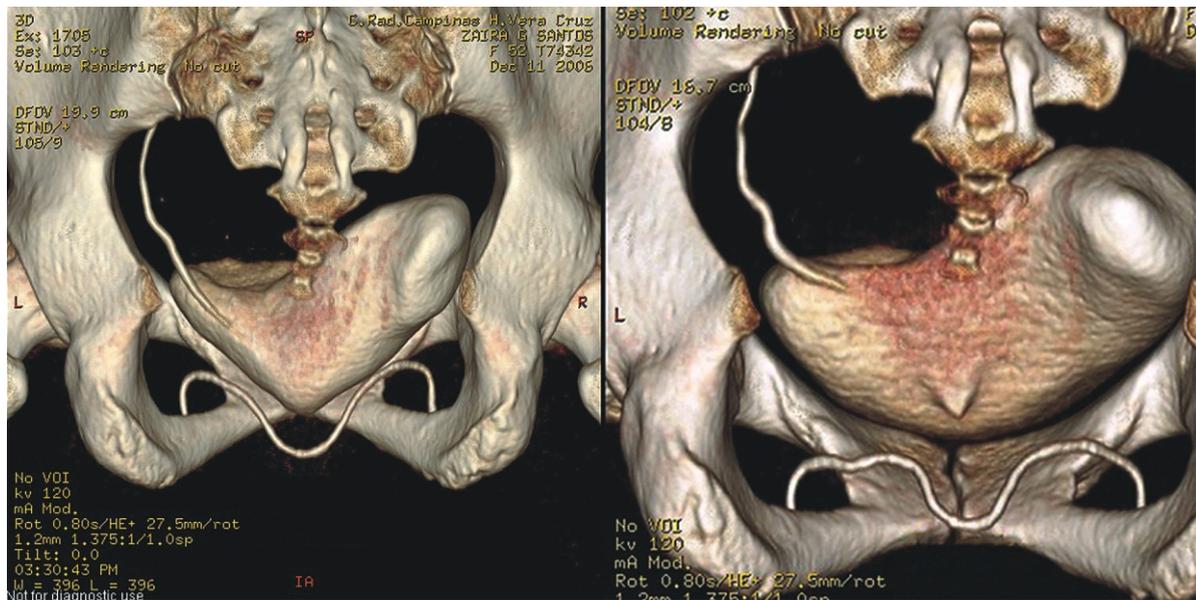




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Posterior views of a transobturator sling during strain and relaxation. (Page 209)

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EDITOR'S COMMENT

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Dynamic Evaluation of Pelvic Floor Reconstructive Surgery

The March – April 2010 issue of the International Braz J Urol presents original contributions and editorials from many different countries, such as USA, India, Turkey, Germany, Thailand, France, Greece, Australia, Indonesia, Canada, Brazil, etc., and as usual, the editor's comment highlights some papers.

Doctor Palma and colleagues, from State University of Campinas, Sao Paulo, Brazil, performed on page 209 a prospective study to achieve visualization of the reestablishment of anatomy after reconstructive surgery in the different pelvic compartments. They studied a total of 30 female patients with stress urinary incontinence (SUI), anterior and posterior vaginal wall prolapse, or both, that underwent surgical repair using radiopaque meshes. Three-dimensional reconstruction using helical CT was performed 4 weeks post-operatively. The authors clearly visualized the mesh in all cases. It was concluded that 3-dimensional helical tomography images of the female pelvis using radiopaque meshes have a potential role in improving the understanding of pelvic floor reconstructive surgeries.

Dr. Soloway and co-workers from University of Miami, Florida, USA, assessed on page 177 whether the time interval between prostate biopsy and total prostatectomy (TP) has an impact on the surgical outcome. They performed a retrospective analysis on patients who underwent TP by a single surgeon from 1992 to 2008. Two groups were studied according to the time interval between biopsy and TP; group 1 \leq 6 weeks and group 2 $>$ 6 weeks. Nine hundred and twenty-three patients were included. There was a significant difference between the two groups in the surgeons' ability to perform a bilateral nerve sparing procedure. Those who had a TP within six weeks of the biopsy were less likely to have a bilateral nerve sparing procedure. No significant difference was noted in the other variables, which included Gleason score, surgical margin status, estimated blood loss, postoperative infection, incontinence, erectile function, and biochemical recurrence. Although safe without any increase in complications, it was concluded that a TP within six weeks of a biopsy significantly reduced the surgeon's perception of whether a bilateral nerve sparing procedure was performed.

Doctors Jun-Ou and Lojanapiwat, from Chiangmai University, Thailand, compared on page 171 the efficacy and safety of the tubeless supracostal versus the standard supracostal percutaneous nephrolithotomy (PCNL). After studying 95 patients they found that in the tubeless PCNL group (Group-I) 90.7% were stone-free while those with standard routine postoperative nephrostomy tube (Group-II) 84.6% were stone-free. Additionally, stone fragments of less than 4 mm in diameter were found in 9.3% of patients in group-I and 25.4% in group-II. The success rate, hematocrit change and complication were not significantly different between both groups. The analgesic requirement, operative time and hospital stay were all significantly less in the tubeless supracostal group (Group-I). None of group I and only one patient of group II needed inter-

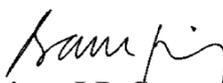
EDITOR'S COMMENT - *continued*

costal drainage. The authors concluded that tubeless supracostal percutaneous nephrolithotomy in selected patients is effective with acceptable rate of complications.

Doctor Labanaris and co-authors, from Martha Maria Medical Center, Nuremberg, Germany, examined on page 141 if elderly patients exhibit comparable outcomes and survival benefits to those achieved in younger patients, concerning radical nephrectomy and nephroureterectomy. They assessed 35 patients over 80 years old treated for malignant and inflammatory conditions. The median age was 83.5 years. Radical nephrectomy with a flank approach was performed in 65.7% of cases and nephroureterectomy with a transabdominal approach in 34.3% of cases. Eighty-eight percent of patients were satisfied with their decision to undergo the operation, 91.4% would undergo it once more if needed and 91.4% would advise it to a patient with their age. The authors concluded that radical nephrectomy and nephroureterectomy are safe and effective in well-selected patients over 80 years old. Elderly patients exhibit comparable preoperative outcomes and survival benefits to those achieved in younger patients.

Doctor Karatas and associates, from Memorial Hospital, Istanbul, Turkey, evaluated on page 190 the efficacy and safety of photoselective vaporization of the prostate (PVP) for benign prostatic hyperplasia (BPH) in cardiac patients receiving anticoagulant therapy. The mean patient age was 71.4 years (range 55-80). Mean prostate volume on transrectal ultrasonography was 73.2 mL (range 44-120). No patient required an additional procedure due to severe bleeding necessitating intervention during the early postoperative phase. The IPSS values and post voiding residual volume decreased and peak urinary flow rate increased ($p < 0.001$). The results showed that the mean prostate volume had decreased by 53% at 6 months. It was concluded that high-power photo selective laser vaporization prostatectomy is a feasible, safe, and effective alternative for the minimal invasive management of BPH, particularly in cardiac patients receiving anticoagulant therapy.

