertion is 5 Newtons. This force deserves validation in a larger population and should be considered when designing urethral catheters or creating catheter simulators. Understanding urethral catheter insertion forces may also aid in establishing competency parameters for health care professionals in training.

*Key words:* urinary catheterization; urethral catheter; educational models

*Int Braz J Urol. 2009; 35: 84-9*

---

## INTRODUCTION

The insertion of a urethral catheter is one of the most commonly performed hospital procedures. For the year 2000, the Center for Disease Control estimated that over five million urethral catheterizations were attempted in the United States (1). In most hospitals, this procedure is performed without a standardized training protocol and by a variety of healthcare workers with varying degrees of experience. We hypothesized that we could establish competency parameters for professionals in-training

by measuring urethral catheter exertion forces and comparing healthcare provider experience. In addition, we would gather information that may affect not only the future design of catheters and virtual simulators but also the rate of urethral trauma and stricture.

## MATERIALS AND METHODS

Healthcare personnel at the Veterans Affairs Medical Center and the University of Minnesota in

Minneapolis, MN, USA, were invited to participate in our study if they could be stratified into one of six groups: Group 1 - Urologist MD; Group 2 - Non-Urologist MD; Group 3 - Urology Resident / Fellow MD; Group 4 - Non-Urology Resident / Fellow MD; Group 5 - Medical Student; and Group 6 - Registered Nurse. Participants were asked, “Push in the catheter until you feel a level of resistance that would make you stop if you were putting in a real urethral catheter”. Participants held the catheter at the same marked area and were instructed and monitored by the same two researchers to ensure procedure conformity. The procedure was repeated five times serially by all groups.

The tube used in simulation was a polyolefin catheter (21F outer circumference, 9F inner circumference) with a metal spring (7/32” x 1” x 0.28” wire thickness) mounted on the distal end of a compression force gauge (Extech™ Digital Force Gauge - model 475040) (Figure-1). Peak compression forces in Newtons (N) were recorded, and participants were blinded to their own results.

The statistical software package SAS was used for all calculations (SAS Institute Inc., Cary, NC, Version 9.0). Group mean comparisons were



**Figure 1** – Photograph of the hand-position taken by a left-handed individual being tested on an Extech™ Digital Force Gauge - model 475040. Participants were asked to hold the silicone portion and press on the tubing similar to advancing a catheter. A plastic shield (not shown) was placed between the force gauge and catheter to blind participants to their results.

calculated by an unpaired, two-sided, Student t-test. Analysis of variance (ANOVA) was applied to compare different groups with respect to continuous variables. Change in force over years of experience was estimated by regressing the force applied by each subject and obtaining a best fit line by linear regression. Results were considered significant if the p-value was  $< 0.05$ .

## RESULTS

Fifty-seven healthcare workers participated in this study (Figure-2). Individual urethral catheter insertion force was averaged by group and ranged from 6.8 to 10.1 N. Urologists (Group-1) had the lowest average force insertion forces ( $6.8 \text{ N} \pm 2.0 \text{ N}$ ), while medical students (Group-5) had the highest average insertion forces ( $10.1 \text{ N} \pm 3.7 \text{ N}$ ). The difference in the amount of simulated force used to insert a catheter was significantly higher for the medical students compared to every other group ( $p < 0.01$ ). The difference in p values was also significant when comparing urologists to urology residents (Group-3,  $p = 0.03$ ) and registered nurses (Group-6,  $p < 0.01$ ).

To evaluate for subject-expectancy effect, one way ANOVA was performed comparing force versus attempt for attempts #1 - 5 (Figure-3). No statistically significant difference was found between means of groups (range 8.14 N - 8.62 N;  $p = 0.96$ ). Experience was then plotted independent of medical group in a bivariate fit graph versus force, and results were examined using ANOVA (Figure-4). In this linear correlation, participant experience alone ( $r = -0.78$ ) explained approximately 78% of the observed variation in force ( $p < 0.001$ ). Health care workers with more than 25 years experience ( $n = 9$ ) had the lowest average force insertion forces ( $4.9 \text{ N} \pm 1.8 \text{ N}$ ) compared to those with less than 25 years experience ( $8.4 \pm 2.5 \text{ N}$ ,  $p = 0.01$ ).

## COMMENTS

The urethral catheter is an instrument as old as the field of urology. Evidence of catheter use in Greece can be found in the Hippocratic Writings (~400 BC)

## Urethral Catheter Insertion Forces

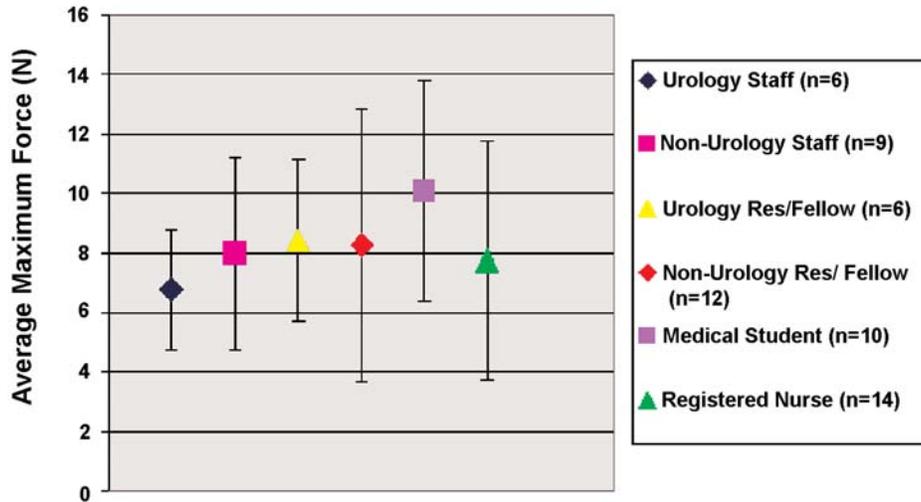


Figure 2 – Average urethral catheter insertion force in Newtons, by group.

(2). In 1929, Dr. Frederick E.B. Foley described the first modern urethral catheter by dipping coagulating latex onto metal forms to create a dual-port balloon catheter (3). Components of modern urethral catheters have evolved into a combination of silicone

and latex-free rubber (mixed in varying proportions to vary catheter rigidity) coated with an elastomer to aid insertion (4).

Despite the publications of a nurse clinical practice guideline (5) and the impact of nursing educa-

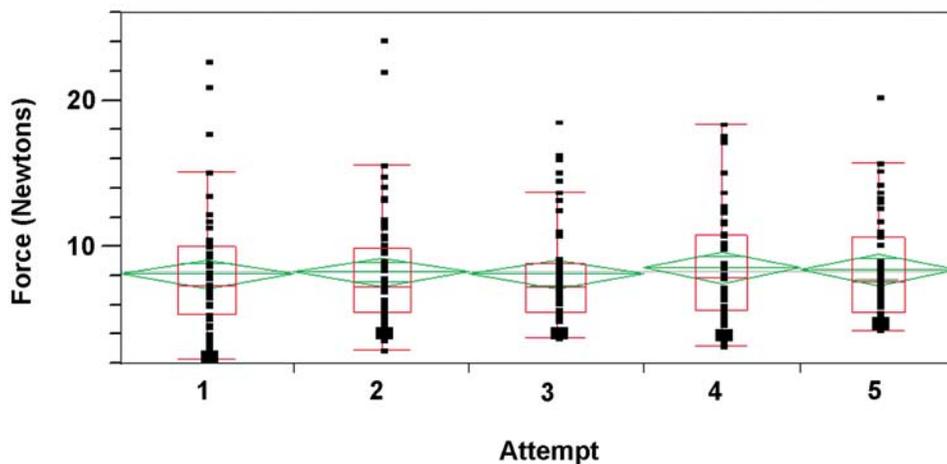
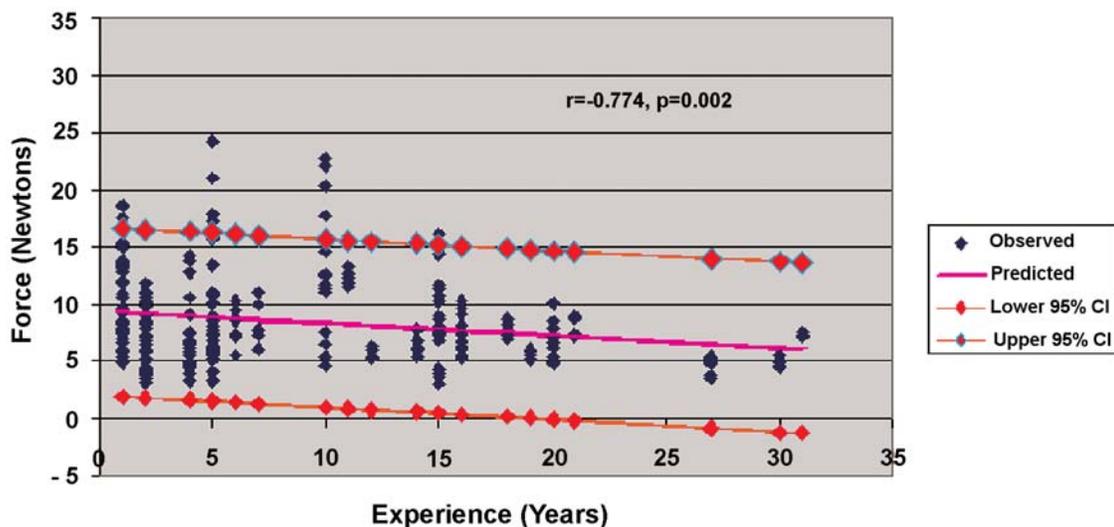


Figure 3 – One way analysis of variance comparing force (y-axis) versus attempt (x-axis). Mean force (green diamond lines) by attempt ranged from 8.14 N - 8.62 N ( $p = 0.96$ ).

## Urethral Catheter Insertion Forces



*Figure 4 – Simple linear regression plot of forces (observed and predicted) and participant experience with 95% confidence intervals for the mean.  $r$  = correlation coefficient.*

tional programs (6), no standardized method for training health care workers in catheter placement exists. Most new health care employees, whether they are students or residents, are guided through the process of patient preparation and catheterization by someone with catheter experience. During the actual procedure, however, only the health care worker advancing the catheter can feel the resistance given by the catheter. Although improvements in catheter design and composition have occurred, iatrogenic urethral injury, in particular urethral stricture, continues to occur far too commonly (7,8). Fenton et al. found that urethral catheter placement was the cause of approximately 30% of all urethral stricture disease (9). In addition, urethral-rectal fistulas, urethral perforation, prostatic bleeding requiring surgical intervention, and bladder perforation have all been reported as consequences of improperly inserted urethral catheters (10-12). Therefore, we attempted to generate a “normal curve” of catheter forces that could be used for modeling purposes and potential competency parameters.

From a design standpoint, it is important to emphasize that we have measured only one element of catheter insertion: force used. Because our method of simulation does not involve resistance, we chose to use the polymer “polyolefin” as it is more firm than a silicone or latex catheter and does not buckle

prior to the participant reaching the point of maximal force. Analysis by attempt (Figure-3) indicated that no more force was applied on the first attempt than on the last attempt, suggesting that both the material used and the study design yielded reproducible and precise results.

Intuitively, it makes sense that a properly placed catheter should not require a great deal of force to traverse the urethra. In support of this, the experienced urologists had the lowest catheter insertion forces of all our groups ( $6.8 \pm 2.0$  N). More surprising was the finding that health care workers with more than 25 years experience had even lower forces ( $4.9 \pm 1.8$  N) with statistical significance. Because of this, we propose that the range of  $4.9 \pm 1.8$  N be considered the standard-of-care model in regards to urethral catheter insertion force. Future clinical studies should evaluate not only force but also the ability for providers to appreciate and adapt to variances in a clinical presentation, such as catheter resistance, anatomy, bloody return, or patient discomfort.

Several catheter methods of simulation have been devised, but no simulation method fully recreates the sense of catheterization of the female or male. Despite their shortcomings, catheter simulators have been shown to reduce both risk and pain experienced by patients in addition to avoiding urethral injuries

(13). Since many U.S. medical schools have the insertion of a urethral catheter as a core clinical competency (14), simulators could likely help students learn this core concept before actually practicing on a real patient. As the use of simulated medical trainers rises in this country, it is our hope that this data can be used to help industry sector and medical programs in designing simulation devices that give feedback during urethral catheter insertion. From a cost standpoint, Morgan et al. showed that medical simulator training devices are worth the extra expense in regards to both student and faculty satisfaction (15). Although most of the medical simulator published data involves medical students, this technology could easily be applied to nursing students (who are much more likely to place routine catheters than physicians are), new surgical or medical residents, and/or as competency testing for physicians.