Doctor Valentine and others, from Université Pierre et Marie Curie, Paris, France, determined on page 218 why community-dwelling women aged 80 years or over were referred for urodynamic evaluation despite their advanced age and which urodynamic diagnosis was made. One hundred consecutive females (80-93 years) were referred to an urodynamics outpatient clinic for evaluation of lower urinary tract symptoms (LUTS). It was found that in this particular community-dwelling with an elderly female population, urodynamics is easily feasible. Incontinence, mainly "complicated" is the more frequent complaint and urgency the more frequent symptom. Urodynamic diagnosis underlines the high incidence of detrusor overactivity as well as impaired detrusor function.


Francisco J.B. Sampaio, M.D.
Editor-in-Chief

Radical Prostatectomy: Evolution of Surgical Technique from the Laparoscopic Point of View

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ABSTRACT

Purpose: To review the literature and present a current picture of the evolution in radical prostatectomy from the laparoscopic point of view.

Materials and Methods: We conducted an extensive Medline literature search. Articles obtained regarding laparoscopic radical prostatectomy (LRP) and our experience at Institut Montsouris were used for reassessing anatomical and technical issues in radical prostatectomy.

Results: LRP nuances were reassessed by surgical teams in order to verify possible weaknesses in their performance. Our basic approach was to carefully study the anatomy and pioneer open surgery descriptions in order to standardized and master a technique. The learning curve is presented in terms of an objective evaluation of outcomes for cancer control and functional results. In terms of technique-outcomes, there are several key elements in radical prostatectomy, such as dorsal vein control-apex exposure and nerve sparing with particular implications in oncological and functional results. Major variations among the surgical teams' performance and follow-up prevented objective comparisons in radical prostatectomy. The remarkable evolution of LRP needs to be supported by comprehensive results.

Conclusions: Radical prostatectomy is a complex surgical operation with difficult objectives. Surgical technique should be standardized in order to allow an adequate and reliable performance in all settings, keeping in mind that cancer control remains the primary objective. Reassessing anatomy and a return to basics in surgical technique is the means to improve outcomes and overcome the difficult task of the learning curve, especially in minimally access urological surgery.

Key words: prostatectomy; laparoscopy; minimally invasive; outcomes

Int Braz J Urol. 2010; 36: 129-40

INTRODUCTION

Radical prostatectomy (RP) remains the gold standard for the surgical treatment of localized prostate cancer. Evolution of the technique was started by the pioneering work done by Walsh and Donker (1). The accurate description of the dorsal vein complex, pelvic plexus and cavernous nerves and pelvic fascia has had a real impact in a number of patients operated for prostate cancer as regards morbidity and mortal-

ity procedure and scientific investigation in prostatic carcinoma (2). Schuessler et al. (3) described their initial experience in laparoscopic radical prostatectomy (LRP), which they initially considered as having no benefits when compared to its open surgery counterpart.

However, they rationalized that technical progress and experience could improve results. In 1998, the Montsouris team began their experience in LRP with their own developed technique. LRP

technique was well standardized (4); however, changes have been gradually introduced as a natural evolution of our surgical performance. The objective was to meet the demanding oncologic and functional objectives of the procedure and verify the efficacy of our technique. Our aim was to update the latest advances in our technique for LRP, at a point where our team had evolved from the steep learning curve of the procedure and arrived at a plateau level in which reevaluation and improvement became mandatory.

UNDERSTANDING THE ANATOMY OF THE PROSTATE AND ITS IMPLICATIONS ON SURGICAL TECHNIQUE

Whether RP is performed in open surgery, laparoscopic or perineal, the anatomy of the gland remains the cornerstone of surgery. Comprehensive understanding of the anatomical landmarks and its implications in the patient's future quality of life are mandatory when attempting the procedure. This issue has propelled a rather wide range of surgical descriptions that subsequently produced a controversy in the anatomic nomenclature. In fact, the endopelvic fascia is also described as: lateral pelvic fascia or parietal layer of the pelvic fascia; the levator fascia is mentioned as outer layer periprostatic fascia and the prostatic fascia is also known as inner layer of periprostatic fascia (5). Furthermore, the arrival of laparoscopy presented the possibility of a magnified surgical field that has allowed urologic surgeons to verify prostatic anatomy and this has also contributed to extensive discussion (6).

OPTIMAL SURGICAL TECHNIQUE

Once the surgical field has been developed, as described by Barré, RP can be summarized in the stages described in Table-1 (7). Laparoscopic and robotic approaches have specific variations, which are shown in Table-1.

We are still far from the well known "Tri-fecta" ideal combination of oncologic success and adequate continence and potency (8), because even when patients should be comprehensively selected for

surgery, a great number of particular variations still remain for each patient, including: large prostate, post transurethral resection setting and the obese patient. The best performances of RRP or LRP show a 11-14% of positive margins, in 50 to 70% of patients with early continence and a maximum of 70% of patients with potency at one year follow-up (4-8).

CONTINENCE PRESERVATION TECHNIQUE

Ligation of the Dorsal Vein

The dorsal vein complex (DVC) approach, aims to reduce blood loss and also to improve functional continence results. As described by Olerich (9), the sphincter complex (SC) responsible for passive urinary control, covers the prostate apex. Therefore, DVC and SC are parallel and transection of the DVC could eventually be excised at the anterior portion of the sphincter with a definite impact in postoperative continence improvement (10,11). For that reason, careful and elective ligation should be achieved in order to expose the prostatic apex and urethra (Figures-1 and 2).

Dissection of the Apex

Apex dissection should be approached with the idea of avoiding both areas by leaving prostatic tissue behind and not damaging the striated sphincter. Once the endopelvic fascia is incised and the puboprostatic ligaments transected, careful dissection to free the muscle fibers from the apex should be performed. Careful observation of the shape of the prostate is important to delineate the borders and therefore guide dissection (2,7), keeping in mind that at the apical region nerve fibers run at 3 and 9 o'clock positions posterolaterally to the urethra (11) (Figure-3).

Nguyen et al. (12) have proposed posterior reconstruction of Denonvilliers' musculofascial plate (PRDMP) to enhance early continence after robotic or laparoscopic radical prostatectomy. These authors suggest that PRDMP leads to improved maintenance

Radical Prostatectomy

Table 1 – Retropubic, laparoscopic and robotic assisted radical prostatectomy techniques.