Our study has some limitations. Though utilization of an in vitro model allows standardization of technique and measurement, it does not account for signs of excess force that could be noted in a clinical trial, such as patient reporting of discomfort, blood at the urethral meatus, or catheter tip resistance. In addition to force, urethral injury rates may increase by higher catheterization intervals or in high risk male populations, such as benign prostatic hyperplasia or prostate cancer (6). Polyolefin material is slightly stiffer than silicone and latex materials used in catheters and was selected specifically so the catheter would not buckle during testing. It would be of value to validate the force range defined in this study in a clinical trial of a larger group of providers using commercially available catheters.

## CONCLUSION

In conclusion, as health care workers acquire more experience, significantly less force is used during urethral catheter insertions. Based on our findings, we propose that the maximum force that should be utilized during urethral catheter insertion is 5 Newtons. This force should be considered the “upper limit” utilized for urethral catheter insertion. Future validation in larger populations, such as measurements in cadavers or anesthetized patients undergoing

non-urologic surgery, would be warranted to evaluate the range of forces used during normal circumstances. However, clinical measurements of this type may not necessarily help refine the “upper limit” that should be avoided unless they are collected from experienced practitioners. Overall, understanding urethral catheter insertion forces may aid in the design of future catheters, in the creation of catheter simulators, and in establishing competency parameters for health care professionals during training and/or recertification.

## ACKNOWLEDGEMENT

To Dr. John J. Carlow who assisted in the statistical analysis.

## CONFLICT OF INTEREST

Financial support by PercSys® (Percutaneous Systems, Inc.; Mountain View, CA)

## REFERENCES

1. Maki DG, Tambyah PA: Engineering out the risk for infection with urinary catheters. *Emerg Infect Dis.* 2001; 7: 342-7.
2. Moog FP, Karenberg A, Moll F: The catheter and its use from Hippocrates to Galen. *J Urol.* 2005; 174: 1196-8.
3. Newman DK: Managing indwelling urethral catheters. *Ostomy Wound Manage.* 1998; 44: 26-32.
4. Carr HA: A short history of the Foley catheter: from handmade instrument to infection-prevention device. *J Endourol.* 2000; 14: 5-8.
5. Clinical Practice Guidelines Task Force; Society of Urologic Nurses and Associates. Male urethral catheterization. *Urol Nurs.* 2006; 26: 315-7.
6. Kashefi C, Messer K, Barden R, Sexton C, Parsons JK: Incidence and prevention of iatrogenic urethral injuries. *J Urol.* 2008; 179: 2254-7; discussion 2257-8.
7. Dobrowolski ZF, Weglarz W, Jakubik P, Lipczynski W, Dobrowolska B: Treatment of posterior and anterior urethral trauma. *BJU Int.* 2002; 89: 752-4.
8. Igawa Y, Wyndaele JJ, Nishizawa O: Catheterization: possible complications and their prevention and treatment. *Int J Urol.* 2008; 15: 481-5.

9. Fenton AS, Morey AF, Aviles R, Garcia CR: Anterior urethral strictures: etiology and characteristics. *Urology*. 2005; 65: 1055-8.
10. Nouri M, Tazi K, el Fassi J, Ibn Attya A, Hachimi M, Lakrissa A: Treatment of urethro-rectal fistulas. Apropos of 5 cases. *Prog Urol*. 1999; 9: 137-41.
11. Donovski L, Ormanov I, Ziad Sh, Farakh N: A case of iatrogenic rupture of the urethra with a retrovesical urinoma. *Khirurgiia (Sofia)*. 1989; 42: 72-4.
12. Basha M, Subhani M, Mersal A, Saedi SA, Balfe JW: Urinary bladder perforation in a premature infant with Down syndrome. *Pediatr Nephrol*. 2003; 18: 1189-90.
13. Gordon JA, Wilkerson WM, Shaffer DW, Armstrong EG: "Practicing" medicine without risk: students' and educators' responses to high-fidelity patient simulation. *Acad Med*. 2001; 76: 469-72.
14. Sanders CW, Edwards JC, Burdenski TK: A survey of basic technical skills of medical students. *Acad Med*. 2004; 79: 873-5.
15. Morgan PJ, Cleave-Hogg DM: Cost and resource implications of undergraduate simulator-based education. *Can J Anaesth*. 2001; 48: 827-8.

---

*Accepted after revision:  
October 13, 2008*

---

**Correspondence address:**

Dr. Benjamin K. Canales  
Dept of Urology, University of Florida  
1600 SW Archer Rd, Rm N-213  
PO Box 100247  
Gainesville, FL, 32610-0247, USA  
Fax: + 1 352 273-7515  
E-mail: benjamin.canales@urology.ufl.edu

## EDITORIAL COMMENT

This work is a highly valuable unprecedented initiative towards systemization of urethral catheter insertion. Although urethral catheter insertion is a common procedure, to date there is no definitive standardization.

The use of diverse groups in the study serves to show that aptitude in catheter placement implicates an extremely long learning curve for all healthcare providers, independent of their specialization. Ul-

timately, this study shows that even if other factors can lead to late complications, the force used in the placement of the catheter is the principal factor leading to acute complications.

Lastly, this study serves as a starting point for creation of catheter simulators designed for healthcare workers. However, as documented by the authors, more studies must be conducted in order to validate all these data.

***Dr. João P. Martins de Carvalho***  
*Section of Urology  
Fluminense Federal University (UFF)  
Niteroi, Rio de Janeiro, Brazil  
E-mail: carvalho.jpm@gmail.com*

## Re: Appendiceal Substitution Following Right Proximal Ureter Injury

To the Editor,

Use of the appendix as a ureteral substitute was first described by Melnikoff in 1912 (1). However, the technique has been used only in a handful of patients since its introduction (2,3). We present the case of a 66 year-old male who presented with abdominal pain three weeks after undergoing lysis of small bowel adhesions, and was found to have an 8-10 cm defect of the right proximal ureter upon undergoing retrograde pyelogram.

There are numerous techniques for the repair of ureteral injuries. Primary end-to-end anastomosis, psoas hitch ureteral reimplantation, and Boari flap were not feasible in this case due to the length and location of the injury. Ileal interposition has been successfully used to repair large defects, but requires a bowel anastomosis, which we wished to avoid. Auto-transplantation of the kidney is technically challenging and associated with unique morbidities. Appendiceal substitution was chosen due to the amenable location of the injury and favorable operative risks.

In the operating room, we injected methylene blue through a previously placed nephrostomy tube in order to better delineate the proximal margin of the injury. The appendix was then ligated at its base and

tip and detached from the cecum. Special attention was given to preserving the appendicular arteries and mesoappendix (Figure-1). The appendix was cannulated to accommodate a 14 French endopyelotomy stent. Next, the appendix was rotated up to the level of the renal pelvis to ensure a tension free anastomosis. It was then oriented in isoperistaltic fashion with its distal tip abutting the renal pelvis. A spatulated uretero-appendiceal anastomosis was performed on both ends of the graft (Figure-2). The anastomosis was then tested



**Figure 1** – Proximal ureteral defect measuring 8-10 cm with appendix rotated into position (black arrow). Dark suture at right renal pelvis (white arrow).



**Figure 2** – Completed appendiceal interposition (arrows). K = right kidney.



**Figure 3** – Intravenous pyelogram at eight months postoperatively showing a patent graft with no evidence of stricture or hydronephrosis.

for leakage by injecting methylene blue through the indwelling nephrostomy tube.

The patient was discharged from the hospital on postoperative day six and the stents were removed four weeks later. Intravenous pyelogram at eight months postoperatively showed a patent appendiceal graft with no evidence of stricture or hydronephrosis (Figure-3).

Long-term data in the small body of literature devoted to this procedure demonstrates excellent autograft performance and preserved renal function up to fifteen years postoperatively (2). While traumatic injury is the most commonly reported indication for this procedure, it has also been employed successfully in other settings such as ureteral necrosis secondary to dermatomyositis. This technique has also been proven effective in pediatric as well as adult populations (2).

The majority of case reports of appendiceal interposition involve the right ureter due to the ipsilateral location of the appendix. However, there is at least one description of a proximal left ureteral repair by Zargar et al. 2004 (3). To accomplish the left-sided reconstruction the author mobilized the appendix with the right colon and distal ileum into the left ureteral fossa.

This case supports appendiceal substitution as a reasonable option for patients with right-sided ureteral defects not amenable to primary end-to-end anastomosis. Limiting factors for the procedure include presence and length of appendix, impaired renal function, and history of pelvic irradiation.

#### REFERENCES

1. Melnikoff AE: Sur le remplacement de l'uretere par anse isolée de l'intestin grêle. Rev Clin Urol. 1912; 1: 601-05.
2. Richter F, Stock JA, Hanna MK: The appendix as right ureteral substitute in children. J Urol. 2000; 163: 1908-12.
3. Zargar MA, Mirzazadeh M, Zargar K: The appendix, an acceptable substitute for all segments of both ureters: a report of two cases. Med J Islam Repub Iran. 2004; 18: 177-180.

**Matt S. Ashley, BA &  
Dr. Siamak Daneshmand**

*Division of Urology & Renal Transplantation  
Oregon Health & Science University  
Portland, Oregon, USA  
E-mail: daneshma@ohsu.edu*

## Re: Initial Complete Laparoendoscopic Single-Site Surgery Robotic Assisted Radical Prostatectomy(LESS-RARP)

To the Editor,

Laparoendoscopic single-site surgery (NOTES-LESS) has been gaining momentum in minimally access urological surgery. The incorporation of the robotic interface into the NOTES-LESS arena, proposes a symbiosis with promising future; Haber et al. (1), presented their experience with experimental with NOTES and robot in pigs for nephrectomies and pyeloplasties. Their results were encouraging in terms of feasibility. More recently, Desai et al. (2) presented an interesting work of transvesical radical prostatectomy (RP) in a cadaver model. Our group has previously report on a transitional experience to LESS-RP including both cadaver experimental and clinical experiences (3).

Previous detailed explanation and consent of the procedure, we have performed LESS-RARP in a 69 years old patient with prostatic cancer T1c. Patient's PSA and Gleason score were 8.50 ng/mL and 3+3, respectively. Patient was fully continent preoperatively and reported active sexual life. Operation was performed with daVinci® interface and standard trocars (Figure-1). Ports were placed in a rhomboid fashion with the endoscope in the upper corner (12 mm), a 5 mm trocar in the lower corner for suction and traction purposes and 8 mm working ports at either side, without need of any other instrument. Clashing between instruments was verified externally and this hardened assistant's performance. Total operative time was 210 min. Dorsal venous control was accomplished in 3 min. with one figure of eight stitch. Urethrovesical anastomosis was performed in 35 min. by separate stitches. An antegrade interfascial bilateral neurovascular bundle dissection was performed. Bipolar energy and metallic clips were used for hemostasis. Blood loss was 300 cc and final pathology reported a surgical specimen of 66 g, Gleason score 3+4 with negative surgical margins. No perioperative complications were observed.

RP has been previously assessed in NOTES-LESS urological surgery. Desai et al. (2) presented

an interesting work of transvesical RP in a cadaver model. The procedure was performed in two fresh male cadavers. They employed four laparoscopic transvesical trocars and single-port device for their first and second cases, respectively, using the daVinci-S robot (Intuitive Surgical, Sunnyvale, CA, USA). Both operations were completed transvesically and robotically. There was no need for additional ports. Operative time for the multi-port procedure was 3 h and for the single-port procedure was 4.2 h. External conflict with robotic interface was experienced as a technical difficulty with the single-port procedure.



**Figure 1** – Rhomboid trocar positioning for LESS robotic assisted. Dissection of aponeurosis allowed a separation of 3.5 cm between ports.

In the clinical arena, Kaouk et al. (4) presented a series of single-port laparoscopic RP in 4 patients diagnosed with prostate cancer. They treated patients with localized disease, no previous pelvic surgery, and a body mass index < 35 kg/m<sup>2</sup>. A single port device was placed transperitoneally through a 1.8-cm incision located at the umbilicus without any other instruments or ports needed to complete operations. Urethrovesical anastomosis was performed using free-hand interrupted suturing and extracorporeal knot tying. This work is an impressive publication verifying feasibility of this procedure with the use of single port and articulated instruments. Kaouk et al have also presented a previous experience in LESS-RARP using the R-port with adequate results.

We report to our the first clinical report of LESS-RARP. The procedure was successfully completed with the initial approach and a change in port triangulation was a key point to accomplish the task. Further evaluation of the technique is warranted.

## REFERENCES

1. Haber GP, Crouzet S, Kamoi K, Berger A, Aron M, Goel R, et al.: Robotic NOTES (Natural Orifice Transluminal Endoscopic Surgery) in reconstructive urology: initial laboratory experience. *Urology*. 2008; 71: 996-1000.
2. Desai MM, Aron M, Berger A, Canes D, Stein R, Haber GP, et al.: Transvesical robotic radical prostatectomy. *BJU Int*. 2008; 102: 1666-9.
3. Barret E, Sanchez-Salas R, Kasraeian A, Benoist N, Ganatra A, Cathelineau X, et al.: A transition to laparoendoscopic single-site surgery (LESS) radical prostatectomy: human cadaver experimental and initial clinical experience. *J Endourol*. 2009; 2. [Epub ahead of print]
4. Kaouk JH, Goel RK, Haber GP, Crouzet S, Desai MM, Gill IS: Single-port laparoscopic radical prostatectomy. *Urology*. 2008; 72: 1190-3.
5. Kaouk JH, Goel R K, Haber GP, Crouzet S, Stein RJ. Robotic single-port transumbilical surgery in humans: initial report. *BJU*. 2008 Sep 3. Epub ahead of print.

***Dr. Eric Barret, Dr. Rafael Sanchez-Salas,  
Dr. Xavier Cathelineau, Dr. Francois Rozet,  
Dr. Marc Galiano & Dr. Guy Vallancien***

*Department of Urology  
Institut Montsouris  
Université Paris Descartes  
Paris, France  
E-mail: eric.barret@imm.fr*

## Re: The Influence of Statins on Prostate-Specific Antigen Levels

To the Editor,

The influence of statin medications on prostate specific antigen levels is somehow controversial. Recently, Hamilton RJ et al. analyzed data of men who were prescribed a statin for a long-term period. The authors reported a statistically significant decline in PSA levels in men without prostate cancer, after they were treated with statins (1). This finding is

in accordance with that of Cyrus-David et al., who also reported an important PSA decline in a small number of healthy men treated with statins for over 5 years (2). In contrast, Mills et al., who assessed the efficacy of statins in the treatment of lower urinary tract symptoms and prostate enlargement in a large, double-blind, placebo-controlled trial did not found

any difference between the effects of statins and placebo on the mean change from baseline in PSA levels after 26 wk of treatment (3). In our recently published study investigating the effects of statins on conventional medical treatment of lower urinary tract symptoms with finasteride, serum PSA values seemed to be generally lower in statin/finasteride arm compared to finasteride arm alone at the end of the study (4). The fact that the change in mean PSA from baseline to end point in patients treated with statins did not achieved statistical significance lead authors to conclude that statins do not seem to boost the finasteride's effect on PSA. However, under the light of the new evidence emerged from the study of Hamilton RJ et al., this could be attributed to the relatively low sample as well as to the relatively low duration of the study and an effect of statins on PSA would be probably detected if the study has been lasted over a longer period of time. In fact, effects of statins on prostate biology, as observed in large prospective cohort studies, are probably associated with higher doses and longer use (5). Although the specific mechanism by which statins influence PSA is not understood, it could be assumed that involves metabolic pathways. Since cholesterol is an important precursor for androgen formation, it is conceivable that by influencing cholesterol metabolism, statins may lower levels of intraprostatic androgens and in consequence they reduce PSA levels. An additional, non-cholesterol mediated effect of statins via anti-atherosclerotic action is not to be excluded also. Effects of statins in both prostate stromal and epithelial cells

have been attributed to the anti-oxidative properties of statins as well. Data suggesting that treatment with statins lower serum PSA with time may also indicate new possible drug mechanisms acting on prostate cells at the receptor level and may indicate a novel approach in both prostate cancer chemoprevention and benign prostate hyperplasia treatment. Therefore, further experimental studies are needed in order to investigate the exact mechanism by which statins impact on prostate cells.

#### REFERENCES

1. Hamilton RJ, Goldberg KC, Platz EA, Freedland SJ: The influence of statin medications on prostate-specific antigen levels. *J Natl Cancer Inst.* 2008; 100: 1511-8.
2. Cyrus-David MS, Weinberg A, Thompson T, Kadmon D: The effect of statins on serum prostate specific antigen levels in a cohort of airline pilots: a preliminary report. *J Urol.* 2005; 173: 1923-5.
3. Mills IW, Crossland A, Patel A, Ramonas H: Atorvastatin treatment for men with lower urinary tract symptoms and benign prostatic enlargement. *Eur Urol.* 2007; 52: 503-9.
4. Stamatiou KN, Zaglavira P, Skolarikos A, Sofras F: The effects of lovastatin on conventional medical treatment of lower urinary tract symptoms with finasteride. *Int Braz J Urol.* 2008; 34: 555-61; discussion 561-2.
5. Platz EA, Leitzmann MF, Visvanathan K, Rimm EB, Stampfer MJ, Willett WC, et al.: Statin drugs and risk of advanced prostate cancer. *J Natl Cancer Inst.* 2006; 98: 1819-25.

**Dr. Konstantinos N. Stamatiou**  
*Department of Urology*  
*University of Crete, Greece*  
*Piraeus, Greece*  
*E-mail: stamatiouk@gmail.com*

---

## UROLOGICAL SURVEY

---

**Francisco J.B. Sampaio**  
Urogenital Research Unit  
State University of Rio de Janeiro

**Athanase Billis**  
State University of Campinas  
Campinas, SP, Brazil

**Andreas Böhle**  
Helios Agnes Karll Hospital  
Bad Schwartau, Germany

**Steven B. Brandes**  
Washington University in St. Louis  
St. Louis, Missouri, USA

**Fernando J. Kim**  
Univ Colorado Health Sci Ctr  
Denver, Colorado, USA

**Manoj Monga**  
University of Minnesota  
Edina, MN, USA

**Steven P. Petrou**  
Mayo Medical School  
Jacksonville, Florida, USA

**Adilson Prando**  
Vera Cruz Hospital  
Campinas, SP, Brazil

**Brent W. Snow**  
University of Utah  
Salt Lake City, Utah, USA

**Arnulf Stenzl**  
University of Tuenbingen  
Tuebingen, Germany

## STONE DISEASE

---

### **Impact of real-time visualization of cystoscopy findings on procedural pain in female patients**

Patel AR, Jones JS, Babineau D

*Glickman Urological and Kidney Institute, The Cleveland Clinic, Cleveland, Ohio 44195, USA*

*J Endourol. 2008; 22: 2695-8*

**Background and Purpose:** We have previously shown that men tolerate office flexible cystoscopy better when they simultaneously view the monitor during their procedure. We sought to demonstrate similar effects of distraction on women undergoing rigid office cystoscopy.

**Patients and Methods:** 100 consecutive women underwent diagnostic office based rigid cystoscopy. All patients consented to inclusion in the study. Patients were randomized to two groups. The study group consisted of patients who were allowed to view their procedure real-time on the video monitor. The control group patients had the video screen positioned such that only the surgeon could visualize the procedure. Patients underwent rigid cystoscopy using a 17F cystoscope introduced with an obturator. Water-soluble lubricant was liberally applied to all cystoscopes immediately before the procedure. Patients who needed additional procedures, including cystodiathermy or stent extraction, were excluded from the study groups. Postprocedure, patients were asked to record their experience on a 100-mm visual analog pain scale as soon as the surgeon left the room.

**Results:** Women who were able to view their cystoscopy findings simultaneously during the procedure did not demonstrate lower pain scores compared with those who did not view the screen (median pain score of 19 v 10;  $P = 0.16$ , based on Wilcoxon rank sum test).

**Conclusions:** In contrast to the decreased pain scores demonstrated when tested in men, use of distraction by allowing patients to simultaneously view their procedure may not affect procedure tolerance for women undergoing office-based rigid cystoscopy.

#### **Editorial Comment**

The authors present a well-designed and conducted randomized prospective clinical trial to evaluate the impact of video-endoscopic visualization on procedural pain during rigid cystoscopy in females. They do not report if a power analysis was conducted - it is possible that a Type 2 error may be encountered due to small sample size.

The authors have previously reported decreased pain scores in men undergoing flexible cystoscopy when the patients are allowed to visualize the cystoscopic findings on the video tower. As the authors note, the lack of a difference in pain scores in women may be related to the use of rigid cystoscope or positioning in a lithotomy as opposed to supine position.

It would be helpful to document at what point during the procedure did the women report the most discomfort - if during insertion, this would support the hypothesis that the use of an obturator during blind insertion of the cystoscope eliminates the value of visualization during the procedure. Alternatively, if discomfort was reported during filling with irrigant, was this more common in women with voiding dysfunction and did it correlate with the volume of irrigant instilled or patient's bladder capacity?

It would be important to exclude patients who have previously undergone cystoscopy - as pre-procedural anxiety has been reported to correlate with procedural pain. It would be interesting to repeat the study in men using a television show as a sham control - is it distraction that diminishes pain, or is it "visual feedback" that facilitates relaxation as the scope is passed through the bulbar, membranous and prostatic urethra?

**Dr. Manoj Monga**

*Professor, Department of Urology*

*University of Minnesota*

*Edina, Minnesota, USA*

*E-mail: endourol@yahoo.com*

### **Retrograde, antegrade, and laparoscopic approaches for the management of large, proximal ureteral stones: a randomized clinical trial**

Basiri A, Simforoosh N, Ziaee A, Shayaninasab H, Moghaddam SM, Zare S

*Urology and Nephrology Research Center, Tehran, Iran*

*J Endourol.* 2008; 22: 2677-80

**Background and Purpose:** Multiple procedures have been introduced for the management of urinary stones in the upper ureter. In this randomized clinical trial, we compared three surgical options in this regard.

**Patients and Methods:** From September 2004 to May 2006, we enrolled in the study 150 patients with upper ureteral stones who were referred to our center. We included patients with a stone size  $\geq 1.5$  cm in the greatest diameter. Using the random table, patients were divided into three 50-patient groups by treatment: Group A, retrograde ureteroscopic lithotripsy using a semirigid ureteroscope; group B, transperitoneal laparoscopic ureterolithotomy; and group C, percutaneous nephrolithotripsy. All procedures were performed in a training program.

**Results:** The stone-free rates for patients in groups A, B, and C, at discharge and 3 weeks later, were 56%, 88% and 64% and 76%, 90% and 86%, respectively. Conversion to open surgery and repeated laparoscopy was necessary for two and one patients in group B. Urinary leakage continued more than 3 days in eight (16%) and nine (18%) patients in groups B and C after operation, respectively ( $P = 0.7$ ). **Conclusions:** Although the success rate of ureteroscopy was not significantly lower than the two other options, the complications seen with this technique were negligible. Consequently, the procedure of choice for large proximal ureteral stones seems to depend on surgeon expertise and availability of equipment.

#### **Editorial Comment**

The authors are to be commended for conducting a randomized prospective study of a difficult clinical situation. Indeed, it is note-worthy that they were able to recruit 150 patients with  $> 1.5$  cm proximal ureteral calculi in less than 2 years. Similarly, it is a challenge to consent patients to be randomized to procedures that vary greatly in the degree of invasiveness and risk.

The authors concluded that ureteroscopy is a reasonable first alternative as the severity of potential complications is lower than the other procedures tested. Indeed, patients would tend to agree with this assessment, and if given the alternative of shockwave lithotripsy (not tested in the current study due to concerns of efficacy) would often select SWL over more effective procedures.

The study is somewhat limited by the choice of technology. The authors did not utilize flexible endoscopy - either flexible ureteroscopy as an adjunct to the ureteroscopic approach, or flexible cystoscopy/ureteroscopy as an adjunct to the antegrade percutaneous approach. One would anticipate that these modalities would significantly improve the initial post-procedural stone-free rates. Pneumatic lithotripsy has been demonstrated to lead to greater stone migration and larger stone fragments. Intraoperative ultrasound may have facilitated identification of the "missed stone" in the laparoscopic group.