Open Radical Prostatectomy (Extraperitoneal) Barré (7)	Laparoscopic Radical Prostatectomy (Transperitoneal) Institut Montsouris Initial Technique	Robotic Assisted Radical Prostatectomy (Transperitoneal) Kaul & Menon (19)
Bilateral pelvic lymphadenectomy is selectively performed based on Gleason grade and PSA		
1. Incision and exposure	1. Dissection of the seminal vesicles, via direct approach.	1. Peritoneoscopy and mobilization of the bladder
2. Exposure of the prostate apex	2. Dissection of the bladder to approach the space of Retzius	2. Preservation of endopelvic fascia and control of dorsal venous complex. Prostatic fascia preservation.
3. Preservation of the striated sphincter (Control of dorsal vein)	3. Dissection of the bladder neck	3. Dissection and division of the bladder neck
4. Nerve-sparing (retrograde, interfascial). Using clips for hemostasis.	4. Creation of space between the rectum and the prostate.	4. Dissection of vas deferens and seminal vesicles
5. Dissection of the seminal vesicles and division of the bladder neck	5. Control of dorsal vein complex, exposure and dissection of the prostate apex and urethra.	5. Nerve sparing (antegrade, interfascial), athermal technique
6. Excision of the seminal vesicles	6. Nerve sparing (antegrade, interfascial). Using clips and micro bipolar energy.	6. Apical dissection and urethral transection.
7. Extraction and inspection of the specimen	7. Extraction and inspection of the specimen	7. Vesicourethral anastomosis (running anastomosis)
8. Vesicourethral anastomosis (separate stitches)	8. Vesicourethral anastomosis (separate stitches)	8. Retrieval of the specimen

of membranous urethral length and significantly higher early continence rates.

NERVE SPARING TECHNIQUE: MARGINS VS. POTENCY. ON WHICH SIDE OF THE FASCIA DO WE STAND?

Walsh et al. have stated that: “The Lateral fascia is divided into 2 layers - the prostatic fascia and the levator fascia- and when the nerve sparing is properly performed the prostatic fascia must remain on the prostate” (13). The distinction between interfascial, interfascial and extrafascial dissection has been described by open surgery surgeons (1,7), however there is still controversy as to whether or not a clear distinction of the layers of tissue can

be accomplished by open surgery, even by using operating loupes (6). As described by Martínez-Piñeiro et al., (14) the interfascial plane would be a plane between the prostatic fascia and Denonvilliers fascia posterior and between the prostatic fascia and the anterior extension of Denonvilliers’ fascia at the posterolateral aspect of the prostate.

In our experience, we have been able to obtain a highly detailed view of the anatomy with the endoscopic approach and more recently, lenses provided by the robotic interface do in fact improve the surgical field due to a three-dimensional perspective. Although the improvements accomplished since Walsh’s first operation over 25 years ago, radical prostatectomy remains a challenging procedure with a steep learning curve and two objectives that are contradictory. The idea is to obtain reliable cancer

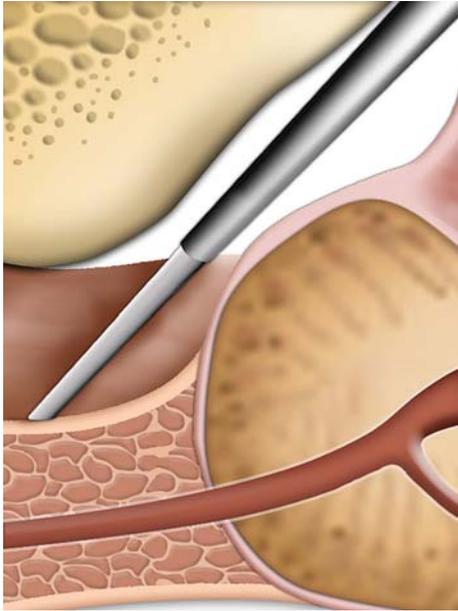


Figure 1 – Clamping and cutting of dorsal vein complex.

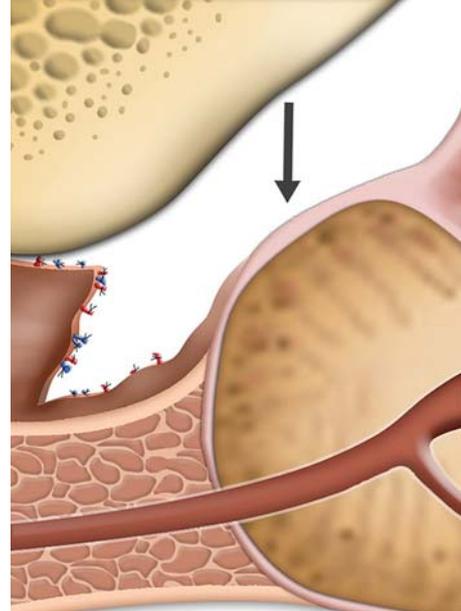


Figure 2 – Clamping and cutting of dorsal vein complex. Arrow shows placement of back bleeding control stitch.

control, which means avoidance of positive surgical margins while preserving as much as possible functionality in terms of continence and potency. Excellent rates of cancer control for patients with organ-confined disease (5-year recurrence free probabilities close to 100%) are accomplished by dedicated surgeons only when a surgical technique is properly performed (15). Complete preservation of the neurovascular bundles (NVB) is performed either with intrafascial or interfascial dissection technique (6), however, we believe that the interfascial plane would be the elected plane for comprehensive nerve sparing in order to be oncologically safe while preserving functionality (Figures-4 and 5). Secin et al., (16) have described the intrafascial technique as the reference procedure for preservation of NVB in selected patients based on pre- and intraoperative findings. Several authors have also supported the idea of an intrafascial dissection (17-19). We agree that comprehensive and judicious preoperative evaluation and adequate interpretation of operative findings are crucial in final results of the prostatectomy, but there is also a need to state a technical approach that might not only spread LRP even more, but offer safety to

patients in all settings. See Table-2 for variations on technique, approach and type of nerve sparing technique for radical prostatectomy.

Antegrade and Retrograde Dissections

There are two nerve sparing techniques, the antegrade dissection that starts at the base of the prostate and continues along the posterolateral contour to end in the posterior edge (7,20), and the retrograde, which starts at the apex and develops a plane between the rectum and the prostate to expose the medial border of the NVB. Retrograde dissection was the initially described technique for RRP, and it is characterized by a high incision of the fascia. The antegrade dissection has been applied primarily in LRP and it has been criticized because of the starting point of dissection that can be rather high, creating an intrafascial dissection, or very low, which would injure the nerves (7). In the principles of interfascial dissection of the NVB, skilled dissection and avoiding energy sources around the NVB are more important factors than the nerve-preservation technique used (20).

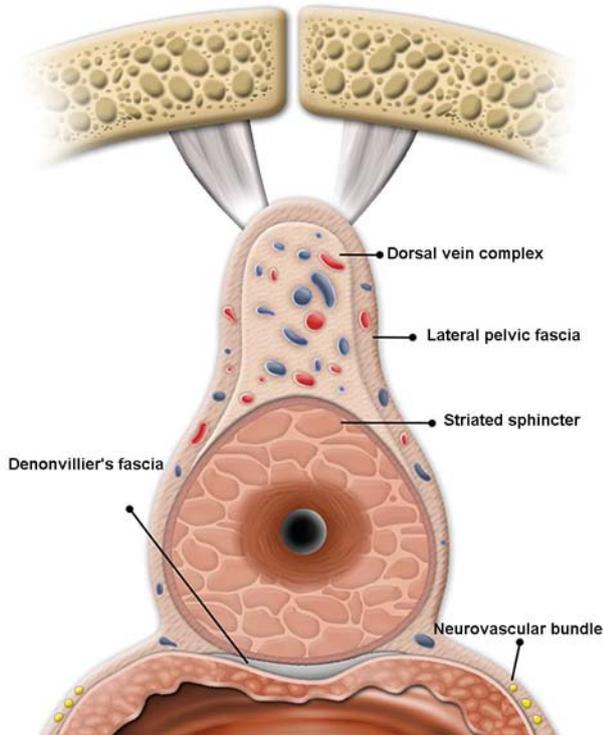


Figure 3 – Diagram showing urethra and its relations with dorsal vein complex.

ANATOMICAL RATIONALE FOR A PROSTATIC VEIL

There is objective evidence that supports the fact of the existence of a neurovascular network that surrounds the prostate and that it could have an impact in postoperative evaluated issues. However, the idea of giving it a cumbersome name, has just add more to the already crowded world of nomenclature in radical prostatectomy and therefore we agree with Rassweiler [5] to avoid using the so-called term “Veil of Aphrodite”. Ganzer et al. (21) have objectively verified that the highest percentage (74-84%) of the total nerve surface of the prostate is located dorsolaterally, with up to 39% of nerve surface area, found ventrolaterally. In their study, computerized planimetry offered a basic view that periprostatic nerve distribution is variable with a high percentage of nerves in the ventrolateral and dorsal position. They also verified an interesting decrease

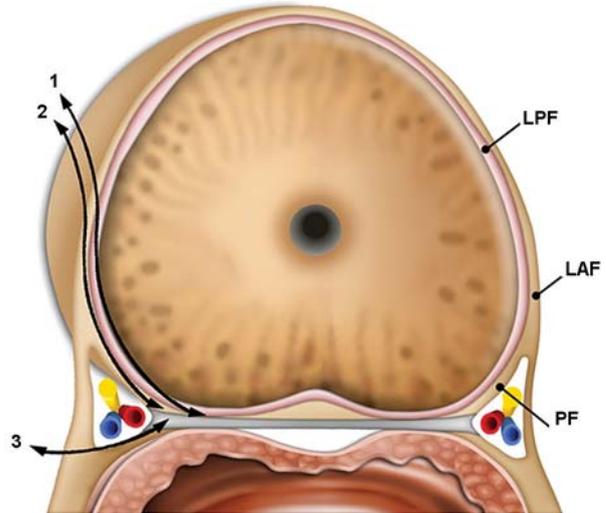


Figure 4 – Neurovascular bundle sparing.

in total periprostatic nerve surface area from the base to the apex. Several researchers have also addressed the subject of periprostatic nerve distribution with comparable results in terms of most frequent localization of nerves (dorsolaterally) and a high percentage of variation from case to case (22-24).

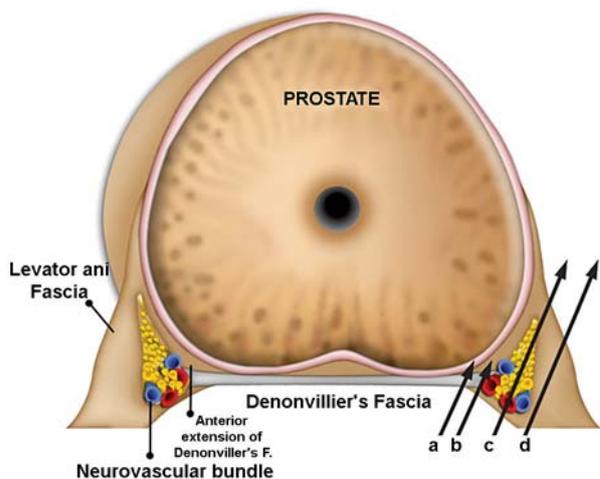


Figure 5 – Grades of neurovascular bundle preservation.

Table 2 – Variations on technique, approach and type of nerve sparing for radical prostatectomy.

Authors	Radical Prostatectomy Technique	Type of Nerve Sparing
Barré C (7)	Open/extraperitoneal	Retrograde/Interfascial
Secin et al. (16)	Laparoscopic/transperitoneal	Antegrade/Intrafascial
Stolzenburg et al. (37)	Laparoscopic /extraperitoneal	Antegrade/Intrafascial
Kaul & Menon (19)	Robotic assisted Laparoscopy	Antegrade/Intrafascial
Institut Montsouris 2008	Laparoscopic or robotic, extraperitoneal	Antegrade/ Interfascial

ROBOTIC INTERFACE OFFERINGS FOR RADICAL PROSTATECTOMY LEARNING CURVE

As we have previously mentioned, laparoscopic radical prostatectomy far from dying is rapidly evolving (25). The use of the robot has reduced the learning curve due to EndoWrist® technology, three-dimensional imaging and magnification but there is still a need for solid evidence to back up the analysis of the learning curve, as completing the procedure or being able to perform it does not necessarily mean it is done well. The robot represents a useful instrument for the surgeon and it should be regarded as a procedure to be followed in the future, as its results will certainly improve in the years to come.

Meanwhile, how many cases do we need to become expert surgeons in the technique we perform on a daily basis? or perhaps more importantly, how many cases do the fellows standing by our sides need to become safe and reliable operators?

These remain controversial questions that we still need to address, not only in radical prostatectomy but also as regards minimal urological access surgery. The arrival of both, laparoscopy and more recently the robotic interface has focused our attention on the term learning curve. In fact, laparoscopic series brought with it a tremendous enthusiasm in terms of validation of the technique and therefore extensive work in the procedure's learning curve.

Is there a formal definition for learning curve? Probably not. However, let us see:

The Ross procedure is a challenging operation for patients with aortic valve disease. The principle is to

remove the patient's normal pulmonary valve and used it to replace the patient's diseased aortic valve. In Dr. Ross's own series, 23% of the patients died during the first year of the operation and 18% in the second year. In the following 10 years, the surgical mortality in a series of 188 patients dropped to 9%. This is a learning curve. The message: It requires time and hard work (26). The incorporation of new devices into surgical practice - such as the robot - requires that surgeons acquire and master new skills. As in any new technology, robotic surgery demands dedication to achieve expertise. For a skilled laparoscopic surgeon the learning curve to achieve proficiency with robotic radical prostatectomy is estimated at between 40 to 60 cases. For the laparoscopically naive surgeon the curve is estimated at 80 to 100 cases (27). The Da Vinci assisted approach incorporates the advantages of minimally invasive approach while presenting comparable results to the open surgical approach. However, we do not believe that proficiency could be achieved within the first 20 or 25 cases of robotic experience, as has previously been stated (28). Robotic interface appears to offer a significant benefit to the laparoscopically naive surgeon with respect to learning curve, at an increased cost. We have previously demonstrated that laparoscopic extraperitoneal radical prostatectomy is equivalent to the robotic assisted laparoscopic prostatectomy in the hands of skilled laparoscopic urological surgeons with respect to operative time, operative blood loss, hospital stay, length of bladder catheterization and positive margin rate (29). Improvement of our technique is found on a daily basis and there is considerable experience needed to reach the best quality in both open and laparoscopic standards. The latter is in agreement with

the study by Vickers et al. in their timely publication assessing surgical learning curve for prostate cancer control (30). These investigators found a statistical significance related to the surgeon's experience and cancer control after radical prostatectomy. This study is a return to the basic concept of learning curves and suggests a real link between surgical technique and cancer control. Its analysis showed a dramatic improvement in cancer control with increasing surgeon experience up to 250 previous treated cases. As presented in a recent review of the robotic literature by Ficarra et al., positive surgical margin rates decreased with the surgeon's experience and improvement in technique; reaching percentages similar to those of retropubic and laparoscopic series (31).