The authors did not stratify results based on the severity of hydronephrosis - it is our practice to consider the antegrade approach if we anticipate that the severity of hydronephrosis will preclude manipulation of the flexible ureteroscope for stone retrieval. The authors report a high secondary procedure rate in all groups in this study (10-20%); underscoring the challenge of the large ureteral calculus. Most importantly, it tempers the enthusiasm of prior reports of laparoscopic ureterolithotomy.

In summary, the addition of a flexible ureteroscope and decreased reliance on pneumatic lithotripsy may have placed ureteroscopy more solidly as the front-runner for large proximal ureteral stones.

***Dr. Manoj Monga***

*Professor, Department of Urology*

*University of Minnesota*

*Edina, Minnesota, USA*

*E-mail: endourol@yahoo.com*

## ENDOUROLOGY & LAPAROSCOPY

---

### **Robot assisted laparoscopic partial nephrectomy: a viable and safe option in children**

Lee RS, Sethi AS, Passerotti CC, Retik AB, Borer JG, Nguyen HT, Peters CA

*Department of Urology, Children's Hospital Boston, Boston, Massachusetts, USA*

J Urol. 2009; 181: 823-8; discussion 828-9

**Purpose:** The safety, benefits and usefulness of laparoscopic partial nephrectomy have been demonstrated in the pediatric population. We describe our technique, and determine the safety and feasibility of robot assisted laparoscopic partial nephrectomy based on our initial experience.

**Materials and Methods:** We retrospectively reviewed robot assisted laparoscopic partial nephrectomy performed at our institution between 2002 and 2005. The technique was conducted via a transperitoneal approach with the da Vinci Surgical System using standard laparoscopic procedural steps. Clinical indicators of outcomes included estimated blood loss, complications, in hospital narcotic use and length of stay.

**Results:** Robot assisted laparoscopic partial nephrectomy was completed successfully in 9 cases. Mean patient age was 7.2 years and mean follow-up was 6 months. Mean operative time was 275 minutes and mean estimated blood loss was 49 mL. Operative times improved significantly with experience. Overall patients had a mean hospitalization of 2.9 days and required 1.3 mg morphine per kg. All patients had a normal remaining renal moiety confirmed on Doppler ultrasound. The only complication was an asymptomatic urinoma discovered on ultrasound, which was treated with percutaneous drainage and ultimately resolved.

**Conclusions:** Our initial experience shows the safety and feasibility of robot assisted laparoscopic partial nephrectomy in children. Operative time decreases with experience. The enhanced visualization and dexterity of a robotic system potentially offer improved efficiency and safety over standard laparoscopy. Robot assisted laparoscopy is an option for partial nephrectomy and may become the minimally invasive treatment of choice.

### **Editorial Comment**

This report on robotic assisted laparoscopic partial nephrectomy in the pediatric population is another pioneering manuscript that raises the everlasting question of minimally invasive surgery in children and the true benefits that this treatment modality offers. Another similar major query is the advantage of robotic surgery versus standard laparoscopic procedure.

The later would allow the surgeon to reach the lowest more distal ureteral cuff when performing the ureterectomy to prevent stump infection and other complications, with ease without docking and docking the robot to re-position the patient. Cost is also a major consideration since the economics of health care has been influencing somewhat how we practice medicine today. These issues do not take any merit from the authors that developed a very nice minimally invasive approach to a common pediatric dilemma with minimal complications.

***Dr. Fernando J. Kim***

*Chief of Urology, Denver Health Med. Ctr.*

*Assistant Professor, Univ. Colorado Health Sci. Ctr.*

*Denver, Colorado, USA*

*E-mail: fernando.kim@uchsc.edu*

### **Histological evaluation of cold versus hot cutting: clinical impact on margin status for laparoscopic partial nephrectomy**

Phillips JM, Narula N, Deane LA, Box GN, Lee HJ, Ornstein DK, McDougall EM, Clayman RV

*Department of Urology, University of California-Irvine, Irvine, California, USA*

J Urol. 2008; 180: 2348-52

**Purpose:** While most laparoscopic nephron sparing surgery is performed using cold scissors, energy based devices may also be used. A criticism of this approach has been the potential thermal destruction of the cellular architecture at the tumor margin, precluding the ability to accurately determine whether tumor cells are present. We clinically characterized the histological appearance of tumor margins excised with cold scissors, and bipolar and ultrasonic shears.

**Materials and Methods:** We evaluated 40 renal mass excisions performed by a total of 3 urologists at our institution between February 2003 and March 2007. There were 10 bipolar (5 mm LigaSure), 20 ultrasonic (Harmonic Scalpel) and 10 cold excisions. All slides were randomly evaluated twice by a single pathologist blinded to surgeon and excision method. Histological interpretation of the margin was scored as clear vs. indeterminate. Variables, including margin fragmentation, artifact, extravascular blood clot, parenchymal hemorrhage, capillary congestion and vessel sealing, were assessed and scored on a scale of 0 to 3, that is 0--none, 1-1% to 25%, 2-26% to 50% and 3--greater than 50%.

**Results:** The pathologist was able to confidently identify cells at the margin as being malignant or benign in all cases. Histologically the ultrasonic scalpel demonstrated increased fragmentation and extravascular blood clotting compared with those of the other cutting methods ( $p < 0.025$  and  $< 0.026$ , respectively). The ultrasonic scalpel also showed increased artifact depth compared to that of cold cutting ( $p < 0.001$ ). There were no statistical differences between the groups regarding margin artifact, parenchymal hemorrhage or capillary congestion. No statistical significance was observed in any variables between bipolar and cold cutting.

**Conclusions:** Despite some degree of cellular damage the ability to determine whether cells at the margin were benign or malignant was not affected by using an energy based bipolar or ultrasonic device.

### **Editorial Comment**

Laparoscopic partial nephrectomy remains to be challenging technically due to reconstructive steps but also oncological principles should be maintained.

The optimal laparoscopic instrument to excise the renal mass during laparoscopic partial nephrectomy would be the one that not only precisely removes the mass but also performs coagulation of renal parenchymal vessels so bleeding would not be relevant during this procedure.

The dilemma is whether energy could also destroy possible cancer cells during the excision of the mass, allowing coagulation but not disturbing the histology so the pathological examination is well evaluated to accurately grade and stage the tumor and its surgical margins. The authors examined the preference of 3 surgeons and although the possible artifacts maybe increased with the harmonic scalpel when compared to "cold" cut (no energy) and LigaSure, the ultrasonic device did not distort the histological sample to evaluate its margin status.

Finally, renal hilar clamping may decrease margin positivity due to better visualization compared to excision of renal masses with no vascular control.

**Dr. Fernando J. Kim**

*Chief of Urology, Denver Health Med. Ctr.*

*Assistant Professor, Univ. Colorado Health Sci. Ctr.*

*Denver, Colorado, USA*

*E-mail: fernando.kim@uchsc.edu*

## IMAGING

---

### **Prostate cancer: apparent diffusion coefficient map with T2-weighted images for detection - a multireader study**

Lim HK, Kim JK, Kim KA, Cho KS

*Department of Radiology, Asan Medical Center, University of Ulsan, Songpa-gu, Seoul, South Korea*  
*Radiology. 2009; 250: 145-51*

**Purpose:** To retrospectively assess the incremental value of an apparent diffusion coefficient (ADC) map combined with T2-weighted magnetic resonance (MR) images compared with T2-weighted images alone for prostate cancer detection by using a pathologic map as the reference standard.

**Materials and Methods:** This retrospective study was approved by the institutional review board; informed consent was waived. The study included 52 patients (mean age, 65 years +/- 5 [standard deviation]; range, 48-76 years) who underwent endorectal MR imaging and step-section histologic examination. Three readers with varying experience levels reviewed T2-weighted images alone, the ADC map alone, and T2-weighted images and ADC maps. The prostate was divided into 12 segments. The probability of prostate cancer in each segment on MR images was recorded with a five-point scale. Areas under the receiver operating characteristic curve (AUCs) were compared by using the Z test; sensitivity and specificity were determined with the Z test after adjusting for data clustering.

**Results:** AUC of T2-weighted and ADC data (reader 1, 0.90; reader 2, 0.88; reader 3, 0.76) was greater than that of T2-weighted images (reader 1, 0.79; reader 2, 0.75; reader 3, 0.66) for all readers ( $P < .0001$  in all comparisons). AUC of T2-weighted and ADC data was greater for readers 1 and 2 than for reader 3 ( $P < .001$ ). Sensitivity of T2-weighted and ADC data (reader 1, 88%; reader 2, 81%; and reader 3, 78%) was greater than that of T2-weighted images (reader 1, 74%; reader 2, 67%; reader 3, 67%) for all readers ( $P = .01$  for reader 1;  $P = .02$  for readers 2 and 3). Specificity of T2-weighted and ADC data was greater than that of T2-weighted images for reader 1 (88% vs. 79%,  $P = .03$ ) and reader 2 (89% vs. 77%,  $P < .001$ ).

**Conclusion:** The addition of an ADC map to T2-weighted images can improve the diagnostic performance of MR imaging in prostate cancer detection. (c) RSNA, 2008.

### **Editorial Comment**

Nowadays there is a worldwide tendency to perform a multiparametric endorectal magnetic resonance imaging evaluation of patients suspected or having prostate cancer. On multiparametric MRI evaluation, prostate cancer appears as an area with reduced T2 signal intensity on conventional T2-weighted images, increased choline and decreased citrate and polyamines on magnetic resonance spectroscopic imaging, decreased diffusivity on diffusion weighted-imaging (DWI), and increased uptake on dynamic contrast enhanced (DCE) imaging. All techniques are accomplished in a complete, one-stop shop examination that takes place in about 60-min. Each complementary method has inherent advantages and disadvantages; therefore, they should be combined. The best way to combine these techniques however still needs to be determined. The authors found that the addition of DWI (which is quantified by the apparent diffusion coefficient map-ADC) to the conventional T2-weighted images further improves the performance of MRI in prostate cancer detection.

The results of this work support that the best characterization of prostate cancer in individual patients will most like result from a multiparametric examination that combines conventional MRI, spectroscopy, diffusion-weighted images and dynamic contrast enhanced technique.

**Dr. Adilson Prando**

*Chief, Department of Radiology and  
 Diagnostic Imaging, Vera Cruz Hospital  
 Campinas, São Paulo, Brazil  
 E-mail: adilson.prando@gmail.com*

## **Angiomyolipoma with minimal fat on MDCT: can counts of negative-attenuation pixels aid diagnosis?**

Simpfendorfer C, Herts BR, Motta-Ramirez GA, Lockwood DS, Zhou M, Leiber M, Remer EM

*Section of Abdominal Imaging, Imaging Institute, Cleveland Clinic, Cleveland, OH, USA*

AJR Am J Roentgenol. 2009; 192: 438-43

**Objective:** The purpose of this study was to determine whether counts of pixels with subzero attenuation on CT scans can aid in the diagnosis of renal angiomyolipoma with minimal fat.

**Materials and Methods:** Of 33 angiomyolipomas identified among 719 renal masses resected from 702 patients over 4 years, 15 masses in 15 patients were prospectively diagnosed on the basis of the presence of fat at MDCT. The 18 patients with minimal-fat angiomyolipoma and a matched (age, sex, tumor size) cohort of patients with renal cell carcinoma were included in this study. Three radiologists independently counted the number of pixels with attenuation less than -10, -20, and -30 HU. Receiver operating characteristic analysis of the number of pixels at each cutoff was used to calculate sensitivity, specificity, and positive predictive value with the following criteria: 1, more than 10 pixels less than -20 HU; 2, more than 20 pixels less than -20 HU; 3, more than 5 pixels less than -30 HU.

**Results:** Using criterion 1, reader A identified six angiomyolipomas; reader B, five; and reader C, two. The combined sensitivity was 24%; specificity, 98%; and positive predictive value, 69%. Using criterion 2, reader A identified three angiomyolipomas; reader B, four; and reader C, two. The combined sensitivity was 17%; specificity, 100%; and positive predictive value, 100%. Using criterion 3, reader A identified four angiomyolipomas; reader B, four; and reader C, two. The combined sensitivity was 18%; specificity, 100%; and positive predictive value, 100%.

**Conclusion:** CT findings of more than 20 pixels with attenuation less than -20 HU and more than 5 pixels with attenuation less than -30 HU have a positive predictive value of 100% in detection of angiomyolipoma, but most angiomyolipomas with minimal fat cannot be reliably identified on the basis of an absolute pixel count.