Establishing a robotic prostatectomy program is an important challenge to any institution requiring both financial support and a focused operating room team (32), but this must not lead to an aggressive patient acquisition (advertising, commercialization) during the basic learning curve, because cancer care implies offering a product of the highest quality. The learning curve plateaus come with training and experience. Surgeons have always recognized a structured way to introduce new procedures and learning a new technique requires dedication. Unfortunately, as reported by Tooher et al., (33) the laparoscopic learning curve has only been addressed in a limited number of studies.

NEED FOR REVISION AND STANDARDIZATION

As recently described, oncological outcomes after radical prostatectomy improve with the surgeon's experience irrespective of patient risk and inadequate surgical technique leads to recurrence (34). It has been recently reported that patients undergoing minimally access prostatectomy (either pure lap or robotic assisted) vs. open radical prostatectomy (ORP) have a lower risk for perioperative complications and shorter lengths of stay, but they harbor higher probability for salvage therapy and anastomotic strictures (35). These unfavorable outcomes would be diminished by high surgical volume. The main limitation of this study was the comparison of surgical teams that do not necessarily

represent the standard of care in both open and laparoscopic technique. Therefore, the aim is to improve LRP surgical technique and take advantage of the novel surgical instruments to guarantee a solid based concept of minimally access surgery as the most adequate therapeutic option for localized prostate cancer. As described by Touijer and Guillonneau (36) even when all the reports agree and demonstrate the benefits of minimal access surgery, there are no prospective series comparing LRP vs. ORP and there are important variations reported in the characteristics of the procedure: whether or not performing lymph node dissection, a wide range of positive margin rates (6% to 8% for organ-confined disease and from 35% to 60% with extraprostatic extension), lack of evaluation of short term biochemical recurrence and extreme variations in the evaluation and reporting of functional outcomes. Going back to basics, in our understanding, is a reevaluation and deployment of a surgical technique based on both the available knowledge of the subject and experience. Stolzenburg et al. have opened the way in this matter with their recent experience of extraperitoneal LRP with intrafascial dissection, in which they report a low frequency of surgical margins with 80% and 94% of potency and continence, respectively (37). However, Tooher et al. in their systematic review of comparative studies report that stronger evidence is needed when comparing LRP vs. RRP. There is still a desire in the medical community for a randomized control study and LRP still remains as the emerging alternative for the surgical treatment of localized prostate cancer (33).

LRP MONTSOURIS TECHNIQUE

Five trocars are used (three 5 mm, two 10 mm), one in the umbilicus and the others in the iliac fossa. There are no significant differences between the Trans- or extraperitoneal approach as we have previously described (38), however currently we usually perform an extraperitoneal approach with balloon dissection under direct visualization and insufflation of the space, which creates an optimal operative field. Trocars are positioned according to surgeon's preference. Bilateral pelvic lymph node dissection is performed when it is indicated (PSA values > 10 ng/mL and Gleason score > 7 on primary prostatic

Radical Prostatectomy

Table 3 – *Montsouris technique for laparoscopic radical prostatectomy.*

Positioning	Patient is placed in moderate Trendelenburg position with adequate padding and covering on the areas of exposure.
Surgical approach, creation of surgical field and trocar positioning	Extraperitoneal approach with balloon dissection under direct visualization and insufflation of the space, creates an optimal operative field. Trocars are positioned according to surgeon's preference.
Incision of the endopelvic fascia	Bilateral incisions are performed from the prostate base to the puboprostatic ligaments. Levator ani fibers should be gently mobilized and spared from either side of the prostate. This maneuver should avoid the disruption of venous pedicles usually present in the area. Puboprostatic ligaments are sectioned close to its prostate attachment, sparing its attachment to the sphincter complex.
Division of bladder neck and dissection of the seminal vesicles.	<p>Starting in the pericervical area, the bladder neck is carefully dissected towards the prostate delineating the urethral fibers. Bipolar hemostasis should be precise during this step to avoid excessive blood loss. Our aim when possible is to preserve the bladder neck. The anterior wall of the bladder neck is incised and we proceed to find the plane between the posterior wall of the bladder neck and the prostate. This dissection is made in the extending muscle fibers from the detrusor muscle. In cases of a median lobe a reconstruction should be performed.</p> <p>Once the posterior wall of the bladder neck is dissected, we encounter anterior layers of Denonvilliers' fascia, that are incised in order to reach both vas deferens that should be dissected and ligated. Gently traction in the distal end of each vas aids in exposing the seminal vesicles for their dissection. Once again, a reliable hemostasis should be accomplished and dissection is undertaken close the wall of the vesicles. One must remember that the tip of the seminal vesicle is just above the plane of the neurovascular bundle in order to avoid going too wide in the dissection.</p>
Antegrade nerve-sparing dissection	<p>Posterior surface of the prostate should be carefully dissected to create a space between the gland and the rectum. This maneuver will create a "tunnel" under the prostate gland, which demarks the neurovascular bundles at each side. Antegrade dissection starts at the posterior surface of the prostate and goes along the posterolateral contour of the gland. Traction for exposure should be carefully applied to avoid affecting the neurovascular bundles. We agree with the initial pioneer description by Walsh, that as the lateral fascia divides into 2 layers – the prostatic fascia and the levator fascia- nerve sparing is properly performed when the prostatic fascia remains on the prostate, so we perform an interfascial dissection –between the parietal(levator) and visceral(prostatic) fascia- in order to avoid positive surgical margins while preserving potency. There are two key points in the dissection:</p> <ol style="list-style-type: none"> 1. Posterolateral incision of Denonvilliers' fascia. 2. Lateral incision of the levator ani fascia, keeping in mind that initial section should be performed at 2-3 o'clock position and 9-10 for the right and left prostatic sides, respectively.