### **Editorial Comment**

Adequate preoperative imaging characterization of small angiomyolipoma (AML) is essential since 3-7% of suspicious renal masses resected are found to be AML. AML is characterized by the presence of variable amount of fat within a renal mass. From the practical point of view (evidence based medicine), all renal mass containing fat are considered AML. The use of thin-section (2-5 mm) unenhanced CT is the best method for detecting even small amounts of fat. Previous reports have been shown that if fat within a mass is not visually obvious, pixel mapping can be performed, which may reveal the fat as clustered pixels with negative CT numbers (defined as at least 3 adjacent pixels with attenuation -20 HU) (1). The drawbacks of these previous reports are lack of pathologic confirmation and absence of a control group. The authors of this manuscript found that in a study with pathologic correlation the CT findings of more than 20 pixels with attenuation less than -20 HU and more than 5 pixels with attenuation less than -30 HU have a positive predictive value of 100% in detection of angiomyolipoma. These AMLs presented at pathologic examination more than 10% of fat.

AMLs containing less than 10% of fat at pathologic examination could not be characterized on the basis of an absolute pixel count. Perhaps, for the sake of clarity, we should call AMLs with minimal fat those with tiny amount of visible fat and those in which only CT pixel mapping is able to demonstrate negative attenuation. AMLs with less than 10% of fat should be called AMLs without radiologic evidence of fat. The latter category is indistinguishable from renal cell carcinoma and for this reason, imaging guided percutaneous biopsy is indicated.

**Reference**

1. Takahashi K, Honda M, Okubo RS, Hyodo H, Takakusaki H, Yokoyama H, et al.: CT pixel mapping in the diagnosis of small angiomyolipomas of the kidneys. *J Comput Assist Tomogr.* 1993; 17: 98-101.

**Dr. Adilson Prando**

*Chief, Department of Radiology and  
Diagnostic Imaging, Vera Cruz Hospital  
Campinas, São Paulo, Brazil  
E-mail: adilson.prando@gmail.com*

**PATHOLOGY**

---

**Gleason grading of prostatic adenocarcinoma with glomeruloid features on needle biopsy**

Lotan TL, Epstein JI

*Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD 21231, USA*

*Hum Pathol.* 2009; 5: [Epub ahead of print]

Glomerulations in prostatic adenocarcinoma are characterized by dilated glands containing intraluminal cribriform structures with a single point of attachment, resembling a renal glomerulus. On prostate biopsy, glomerulations are exclusively associated with carcinoma and not associated with benign mimickers. However, the Gleason grading of carcinoma with glomerulations on needle biopsy remains controversial. We prospectively collected 45 prostate needle biopsies containing carcinoma with glomeruloid features from our consult files for a 9-month period and examined the association between glomerulations and the presence of concurrent high-grade carcinoma. Glomerulations were overwhelmingly associated with high-grade cancer on the same core, composed of either Gleason pattern 4 (n = 36, 80% of cases) or Gleason pattern 5 (n = 2, 4% of cases). Only a minority of glomerulations were surrounded exclusively by pattern 3 cancer (n = 7, 16% of cases) on the same core. Most of the cases with surrounding pattern 4 cancer were scored as 3 + 4 = 7 (n = 24, 66%), whereas a smaller fraction were scored as 4 + 3 = 7 (n = 9, 26%), and only a minority were 4 + 4 = 8 (n = 3, 9%). In most cases, glomeruloid change was present on the same core as the highest Gleason score carcinoma of the case. None of the pattern 3 cases and only a minority of the pattern 4 cancers had higher Gleason score carcinoma on additional cores (n = 5, 14%). Glomeruloid structures are a rare but diagnostic feature of prostatic carcinoma on needle biopsy. Our data indicate that glomerulations are overwhelmingly associated with concurrent Gleason pattern 4 or higher-grade carcinoma. In several cases, transition could be seen among small glomerulations, large glomeruloid structures, and cribriform pattern 4 cancer. These data suggest that glomerulations represent an early stage of cribriform pattern 4 cancer and, until follow-up data are available, are best graded as Gleason pattern 4.

**Editorial Comment**

The grading of prostatic adenocarcinoma with glomeruloid structures is controversial (1-3). Some urological pathologists do not assign a grade to this pattern and just grade the surrounding tumor. Other experts in the field feel that all glomeruloid structures should be assigned a Gleason pattern 4.

The glomeruloid feature in adenocarcinoma of the prostate refers to an architectural pattern of growth that mimics the renal glomerulus (1,3,4). Glomeruloid structures have been described in Wilm's tumor (5) probably representing differentiation of neoplastic cells toward a primitive form of renal glomerulus and are sometimes present in gliomas (6). In a rare case of adenoma (hamartoma) of bladder in siblings, spaces, often

cystic, lined with neoplastic epithelial cells with hyperchromatic nuclei were crowded at one of the poles which strikingly resembled primitive glomeruli (7).

This distinctive pattern of prostate cancer was first described in 1995 by Epstein in his book Prostate biopsy interpretation and called the lesion glomerulations (8). In 1998, Pacelli et al. (1) published a series of prostatic adenocarcinoma with glomeruloid features in biopsies and radical prostatectomies. The frequency of adenocarcinoma with glomeruloid features in 100 needle prostatic biopsies was 3% in Pacelli's series.

Glomeruloid structures appear to be a specific but uncommon finding in prostate cancer. They are not seen in benign prostatic tissue, nodular hyperplasia, basal cell hyperplasia, atypical adenomatous hyperplasia, or prostatic intraepithelial neoplasia (3,4).

In Lotan and Epstein's study glomeruloid structures were associated to Gleason pattern 4 or 5 in more than 80% of the cases. In only 16% of the cases were associated exclusively to Gleason pattern 3. The authors suggest that glomerulations represent an early stage of cribriform pattern 4 cancer and, until follow-up data are available, are best graded as Gleason pattern 4.

In a similar study based on 264 needle biopsies, we found 28/264 (10.6%) biopsies showing glomeruloid structures; 9/28 (32.14%) biopsies the glomeruloid structures were surrounded by Gleason low-grade tumor and in 19/28 (67.85%) biopsies surrounded by Gleason high-grade tumor (9). All patients in our study were submitted to radical prostatectomy. Comparing the findings for several clinicopathologic variables between patients with and without glomeruloid structures, no statistical significance was found and at 5 years, the PSA progression-free survival rates were 57% and 52% for patients without and with glomeruloid structures (log-rank,  $p = 0.26$ ). Glomeruloid structures were associated more frequently with Gleason high-grade surrounding tumor, however, the presence of this architectural pattern was not associated to any other adverse clinicopathologic findings. It seems in our study that glomeruloid feature per se should not interfere in the grading of a tumor.

### References

1. Pacelli A, Lopez-Beltran A, Egan AJ, Bostwick DG: Prostatic adenocarcinoma with glomeruloid features. *Hum Pathol.* 1998; 29: 543-6.
2. Epstein JI, Allsbrook WC Jr, Amin MB, Egevad LL; ISUP Grading Committee: The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol.* 2005; 29: 1228-42.
3. Epstein JI, Netto GJ: *Biopsy Interpretation of the Prostate*, 4th ed., Philadelphia, Lippincott Williams & Wilkins. 2008.
4. Baisden BL, Kahane H, Epstein JI: Perineural invasion, mucinous fibroplasia, and glomerulations: diagnostic features of limited cancer on prostate needle biopsy. *Am J Surg Pathol.* 1999; 23: 918-24.
5. Murphy WM, Beckwith JB, Farrow GM: Tumors of the Kidney, Bladder, and Related Urinary Structures. In: *Atlas of Tumor Pathology*, 3rd series, fascicle 11. Washington DC, Armed Forces Institute of Pathology. 1994.
6. Haddad SF, Moore SA, Schelper RL, Goeken JA: Vascular smooth muscle hyperplasia underlies the formation of glomeruloid vascular structures of glioblastoma multiforme. *J Neuropathol Exp Neurol.* 1992; 51: 488-92.
7. Billis A, Lima AC, Queiroz LS, Cia EM, Oliveira ER, Pinto W Jr: Adenoma of bladder in siblings with renal dysplasia. *Urology.* 1980; 16: 299-302.
8. Epstein JI. Evaluation in Needle Biopsy Specimens. In: *Prostate Biopsy Interpretation*, 2nd ed., Philadelphia, Lippincott Raven. 1995, pp. 95-6.
9. Quintal MM, Billis A, Meirelles L, Freitas LL, Duarte AG, Silva CA, Bisson MA, Magna LA: Glomeruloid structures on needle prostatic biopsies: should they be assigned a grade or rather just grade the surrounding tumor? *Mod Pathol.* 2009; Abstract [in press].

**Dr. Athanase Billis**  
*Full-Professor of Pathology*  
*State University of Campinas, Unicamp*  
*Campinas, São Paulo, Brazil*  
*E-mail: athanase@fcm.unicamp.br*

## Precursor lesions to prostatic adenocarcinoma

Epstein JI

*Departments of Pathology, Urology and Oncology, The Johns Hopkins Hospital, 401 N. Broadway St., Rm 2242, Baltimore, MD, 21231, USA*

Virchows Arch. 2009; 454: 1-16

High-grade prostatic intraepithelial neoplasia (PIN) is the one well-documented precursor to adenocarcinoma of the prostate. This review article defines both low- and high-grade PIN. Unusual variants of high-grade PIN are illustrated. Benign lesions that may be confused with high-grade PIN, including central zone histology, clear cell cribriform hyperplasia, and basal cell hyperplasia are described and illustrated. High-grade PIN is also differentiated from invasive acinar (usual) and ductal adenocarcinoma. The incidence of high-grade PIN, its relationship to carcinoma (including molecular findings), and risk of cancer on rebiopsy are covered in detail. Finally, intraductal carcinoma of the prostate, a controversial entity, is discussed and differentiated from high-grade PIN.

### Editorial Comment

This is a nice review on precursor lesions to prostatic carcinoma. High-grade prostatic intraepithelial neoplasia (PIN) (Figure-1) was previously described by many authors using such terms as atypical epithelial proliferation, atypical glandular hyperplasia, atypical glandular proliferation, atypical hyperplasia, dysplastic lesions, dysplastic hyperplasia, cribriform hyperplasia, and atypical primary hyperplasia (1-6). These lesions were of interest for German authors and in the 80s studied by American authors. Bostwick described 3 grades for the lesion: low, intermediate and high-grade - grades 1, 2, and 3 (7). In 1989 during an international workshop in Bethesda, USA, sponsored by the American Cancer Society in an attempt to unify nomenclature it was introduced the term prostatic intraepithelial neoplasia (PIN) (8). In the same workshop it was suggested to refer in the pathology reports only to high-grade PIN (grades 2 or 3) due to the fact that low-grade PIN (grade 1) lesions have poor reproducibility among pathologists and lack any significant association with concomitant cancer.

The presence of PIN in a biopsy means a high frequency for finding cancer in a second biopsy. This frequency varies in the literature between 26% and 53%, however, with the advent of extended biopsies this frequency today is 27%-31% (9). In a study by Herawi et al. (10) the risk of cancer on biopsy within 1 year following a diagnosis of high-grade PIN in extended biopsies was very low (13.3%). Herawi et al. concluded that for patients diagnosed with high-grade PIN on extended initial core sample, a repeat biopsy within the first year is unnecessary in the absence of other clinical indicators of cancer.

### References

1. Neller VK, Neüburger K: Ueber atypische Epithelwucherungen und beginnende Karzinome in der senilen Prostata. *Munchen Med Wschr.* 1926; 73: 57-9.
2. Oertel H: An Address on Involutionary Changes in Prostate and Female Breast in Relation to Cancer Development. *Can Med Assoc J.* 1926; 16: 237-241.
3. Tannenbaum M: Histopathology of the Prostate Gland. In: Tannenbaum M (ed.), *Urologic Pathology, The Prostate.* Philadelphia, Lea and Febiger. 1977, p. 305.
4. Helpap B: The biological significance of atypical hyperplasia of the prostate. *Virchows Arch A Pathol Anat Histol.* 1980; 387: 307-17.
5. Kastendieck H, Altenähr E: Dysplasieformen in der menschlichen Prostatadrüse. *Verh Dtsch Ges Pathol.* 1976; 60: 462.
6. Kastendieck H: Correlations between atypical primary hyperplasia and carcinoma of the prostate. A histological study of 180 total prostatectomies. *Pathol Res Pract.* 1980; 169: 366-87.

7. Bostwick DG, Brawer MK: Prostatic intra-epithelial neoplasia and early invasion in prostate cancer. *Cancer*. 1987; 59: 788-94.
8. Drago JR, Mostofi FK, Lee F: Introductory remarks and workshop summary. *Urology*. 1989 (suppl); 34: 2-3.
9. Amin M, Boccon-Gibod L, Egevad L, Epstein JI, Humphrey PA, Mikuz G, et al.: Prognostic and predictive factors and reporting of prostate carcinoma in prostate needle biopsy specimens. *Scand J Urol Nephrol Suppl*. 2005; 216: 20-33.
10. Herawi M, Kahane H, Cavallo C, Epstein JI: Risk of prostate cancer on first re-biopsy within 1 year following a diagnosis of high grade prostatic intraepithelial neoplasia is related to the number of cores sampled. *J Urol*. 2006; 175: 121-4.

**Dr. Athanase Billis**  
*Full-Professor of Pathology*  
*State University of Campinas, Unicamp*  
*Campinas, São Paulo, Brazil*  
*E-mail: athanase@fcm.unicamp.br*

## BASIC AND TRANSLATIONAL UROLOGY

---

### **Botulinum toxin-A to improve urethral wound healing: an experimental study in a rat model**

Sahinkanat T, Ozkan KU, Ciralik H, Ozturk S, Resim S

*Department of Urology, University of Kahramanmaraş Sutcu Imam School of Medicine, Kahramanaras, Turkey*

*Urology*. 2009; 73: 405-9

**Objectives:** Tensile distracting forces caused by elements such as a muscle pull can cause widening of scars in the tissue during the wound healing process. The aim of the present study was to investigate whether induced immobilization of the urethral muscle using botulinum toxin-A (BTX-A) enhances wound healing and also reduces the amount of scar formation in an experimentally induced urethral injury in a male rat model.

**Methods:** Prepubertal male albino rats were divided into 2 groups: 20 rats in the BTX-A group received BTX-A injection treatment during surgery and 10 rats in the control group received 0.9% saline solution injection. The penile skin was incised circumferentially and degloved. To make the urethral injury at a location approximately 15 mm proximal to the external meatus, the urethra was cut transversally with scissors, from the 2-o'clock to the 10-o'clock position and then sutured by a single suture at the 6-o'clock position. To evaluate chronic inflammation and fibrosis, the rats were killed, and the injured portions of the urethras were harvested for histopathologic examination after a follow-up period of 21 days.

**Results:** On histopathologic evaluation, the control group rats had a more severe fibrotic change in the urethral tissue compared with the BTX-A injected rats, which showed a mild fibrotic change. The mean +/- SD and median fibrosis score was 2.4 +/- 0.5 and 2 in the control group and 1.5 +/- 0.5 and 1 in the BTX-A group, respectively ( $P < .01$  and  $P < .01$ , respectively).

**Conclusions:** The results of our study have shown that BTX-A prevented increases in collagen content during urethral wound healing.

### **Editorial Comment**

This is a very interesting and inventive study that certainly will open new avenue for treatment of urethral stricture disease. In fact, using biochemical and stereological methods, we have recently found that, when compared to age-matched controls, there is no fibrosis and no collagen increase in the urethral edges of

male patients submitted to end-to-end anastomosis for treating bulbar urethra stenosis (1). Therefore, in well conducted cases, with anastomosis of fibrosis-free urethral edges, the fibrosis that could compromise the results may be a consequence of tensile forces in the anastomotic area and probably BTX-A would help in avoiding it.

#### Reference

1. Carvalho JP, Cavalcanti AG, Costa WS, Cardoso LE, Favorito LA, Sampaio FJ: Stereological and biochemical analysis of the urethral edges in patients submitted to end-to-end anastomosis for bulbar urethral stricture. *J Urol.* 2009 [submitted]

**Dr. Francisco J. B. Sampaio**  
*Full-Professor and Chair, Urogenital Research Unit  
State University of Rio de Janeiro  
Rio de Janeiro, RJ, Brazil  
E-mail: sampaio@urogenitalresearch.org*

#### **Comparisons of the responses of anterior and posterior human adult male bladder neck smooth muscle to in vitro stimulation**

Bolton JF, Whittlestone TH, Sibley GN

*Department of Urology, University of Bristol, Bristol Royal Infirmary, Bristol, UK.*

*BJU Int.* 2008; 102: 1737-42

**Objective:** To evaluate differing methods of stimulation on strips of human bladder neck smooth muscle and compare muscle taken from the anterior and posterior aspects.

**Materials and Methods:** Samples of adult human male bladder neck muscle were obtained from patients undergoing open radical prostatectomy. Muscle was taken from either the anterior or posterior (nine and six patients, respectively) aspects of the bladder neck. Muscle strips dissected from these samples were suspended in the Brading-Sibley organ bath. The strips were superfused with 100 mm KCl-enriched Krebs' solution for 4 min to determine viability. This allowed experimentation on 17 strips from the anterior aspect of the bladder neck and 13 from the posterior bladder neck. These remaining strips were then superfused either with various concentrations ( $\times 10^{-7}$ ) to  $\times 10^{-3}$ m) of carbachol or noradrenaline in Krebs' solution, for 15 s. A further set of strips (eight from anterior, six from posterior) was suspended and responses to electrical field stimulation (EFS) with varying parameters were measured. Each EFS experiment was repeated after a 15 min exposure to  $10^{-3}$ m atropine, and again after a 15 min exposure  $10^{-7}$ m tetrodotoxin (TTX). Tension responses produced in these series of experiments were measured using strain gauges and analysed using data acquisition software. Student's t-test was used for the statistical analysis.

**Results:** All muscle strips included in the study responded to EFS. The magnitude of this contraction is frequency dependent. The contractions were abolished by superfusion of the muscle strips with atropine. There was no further suppression of the contractile response on addition of TTX. Posterior bladder neck samples had a greater mean contractile response per unit mass than anterior strips at all frequencies of  $>1$  Hz, and significantly more at 20 and 30 Hz. There was a concentration-dependent response in bladder neck contraction to carbachol but only in the strips from the anterior bladder neck at concentrations of  $<10^{-3}$ m. Posterior bladder neck strips did not significantly contract upon application of carbachol. Similarly, there was a concentration-dependent response to noradrenaline. Responses to noradrenaline were not uniform around the bladder neck, but not significantly different. Carbachol was the more 'potent' stimulator in anterior smooth muscle strips, but again the differences between agonists were not statistically significant.

Conclusion: These experiments show physiological variability around the circumference of the human male bladder neck. The posterior bladder neck shows significantly stronger contraction to alpha-adrenergic agonists compared with cholinergic agonists; the anterior bladder neck does not have a similarly significant differential response. The uniform response to noradrenaline may underlie the bladder neck's role in the prevention of retrograde ejaculation. The differential responses to carbachol may reflect differences in the embryological derivation of the anterior and posterior bladder neck fibres or in their innervation. Some of these differences may have clinical importance through the action of therapeutic agents.

### Editorial Comment

The authors of this elegant *in vitro* study show by the first time, in the best of my knowledge, that exist important physiological variability in the human male bladder neck. They found that the posterior bladder neck presented significantly stronger contraction to alpha-adrenergic agonists when compared with cholinergic agonists. On the other hand, the anterior bladder neck did not have a similarly significant differential response. The authors also found a uniform response to noradrenaline and this might underlie the role of bladder neck in avoiding retrograde ejaculation. Also, the authors speculated that differential responses to carbachol may reflect differences in the embryological origin of anterior and posterior bladder neck fibers or in their innervation.

**Dr. Francisco J. B. Sampaio**

*Full-Professor and Chair, Urogenital Research Unit*

*State University of Rio de Janeiro*

*Rio de Janeiro, RJ, Brazil*

*E-mail: sampaio@urogenitalresearch.org*

## RECONSTRUCTIVE UROLOGY

---

### **A new suture material for hypospadias surgery: a comparative study**

Guarino N, Vallasciani SA, Marrocco G

*Division of Pediatric Surgery, Ospedale San Camillo-Forlanini, Rome, Italy*

J Urol. 2009; 19. [Epub ahead of print]

Purpose: We compared the results of hypospadias repair using polyglytone versus polydioxanone to evaluate the potential benefit of using a suture with a rapid absorption time.

Materials and Methods: A total of 100 patients 8 to 24 months old affected by distal isolated penile hypospadias were considered for this study. Patients were randomized and assigned to 2 different groups according to the suture material used during the surgical procedure (tubularized incised plate repair with or without preputial reconstruction). Polyglytone was used in group A and polydioxanone was used in group B. All patients were evaluated at 4 intervals (1 week, 1 month, 6 months and 2 years postoperatively). Persistence of sutures on penile skin, urethral fistulas, skin dehiscence, infection and skin tracks were recorded. Statistical analysis was performed using chi-square test.

Results: Follow-up data documented the absence of significant differences in terms of urethral fistula rate, skin dehiscence and acute skin infection. Persistence of sutures and multiple skin tracks at long-term follow-up were significantly greater in patients in group B.

Conclusions: Both sutures are adequate for hypospadias surgery in small children. The use of a rapid absorption monofilament may allow much more rapid disappearance of the skin sutures. In the long term this outcome means almost complete absence of suture tracks. No statistically significant difference in terms of urethrocutaneous fistula was observed, suggesting that the tensile strength of polyglytone is adequate.

### Editorial Comment

The suture material used in reconstructive surgery has always been problematic where durability, fineness and effect to the tissue are critical, especially for use in infants. A significant improvement was attained with the introduction of microsurgical instruments and sutures used with magnification (1).

Guarino et al. compared monofilament sutures (polyglytone vs. polydioxanone) with different strengths (6/0 vs. 7/0) (2). The authors observed an increased risk in knot breakdown; however, the most important difference noted was the duration time: 56d for polyglytone vs. 120-180d for polydioxanone. Polyglytone's long duration time might explain the higher proportion of granuloma, fistula and dehiscence when compared with polydioxanone.

Recently we reported our experiences in hypospadias reconstruction where the MEMO technique was used (3). Although only one suture material (plated polyglytone 7/0) was used in our study, the outcome was similar to the report by Guarino using monofilament polyglytone 6/0. The polyglytone 7/0 material we used is thinner but we did not experience knot break down nor did we note inflammatory reaction substantial developments such as granuloma, fistula or dehiscence.

A long-lasting (120-180d) suture material is not required to facilitate healing at the reconstructed glans location. With the reported experience in our patient group, we also noted, but we did not report in the MEMO paper (3), that monofilament sutures cause discomfort and irritation for the child and the parent because the monofilament suture tip snags easily against the child's diaper.

### References

1. Seibold J, Nagele U, Sievert KD, Stenzl A: Complicated urethral reconstruction in the adult and adult and infant males. *Urologe A*. 2005; 44: 768-73.
2. Guarino N, Vallasciani SA, Marrocco G: A New Suture Material for Hypospadias Surgery: A Comparative Study. *J Urol*. 2009; 19. [Epub ahead of print]
3. Seibold J, Boehmer A, Verger A, Merseburger AS, Stenzl A, Sievert KD: The meatal mobilization technique for coronal/subcoronal hypospadias repair. *BJU Int*. 2007; 100: 164-7; discussion 167.

**Dr. Joerg Seibold,  
Dr. Karl-Dietrich Sievert & Dr. Arnulf Stenzl**  
*Department of Urology  
Eberhard-Karls-University Tuebingen  
Tuebingen, Germany  
E-mail: arnulf.stenzl@med.uni-tuebingen.de*

### Recovery of erectile function after unilateral and bilateral cavernous nerve interposition grafting during radical pelvic surgery

Satkunasivam R, Appu S, Al-Azab R, Hersey K, Lockwood G, Lipa J, Fleshner NE  
*Departments of Surgical Oncology (Division of Urology) (RS, SA, RAA, KH, NEF), Biostatistics (GL) and Plastic Surgery (JL), University Health Network, University of Toronto, Toronto, Ontario, Canada*  
*J Urol*. 2009; 17. [Epub ahead of print]

Purpose: The use of cavernous nerve interposition grafting to preserve erectile function in men who require neurovascular bundle resection for cancer control is controversial. We report outcomes and predictors of cavernous nerve interposition grafting in men undergoing unilateral grafting during radical prostatectomy or bilateral grafting during radical cystectomy and prostatectomy with autologous nerve grafts.