Table 3 – Montsouris technique for laparoscopic radical prostatectomy. (continued)

Dorsal vein control and apex exposure	We performed a stitch over the anterior surface of the prostate to stop back bleeding, then, we proceed to clamp the dorsal vein above the striated sphincter (\pm 15 mm depth) and incise the dorsal vein complex with cold scissors. A control bleeding stitch is placed behind the clamp, avoiding going deep in order to protect anterior part of the sphincter. Remaining portion of the dorsal vein is divided under direct vision and hemostasis accomplished with superficial stitches (Vicryl® 2-0). This, exposes the prostate apex and the urethra's surrounding sphincter. Extensive dissection at the lateral sides of the apex is avoided. The urethra is divided step by step, in order to visualize the muscle fibers of the sphincter and its relations with the apex. After the urethra is fully transected, the apex dissection is carefully accomplished in both the anterior and posterior surfaces of the prostate, aiming to avoid excessive traction.
Extraction and inspection of the specimen	The specimen is extracted and verified by the surgical team. Frozen section if indicated.
Vesicourethral anastomosis	It is performed with separate Vicryl® 3-0 stitches and 5/8 needle, starting in the posterior wall and going from side to side, until completing a watertight closure (verified by fulfilling the bladder with 80 cc of solution). During the anastomosis both the grade of Trendelenburg position and also the pneumoperitoneum are decreased.

biopsy) (39,40). In such cases, we rather perform a transperitoneal approach for the procedure. Table-3 shows a detailed description of the most recent surgical technique performed at our institution.

POINTS OF CHANGE. STAYS AND GOES

It has been over 25 years since the Walsh and Donker anatomical description and over 10 years since the Montsouris experience in LRP started. The rapid evolution of surgical technique has been the rule and several variations for RP have been described. After years of experience, we would like to share the elements of the operation that we have kept overtime and others that we have discarded.

Stays:

- Opening of the pelvic fascia.
- Preservation of the bladder neck for cases with

negatives biopsies at prostatic base.

- Effective hemostasis by means of small clips and elective micro bipolar energy.
- Antegrade nerve sparing dissection.

Goes:

- Direct dissection of the seminal vesicles after incising the peritoneum above the pouch of Douglas
- Deep stitching without clamping of the dorsal vein complex to accomplish hemostasis.
- Extensive lateral dissection of the apex and urethra.
- Intrafascial dissection during nerve sparing.

CONCLUSIONS

Radical prostatectomy is a complex surgical operation with difficult objectives; surgical technique should be standardized in order to allow an adequate

and reliable performance in all settings, keeping in mind that cancer control remains objective number one. There is no unique way to attain the highest surgical quality (open or lap, antegrade or retrograde, intra- or interfascial), but there are several concepts and rules to be followed. Reassessing anatomy and going back to basics in surgical technique is the path to improve outcomes and overcome the difficult task of learning curve.

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CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

Open radical prostatectomy is the gold standard and most widespread treatment for clinically localized prostate cancer. However, in recent years laparoscopic and robot-assisted laparoscopic prostatectomy has rapidly been gaining acceptance among urologists worldwide and has become an established treatment for organ-confined prostate cancer.

Schuessler et al. in 1997 (1), described the initial experience in laparoscopic radical prostatectomy (LRP), which they concluded that this technique did not provide any advantages over open surgery.

As the authors described in this revision, in 1998, the Montsouris team started their experience in LRP. LRP technique was well standardized and changes have been gradually introduced as a natural evolution of the technique.

A better understanding of the periprostatic anatomy and further modification of surgical technique will result in continued improvement in functional outcomes and oncological control for patients undergoing radical prostatectomy, whether by open or minimally-invasive surgery. The oncologic results are in line with those reported with the use of the retropubic approach (2).

Today patients diagnosed with clinically localized prostate cancer have more surgical treatment options than in the past including open, laparoscopic and robot-assisted laparoscopic radical prostatectomy.

However, cost-efficacy, learning curves and oncologic outcomes and remain important considerations in the dissemination of minimally-invasive prostate surgery.

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Radical Nephrectomy and Nephroureterectomy in Patients Over 80 Years Old

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ABSTRACT

Purpose: The aim of this study was to discover if elderly patients exhibit comparable outcomes and survival benefits to those achieved in younger patients.

Materials and Methods: We assessed 35 patients over 80 years old treated by radical nephrectomy or nephroureterectomy for malignant and inflammatory conditions within the previous 4 years. A multivariate analysis regarding survival and recovery was conducted and included various preoperative parameters. The subjective opinion of patients or patient's relatives (in cases where the patient had past away) was estimated by answering the following questions: (a) are you satisfied with your decision to undergo the operation? (b) would you undergo it once more if needed? (c) would you advise it to a patient your age?

Results: The median age was 83.5 years. Radical nephrectomy with a flank approach was performed in 65.7% of cases and nephroureterectomy with a transabdominal approach in 34.3% of cases. The median recovery was 13 weeks. During a median follow-up of 31 months (range 12 to 53), 80% of patients were disease free. The remaining 20% passed away demonstrating a median survival of 25 months (range 13-38). Eighty-eight percent of patients were satisfied with their decision to undergo the operation, 91.4% would undergo it once more if needed and 91.4% would advise it to a patient their age.

Conclusions: Radical nephrectomy and nephroureterectomy are safe and effective in well-selected patients over 80 years old. Elderly patients exhibit comparable preoperative outcomes and survival benefits to those achieved in younger patients. Various preoperative clinical variables that effect the survival of patients but not their recovery could be identified.

Key words: renal neoplasms; morbidity; mortality; prognosis; convalescence; patient satisfaction

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INTRODUCTION

Improvements in the healthcare delivery system and of medical interventions have resulted in a significant increase of the average life span. As the

population ages, urologists are faced with the need to counsel older patients on the risks and benefits of surgical procedures. Although the elderly present with unique health-care challenges, currently available data indicate that well-selected elderly patients do

not have a significantly higher risk of morbidity or mortality from major urologic surgery in comparison to younger patients and can potentially gain survival benefits from surgery (1). Nevertheless, three critical questions that arise are (a) are there any preoperative clinical variables that effect survival? (b) are the any preoperative clinical variables that could reveal the length of time required in order for patients to resume usual physical activities? and (c) do the patients themselves believe that they truly benefit from surgery?

The aim of the present study was to find answers to these questions and additionally to do discover if elderly patients exhibit comparable preoperative outcomes and survival benefits to those achieved in younger patients, by analyzing a contemporary series of 35 patients over 80 years old treated by radical nephrectomy or nephroureterectomy at our institution within the previous 4 years.

MATERIALS AND METHODS

Between April 2004 and September 2008, 35 consecutive patients over 80 years old underwent radical nephrectomy or nephroureterectomy for inflammatory and malignant conditions at our institution within the last 4 years. Patient demographics as well as preoperative and postoperative data were recorded in a computer database. The data were collected by chart review and telephone interviews. The parameters assessed included: age, gender, reason of surgery (curative or palliative treatment), type of surgery (radical nephrectomy or radical nephroureterectomy with lymph node dissection), surgical approach (flank or transabdominal), size of renal mass, symptoms (macrohematuria/pain/fever), co-existing diseases (hypertension/diabetes/hypo or hyperthyroidism), laboratory findings (anemia/leucocytosis/increase in serum creatinine levels), median operative time, complication rates (intraoperative and perioperative within 30 days), operative mortality (death within 30 days of surgery), the length of hospital stay, survival, type of renal disease, preoperative American Society of Anesthesiologists (ASA) score (2), preoperative Karnofsky score (3), present Karnofsky score, length of time required in order for patients to resume usual physical activities, and the subjective opinion of pa-

tients or patient's relatives (in patients who past away) regarding the operation.