**Materials and Methods:** We retrospectively reviewed the electronic records of 36 patients who underwent cavernous nerve interposition grafting between 2003 and 2006. Postoperatively erectile function was assessed with the International Index of Erectile Function 15-item questionnaire. Predictors of potency, including age at surgery, time since surgery and prostate specific antigen at surgery, were assessed by univariate analysis.

**Results:** A total of 33 patients (92% response rate) were followed for a median of 32, 25 and 11 months after bilateral grafting during radical cystectomy (10), unilateral grafting during radical prostatectomy (20), and bilateral grafting during radical cystectomy and prostatectomy (3), respectively. The rate of potency, defined as the ability to attain and maintain erection sufficient for penetration at least 50% of the time with or without phosphodiesterase-5 inhibitors, was 31% (5 of 13 men) for unilateral grafts, 38% (5 of 16) for bilateral grafts and 30% (3 of 10) for bilateral grafts during radical cystectomy. Age at surgery was the only significant determinant of potency and it showed an inverse relationship in the bilateral nerve graft group ( $p = 0.02$ ).

**Conclusions:** Cavernous nerve interposition grafting appears to have a role in the recovery of erectile function. To our knowledge this study represents the largest series of cavernous nerve interposition grafting during cystectomy and it suggests that this should be considered during bilateral neurovascular bundle resection.

### Editorial Comment

The reconstructive intraoperative approach of the cavernous nerve during radical prostatectomy or even cysto-prostatectomy represents a challenge for the surgeon. Satkunasivam et al. report in this paper their experience with unilateral and bilateral nerve grafting for the cavernous nerve reconstruction.

Although it might still be a point of discussion which material is the best for the graft to re-establish erectile function; sural nerve, genitofemoral nerve or other sources (1,2). The authors used the genitofemoral nerve in 94% of the cases and in the remaining cases, the sural nerve. In a comparison of all cases with a bilateral graft, those patients that received the sural nerve graft were potent; whereas, using the author's definition of potency, only 27.3% of the genitofemoral nerve graft patients were able to successfully maintain erection with a sufficient penetration rate of at least 50%.

Satkunasivam et al. reported on the largest group of radical cystectomy patients who underwent intraoperative nerve grafting. Their findings are consistent with Anastasiadis's report of a 30% success rate after bilateral nerve grafting subsequent to radical cystectomy (3). These reports underline that nerve grafting can be successfully achieved and should be performed if the morbidity of the patient is not endangered by the procedure. Perhaps with the further detailed knowledge about the peripheral nerves concourses on the prostate surface (4-6) and around the bladder, the successful outcome of nerve grafting can be further improved and nerve harvesting can be avoided with the use of regenerated acellular nerve grafts (7).

### References

1. Secin FP, Koppie TM, Scardino PT, Eastham JA, Patel M, Bianco FJ, et al.: Bilateral cavernous nerve interposition grafting during radical retropubic prostatectomy: Memorial Sloan-Kettering Cancer Center experience. *J Urol.* 2007; 177: 664-8.
2. Nelson BA, Chang SS, Cookson MS, Smith JA Jr: Morbidity and efficacy of genitofemoral nerve grafts with radical retropubic prostatectomy. *Urology.* 2006; 67: 789-92.
3. Anastasiadis AG, Benson MC, Rosenwasser MP, Salomon L, El-Rashidy H, Ghafar MA, et al.: Cavernous nerve graft reconstruction during radical prostatectomy or radical cystectomy: safe and technically feasible. *Prostate Cancer Prostatic Dis.* 2003; 6: 56-60.
4. Sievert KD, Hennenlotter J, Laible IA, Amend B, Nagele U, Stenzl A: The Commonly Performed Nerve Sparing Total Prostatectomy Does Not Acknowledge the Actual Nerve Courses. *J Urol.* 2009; 14. [Epub ahead of print]
5. Sievert KD, Hennenlotter J, Laible I, Amend B, Schilling D, Anastasiadis A, et al.: The periprostatic autonomic nerves-bundle or layer? *Eur Urol.* 2008; 54: 1109-16.

6. Ganzer R, Blana A, Gaumann A, Stolzenburg JU, Rabenalt R, Bach T, et al.: Topographical anatomy of periprostatic and capsular nerves: quantification and computerised planimetry. *Eur Urol.* 2008; 54: 353-61.
7. Connolly SS, Yoo JJ, Abouheba M, Soker S, McDougal WS, Atala A: Cavernous nerve regeneration using acellular nerve grafts. *World J Urol.* 2008; 26: 333-9.

**Dr. Karl-Dietrich Sievert &  
Dr. Arnulf Stenzl**

*Department of Urology  
Eberhard-Karls-University Tuebingen  
Tuebingen, Germany*

*E-mail: [arnulf.stenzl@med.uni-tuebingen.de](mailto:arnulf.stenzl@med.uni-tuebingen.de)*

## UROLOGICAL ONCOLOGY

---

### **Secondary cancer after radiotherapy for prostate cancer: should we be more aware of the risk?**

Bostrom PJ, Soloway MS

*Department of Urology, University of Miami Miller School of Medicine, Miami, Florida, USA*

*Eur Urol.* 2007; 52: 973-82

**Objectives:** As the number of prostate cancer survivors is increasing, the long-term health of prostate cancer patients has become a significant health issue. Radiation is known to induce malignant transformation, and prostate cancer radiotherapy is suggested to induce secondary malignancies. This report reviews the available data regarding the risk of secondary cancer after radiation for prostate cancer.

**Methods:** Epidemiological studies of the secondary cancer risk in patients with a history of prostate cancer radiation and the literature regarding radiation-induced carcinogenesis were reviewed.

**Results:** Prostate cancer is not associated with an increased number of additional malignancies. The data suggests a modest increase in secondary cancers associated with radiation for prostate cancer, as approximately one in 70 patients undergoing radiation and surviving more than 10 yr will develop secondary cancer. The most common sites for secondary cancers are bladder and rectum. In addition to the cancers adjacent to the radiation field, there is also an increase of cancers in distant sites, such as lung. The increased risk for secondary cancers is reported after external radiation, not after brachytherapy. The available data originated from studies of patients undergoing conventional radiotherapy. New treatment methods, such as intensity-modulated radiotherapy, may be associated with a higher risk of secondary cancers.

**Conclusion:** Although the incidence of secondary cancers after prostate cancer radiotherapy is not dramatically different from the overall population, patients should be informed about this risk. Other treatment modalities should be considered for patients with long life expectancy and for patients with additional risk factors.

### **Editorial Comment**

Long-term survival after radiotherapy for prostate cancer is not uncommon. The risk of secondary cancers contributable to radiotherapy was analyzed in this review of the literature.

First, the authors analyzed the association of prostate cancer with secondary cancers. In 7 reports on roughly 90,000 patients, no elevation of risk for secondary cancers was obvious. The next analysis involved

roughly 32,000 patients who had received radiation therapy for prostate cancer. In this cohort, the authors found a slight increase of the risk to develop a secondary cancer in areas involving the radiation field, specifically the bladder and rectum with a risk ratio of approximately 1:5. Interestingly, an increased risk was also seen for lung cancer. These data mandate long-term follow-up examinations of the specific sites, that are bladder, rectum and lung, after radiotherapy for prostate cancer.

**Dr. Andreas Bohle**

*Professor of Urology*

*HELIOS Agnes Karll Hospital*

*Bad Schwartau, Germany*

*E-mail: boehle@urologie-bad-schwartau.de*

### **Outcome of prostate cancer patients with initial PSA > or =20 ng/ml undergoing radical prostatectomy**

Zwergel U, Suttman H, Schroeder T, Siemer S, Wullich B, Kamradt J, Lehmann J, Stoeckle M  
*Department of Urology and Pediatric Urology, University of Saarland, Hamburg/Saar, Germany*  
Eur Urol. 2007; 52: 1058-65

**Objectives:** To retrospectively assess the outcome of patients with initial PSA of 20 ng/ml or higher undergoing radical prostatectomy (RP) for prostate cancer (pCA).

**Methods:** Between January 1986 and June 2005, 275 patients with preoperative PSA > or =20 ng/ml underwent RP for pCA at our institution. Overall, disease-specific and biochemical progression-free survival rates for the entire cohort and for particular subgroups were determined.

**Results:** Median patient age at time of surgery was 64 yr (range: 44-75). Fifty-seven patients (20.7%) had pT2 stage, 206 (74.9%) pT3, and 10 (3.7%) pT4; 78 (28.4%) presented with local nodal metastases (pN+). To date, 40 patients have died (14.5%), 22 of pCA and 18 of other causes. Biochemical progression occurred in 92 patients (33.5%). Overall (and disease-specific) survivals at 5, 10, and 15 yr were 87% (93%), 70% (83%), and 58% (71%), respectively. These survival rates did not significantly differ between patients receiving immediate versus deferred hormonal therapy (in case of progression). Five-year PSA progression-free survival in patients on surveillance (receiving deferred hormonal treatment at the onset of rising PSA values) was 53%. For patients on immediate hormonal treatment following RP, the 5-yr hormone-refractory PSA progression rate was 76%.

**Conclusions:** According to long-term follow-up results in this high-risk cohort of patients with preoperative PSA > or = 20 ng/ml, RP can be considered a viable therapeutic option. With regard to combining immediate hormonal therapy with surgery, the optimal treatment following RP remains to be defined.

### **Editorial Comment**

The authors report on a series of 275 prostate cancer patients who received radical prostatectomy (RP) with a preoperative PSA of > 20 ng/ml. The patients had bone scans preoperatively, but MRI or CT was offered only in case of clinically suspected metastatic disease. Only 20.7% of patients had organ-confined disease, whereas 74.9 % had pT3 cancer (with pT3b in 43.9%). Only 7.6% had Gleason sum score of 5 and 6 whereas Gleason 7 was seen in 43.3% and Gleason 9 in 28.1 %. Interestingly, even in this high-risk group of patients, cancer-specific survival after 5, 10 and 15 years was 93%, 83% and 71%, respectively. No difference was

seen between cohorts receiving immediate versus deferred hormon-ablative therapy. These data support active therapy in patients with high-risk cancer.

**Dr. Andreas Bohle**  
Professor of Urology  
HELIOS Agnes Karll Hospital  
Bad Schwartau, Germany  
E-mail: boehle@urologie-bad-schwartau.de

## NEUROUROLOGY & FEMALE UROLOGY

---

### **Correlation of morphological alterations and functional impairment of the tension-free vaginal tape obturator procedure**

Yang JM, Yang SH, Huang WC

*Division of Urogynecology, Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan, Republic of China*

J Urol. 2009; 181: 211-8

**Purpose:** We explored the morphological features associated with functional impairment in patients undergoing the tension-free vaginal tape obturator procedure. **Materials and Methods:** We retrospectively reviewed the records of 98 women who underwent the tension-free vaginal tape obturator procedure alone or with concomitant pelvic surgery. Postoperative assessment included a symptom questionnaire, ultrasound cystourethrography and a cough stress test. During followup the measures of postoperative functional impairment included a positive cough stress test, new onset voiding dysfunction and the worsening or progression of urge symptoms.

**Results:** Median follow-up was 22 months. During follow-up 11 women had a positive cough stress test, 22 had voiding dysfunction and 12 had worsening or new onset urge symptoms. Failure was associated with 4 variables on multiple logistic regression analysis, including absent urethral encroachment at rest (OR 16.63, 95% CI 1.87-147.85,  $p = 0.01$ ), bladder neck funneling (OR 8.27, 95% CI 1.99-34.26,  $p < 0.01$ ), a urethral location of less than the 50th percentile (OR 6.01, 95% CI 1.43-25.25,  $p = 0.01$ ) and a resting tape angle of less than 165 degrees (OR 5.21, 95% CI 1.15-23.54,  $p = 0.03$ ). A resting tape distance of less than 12.0 mm (OR 3.00, 95% CI 1.44-6.26,  $p < 0.01$ ) and urethral encroachment at rest (OR 2.86, 95% CI 1.30-6.30,  $p < 0.01$ ) were the variables predictive of postoperative voiding dysfunction. Bladder neck funneling was the only risk factor for postoperative urge symptoms ( $p < 0.01$ ).

**Conclusions:** The tension-free vaginal tape obturator procedure achieves its effectiveness in a process of biological reaction and mechanical interaction between the tape and urethra. When this mechanical interaction is too great or too little, there is functional impairment after the procedure.

### **Editorial Comment**

The authors describe their experience and findings when examining a patient population who has undergone a transobturator tape procedure. Postoperative follow-up included questionnaire analysis, physical examination and ultrasound cystourethrography. The surgeons used transvaginal ultrasound at the time of surgery to assure that there was not indentation of the urethra on initial placement. Postoperatively, their success rate for stress urinary incontinence was approximately 90% with approximately 75% having resolved their urinary urge incontinence with a 3% de novo development of urinary urge incontinence. They found that urethral encroachment at rest and a distance between the tape and the symphysis pubis of  $< 12$  mm were associated with obstructive voiding symptoms in their patient population.

The authors publish an excellent manuscript describing their observations of the dynamic forces and reaction of the transobturator suburethral tape during Valhalla maneuvers. They further break down the movement of the tape and its' effect on the urethra into 5 types. That they were able to identify urethral encroachment while the tape at rest as being significantly associated with obstructive voiding phenomenon definitely lends support to the consideration of using transvaginal ultrasound when evaluating for post-procedure urinary obstruction. We currently utilize fluorourodynamics as well temporal association of symptoms to diagnose postoperative urethral obstruction but will consider strongly the incorporation of transvaginal ultrasound in an effort to assist in this sometimes challenging patient population.

**Dr. Steven P. Petrou**

*Associate Professor of Urology*

*Chief of Surgery, St. Luke's Hospital*

*Associate Dean, Mayo School of Graduate Medical Education*

*Jacksonville, Florida, USA*

*E-mail: petrou.steven@mayo.edu*

### **Pubo-urethral ligament injury causes long-term stress urinary incontinence in female rats: an animal model of the integral theory**

Kefer JC, Liu G, Daneshgari F

*Glickman Urological Institute, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, USA*

*J Urol. 2009; 181: 397-400*

**Purpose:** We examined the long-term effects of pubo-urethral ligament deficiency as a potential model of stress urinary incontinence compared to an established model of stress urinary incontinence.

**Materials and Methods:** A total of 21 female Sprague-Dawley rats were randomly assigned to 1 of 3 groups, including pubo-urethral ligament transection, sham pubo-urethral ligament transection and bilateral pudendal nerve transection. Leak point pressure was measured 28 days later via an implanted suprapubic catheter. After leak point pressure measurement all animals were sacrificed. The pubic arch and pelvic organs were harvested for histological examination. The Wilcoxon rank sum test was used to evaluate differences in leak point pressure among the experimental groups. **Results:** At 28 days after pubo-urethral ligament transection mean +/- SD leak point pressure was significantly decreased when comparing pubo-urethral ligament transection and pudendal nerve transection to sham treatment (15.75 +/- 6.46 and 15.10 +/- 4.98 cm H<sub>2</sub>O, respectively, vs. 42.56 +/- 11.58,  $p < 0.001$ ). No difference was noted when comparing pubo-urethral ligament transection to pudendal nerve transection ( $p = 0.76$ ), indicating the long-term durability of pubo-urethral ligament transection on inducing stress urinary incontinence in the female rat. Histological examination of en bloc suprapubic areas demonstrated an absent pubo-urethral ligament in the pubo-urethral ligament transection group, and an intact pubo-urethral ligament in the sham treated and pudendal nerve transection groups.

**Conclusions:** Our results show that pubo-urethral ligament deficiency in the female rat induces long-term stress urinary incontinence that is comparable to that in the established stress urinary incontinence model via pudendal nerve transection. Our novel rat model could be used to investigate mechanisms of stress urinary incontinence in females, including the role of urethral hypermobility and potential therapeutic interventions for stress urinary incontinence.

### **Editorial Comment**

An interesting look into the development of a laboratory model to analyze and evaluate stress urinary incontinence. The authors noted that pubo-urethral ligament transection was very similar to pudendal nerve

transection in Sprague-Dawley rats in developing a model for stress urinary incontinence in the female rat. It is pointed out in the discussion that developing a model of stress urinary incontinence that avoids the use of pudendal nerve injury may help analyze nulliparous women who suffer with stress urinary incontinence. Much appreciation should go to the researchers in our field who help develop the models upon which to expand our ability to treat affected patients. Of note is that the support of structures of the female urethra including the pubo-urethral ligament had been reviewed in this journal in the past with some anatomic researchers noting that the pubo-urethral ligament may not be a ligament but instead mostly tissue containing smooth muscle cells (1). This is food for thought especially when quoting continence rates after suprimeatal transvaginal urethrolisis which takes down the attachments of the urethra to the underside of the pubic bone (2). In a contrary view, this may also explain the rate of incontinence that is noted in patients after therapeutic pubectomy (3).

### References

1. Fritsch H, Pinggera GM, Lienemann A, Mitterberger M, Bartsch G, Strasser H: What are the supportive structures of the female urethra? *Neurourol Urodyn.* 2006; 25: 128-34.
2. Petrou SP, Brown JA, Blaivas JG: Suprimeatal transvaginal urethrolisis. *J Urol.* 1999; 161: 1268-71.
3. Petrou SP, O'Connor MI: Urological assistance during therapeutic pubectomy. *J Urol.* 2001; 165: 1185-7.

**Dr. Steven P. Petrou**

*Associate Professor of Urology*

*Chief of Surgery, St. Luke's Hospital*

*Associate Dean, Mayo School of Graduate Medical Education*

*Jacksonville, Florida, USA*

*E-mail: petrou.steven@mayo.edu*

## PEDIATRIC UROLOGY

---

### **Long-term follow up of enteric bladder augmentations: the risk for malignancy**

Husmann DA, Rathbun SR

*Department of Urology, Mayo Clinic, Rochester MN 55905, USA*

*J Pediatr Urol.* 2008; 4: 381-5; discussion 386

**Objective:** To determine the risk of bladder cancer following enteric bladder augmentation.

**Materials and Methods:** Patients followed for care after an enteric bladder augmentation have been entered into a registry; individuals followed for a minimum of 10 years were evaluated.

**Results:** The study criteria were met by 153 patients. Indications for bladder augmentation were neurogenic bladder in 97, exstrophy in 38 and posterior urethral valves in 18. There was a median follow-up interval of 27 years (range 10-53). A total of seven cases of malignancy developed. Median time to tumor development following augmentation was 32 years (range 22-52). Two patients with neurogenic bladder developed transitional cell carcinoma; both were heavy smokers (> 50 pack per year history). Two patients with a history of posterior urethral valves and renal transplantation developed adenocarcinoma of the enteric augment. Three patients with bladder exstrophy developed multifocal adenocarcinoma of the augmented bladder. Two patients remain alive, 5 and 6 years following radical cystoprostatectomy; five died of cancer-specific causes.

**Conclusions:** Malignancy following enteric bladder augmentation arose in 4.5% (7/153) of our patients and was associated with coexisting carcinogenic stimuli (prolonged tobacco/chronic immunosuppressive exposure), or alternatively with the inherent risk of malignancy existing with bladder exstrophy.

### Editorial Comment

From 1986 to 2007, 153 patients who had greater than 10 years follow up for enterocystoplasties were studied. No patient in the study had a mixture of feces and urine prior to the enterocystoplasty, only patients who were augmented due to neurogenic bladder, exstrophy/epispadias complex or posterior urethral valves were included. The mean follow up was 27 years with a range of 10-53. Seven cases of malignancy occurred. There was no correlation with malignancy and recurrent urinary tract infections. There was no difference in cancer in the ilia or colonic segments. The incidence of asymptomatic bacteriuria did not reach statistical significance. 2 patients who developed cancer had heavy smoking histories. 2 patients developed cancer after prolonged immunosuppression after renal transplantation, and 3 patients in the exstrophy/epispadias group developed multi-focal adenocarcinoma involving the bladder and enteric segments. The study points out that in other countries where schistosomiasis or tuberculosis are common, enterocystoplasty cancers are found frequently. Most of the previous studies do not have a long enough follow up to have any tobacco use history be a significant risk factor. The cancer risk demonstrated in this paper is 4.5%, which is greater than the previous series of 0.6%-2.8%.

This paper reminds us that these patients need continual follow up throughout their adult lives. It was cancer risk in this same range that discouraged urologists from performing ureterosigmoidostomies and I believe this same risk will produce new solutions to the bladder dysfunction that has been an indication for enterocystoplasties in the past.

**Dr. Brent W. Snow**

*Division of Urology*

*University of Utah Health Sci Ctr*

*Salt Lake City, Utah, USA*

*E-mail: brent.snow@hsc.utah.edu*

### **Risk assessment of incidentally detected complex renal cysts in children: potential role for a modification of the Bosniak classification**

Wallis MC, Lorenzo AJ, Farhat WA, Bägli DJ, Khoury AE, Pippi Salle JL

*Division of Pediatric Urology, University of Utah, Salt Lake City, Utah, USA*

*J Urol. 2008; 180: 317-21*

**Purpose:** Incidentally detected complex renal cysts in children are a rare but worrisome occurrence due to the perceived potential risk of malignancy. We examined the natural history of such cysts in a cohort of children. **Materials and Methods:** We obtained access to a database containing all radiology reports generated at a single institution from 1996 to 2004. We used key words to limit our search, subsequently reviewing charts and images to confirm the diagnosis of a complex renal cyst and to collect clinical data. Cases were categorized according to a modification of the Bosniak classification, using ultrasound in most patients and computerized tomography or magnetic resonance imaging when available.

**Results:** Complex renal cysts were identified in 39 children. Mean patient age at presentation was 7 years. Mean cyst size was 1.6 cm. A total of 18 cases diagnosed by ultrasound only were observed with serial imaging. Additional contrast enhanced computerized tomography or magnetic resonance imaging was performed in 21 of 39 patients (54%). Surgical resection was performed in 5 patients and pathological evaluation revealed benign cyst in 3 (modified Bosniak class II in 2 patients and class III in 1) and renal cell carcinoma in 2 (III in 1 and IV in 1). All other patients had modified Bosniak class II cysts, which remained essentially unchanged during a mean follow-up of 26.8 months (range 9 to 70).

Conclusions: While not validated in children, our data suggest the modified Bosniak classification appears useful as a guideline to direct the management of complex renal cysts in the pediatric population.

### **Editorial Comment**

At Hospital for Sick Children in Toronto, radiology reports from 1996 to 2004 were reviewed looking for renal cysts, including those that were complex and septated. Patients were excluded if they had evidence of cystic kidney disease, prior renal trauma, previous kidney surgery or insufficient data. A minimum of six months follow up was required for inclusion. 39 patients with complex renal cysts were identified with the average age of 7 years and range of 4 months to 14 years, with a mean cystic size of 1.6 cm and a range of 0.4 to 5 cm.

Initial diagnosis was made in 36 patients by ultrasound and 3 patients were discovered by CT scan. Of the 36 cases discovered by ultrasound half had a CT or MRI scanning, while 18 only had ultrasound follow up. Interestingly in these children 7 simple cysts on CT scan clearly had septations on sonographic imaging, some of which even had Doppler flow in the septations on the ultrasound.

Five patients had surgical resection and 2 of these patients had renal cell carcinoma in the specimen. All the patients had follow up with a mean of 26.8 months and a range of 9 to 70 months. The cysts were classified according to the adult Bosniak classification.

Even though these numbers don't reach statistical significance, the authors recommend for patients with Class II cysts on the Bosniak scale, 3-6 month follow up with ultrasound for the first year and annual ultrasounds thereafter. They did not have a recommendation for how long the annual studies should continue once the cyst has stabilized.

There is no data in children correlating the predictability of risk factors in the Bosniak classification. However in this study of 39 patients, the worrisome cyst with enhancing margins or septa on CT scan, were the 2 that had renal cell carcinoma found in the specimen. The authors suggest that if there is a concern about an ultrasound cyst, a CT scan should be obtained with contrast to help in classification.

Bosniak risk classifications are based on renal cell carcinoma incidence in adults. In children, renal cell carcinoma is not the most common tumor and so it's hard to know how one should think about complex cysts in children. This manuscript suggests that similar concerns of the adult Bosniak classification may very well be worthwhile and that children with cysts certainly should have follow up until the cysts have stabilized, and perhaps for years after that.

***Dr. Brent W. Snow***  
*Division of Urology*  
*University of Utah Health Sci Ctr*  
*Salt Lake City, Utah, USA*  
*E-mail: [brent.snow@hsc.utah.edu](mailto:brent.snow@hsc.utah.edu)*