A multivariate analysis was conducted in order to detect possible preoperative clinical variables that stratify patients likely to exhibit a prolonged length of time required in order for them to resume usual physical activities and that effect their survival. The analysis included the following parameters: preoperative Karnofsky score, ASA score, symptoms, pathologic laboratory findings, type of surgery (curative or palliative treatment) and type of renal disease and stage. For comparison between 2 groups of continuous values the Student-t-student test was used. For comparison between 3 or more groups the one-way ANOVA with the Tukey correction for multiple comparisons was used. For comparison of binomial values, the Chi-square test was used. Simple linear regression was used to test the effect of one continuous parameter against another. A p value of < 0.05 was considered significant. The subjective opinion of patients or patient's relatives regarding the operation was estimated by answering the following questions: (a) are you satisfied with your decision to undergo the operation? (b) would you undergo the operation once more if needed? (c) would you advise such a therapeutic approach to a patient your age?

RESULTS

Patient characteristics, as well as intraoperative and postoperative data, are presented in Table-1. The median age was 83.5 years (range 80-94). There were 20 male and 15 female patients. A total of 77.2% of patients underwent curative surgery and the remaining 22.8% palliative surgery. Radical nephrectomy with a flank approach was performed in 65.7% of cases and a radical transabdominal nephroureterectomy with a cuff of the bladder wall and lymph node dissection in 34.3% of cases. Lymphadenectomy typically included the para-aortic, paracaval, and interaortocaval nodes from the renal hilum to the bifurcation of the common iliac artery. All patients were routinely treated in an intensive care unit for 24 h after surgery. The median size of the renal mass was 5.2 cm (1.1-13.5 cm). A total of 40% of patients presented with symptoms (51.4% with intractable

Nephrectomy in Patients over 80 Years

Table 1 – Patient characteristics, intraoperative-postoperative data and the subjective opinion of patients regarding the operation.

Age	80-94 (median 83.5)	Gender	Male = 20 (57.1%) Female = 15 (48.9%)
% survival of living patients	12-53 months (median 31 months)	% survival of dead patients	13-38 months (median 25 months)
% Deaths	Yes = 7 (20%) No = 28 (80%)	Tumor related?	Yes = 5 (71.5%) No = 2 (28.5)
Post-op Deaths	Yes = 1 (Stroke) (2.9%) No = 34 (97.1%)	Rehab	Yes = 17 (48.5%) No = 18 (51.5%)
Post-op Complications	No = 30 (85.7%) Yes = 5 (14.3%) Ileus = 1 (2.9%) Lactacidosis = 1 (2.9%) Stroke = 1 (2.9%) Hyperglycemia = 1 (2.9%) Pneumothorax = 1 (2.9%)	ASA score	ASA 1 - 5 (median 3) ASA 1 = 12 (34.2%) ASA 2 = 9 (25.7%) ASA 3 = 4 (11.4%) ASA 4 = 10 (28.5%) ASA 5 = 0 (0%)
Karnofsky Index Pre-op	40 - 100% (median 77%)	Karnofsky Index Now	40 - 100% (median 75%)
OP Type	Palliative = 8 (22.8%) Curative = 27 (77.2%)	Recovery period	3-48 weeks (median 13)
Symptoms	Yes = 14 (40%) No = 21 (60%)	Path Lab find- ings	Yes = 17 (48.5%) No = 18 (51.5%)
Additional Disease	Yes = 18 (51.5%) No = 17 (48.5%)	Hospital stay	8-30 days (median 14.2)
Type of OP	Flank = 23 (65.7%) Abdominal = 12 (34.3%) LN dissection = 12 (34.3%)	Location	Right Kidney = 18 (51.4%) Left Kidney = 13 (37.1%) Left Ureter = 4 (11.5%)
Pathology	RCC = 17 (48,5%) UCC = 12 (34,2%) Pyonephrosis = 3 (11.4%) Adrenal Ca = 1 (2.9%) XGP = 1 (2.9%)	M+ Post-OP	No = 29 (82.9%) Yes = 6 (7.1%) Liver = 2 (33.3%) Lungs = 2 (33.3%) Bladder = 1 (16.6%) Multiple = 1 (16.6%) (Liver/Lungs/Bones)
R1	Yes = 1 (2.9%) No = 34 (97.1%)	Tumor Size	1.1 - 13,5 cm (median 5.2 cm)
M+ Pre-OP	Yes = 1 (Lungs) (2.9%) No = 34 (97.1%)	Repetition of OP	Yes = 32 (91.4 %) No = 3 (8.6%)
pN+	Yes = 4 (88.5%) No = 31 (11.5%)		
Satisfied with OP	Yes = 31 (88.5%) No = 4 (11.5%)	Suggestion of OP	Yes = 32 (91,4 %) No = 3 (8.6%)

ASA score = American Society of Anesthesiologists score; RCC= renal cell carcinoma; LN = lymph node; OP = operation; UCC = urothelial cell carcinoma; XGP = xanthogranulomatous pyelonephritis.

pain, 45.7 % with severe hemorrhage and 5.7% with signs of urosepsis), 48.5% with pathological laboratory findings and 51.5% presented with co-existing diseases. Para-neoplastic symptoms were not encountered in any of the patients. The median operative time for radical nephrectomy via a flank approach was 75 min. The median operative time for radical abdominal nephroureterectomy with lymph node dissection was 145 min. There were no intraoperative complications observed. Intraoperative blood transfusion was not required in any of the patients in this study. Postoperative complications were encountered in 14.3% of patients (1 case each: ileus, lacticidosis, hyperglycemia, pneumothorax and stroke). Postoperative patients (n = 3) received 2 U of packed red blood cells due to dilutional anemia in view of the patients' advanced age and limited cardiac reserve. Operative mortality (14 days postoperative due to a stroke) was encountered in 1 patient (2.9%). The median hospitalization time was 14.2 days (8-30 days). No patients were re-hospitalized. The final pathology specimen revealed renal cell carcinoma (RCC) in 48.5% of patients, upper tract transitional cell carcinoma (TCC) in 34.3%, pyonephrosis in 11.4%, adrenal carcinoma in 2.9% and xanthogranulomatus pyelonephritis in 2.9% of patients. Only 1 patient exhibited positive

surgical margins. Metastatic disease developed in 7.1% of patients (liver n = 2, lungs n = 2, bladder n = 1 and multiple n = 1). After a median follow-up of 31 months (range 12 to 53), 80% of the patients were still alive. The remaining 20% passed away and had a median survival of 25 months (13-38). A total of 71.5% of these patients died from an underlying oncological disease.

The median length of time required in order for patients to resume their usual physical activities was 13 weeks (3-48 weeks). A total of 34.2% of patients were able to resume their regular activities within 3-6 weeks, 34.2% in 8-12 weeks, 28.5% in 16-24 weeks and 2.8% in 48 weeks.

The multivariate analysis conducted in order to detect possible preoperative clinical variables that stratify patients likely to exhibit a prolonged length of time required in order for them to resume usual physical activities demonstrated that: patients with a preoperative Karnofsky index of 30-60 (Figure-1), patients with an ASA score > 3 (Figure-2) and symptomatic patients (Figure-3) exhibited a slight but insignificant tendency to a prolonged recovery time $p = 0.19$, $p = 0.18$ and $p = 0.10$ respectively. Interestingly, there were no preoperative clinical variables that significantly influenced the length of time required

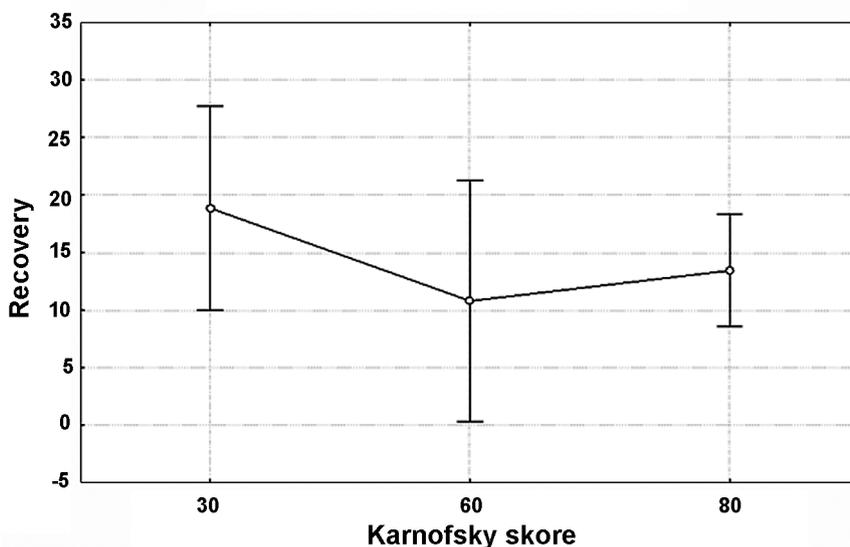


Figure 1 – One way ANOVA with Tuckey correction for multiple comparisons. Patients with a lower preoperative Karnofsky index exhibited a slight but insignificant tendency to a prolonged recovery time.

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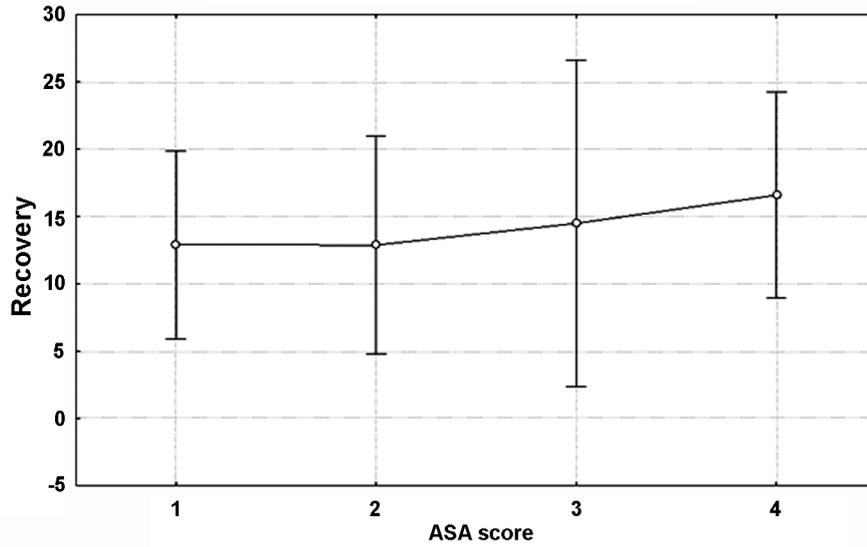


Figure 2 – One way ANOVA with Tukey correction for multiple comparisons. Patients with a higher preoperative ASA score exhibited a slight but insignificant tendency to a prolonged recovery time.

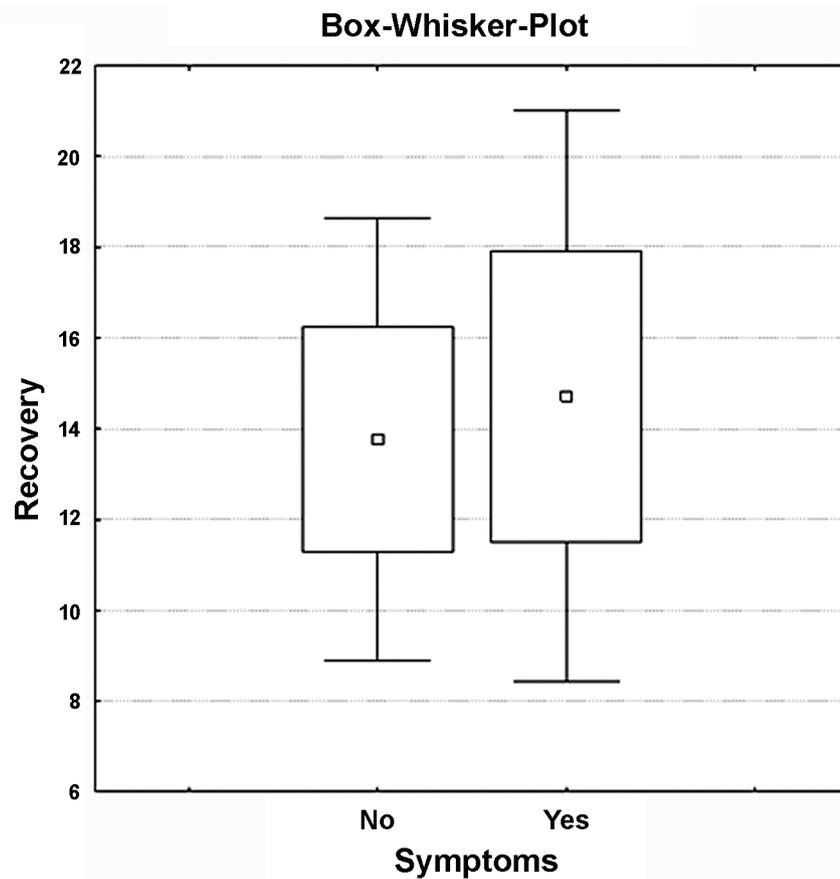


Figure 3 – Student's-t test. Symptomatic patients exhibited a slight but insignificant tendency of prolonged recovery time.

in order for patients to resume to their usual physical activities.

The multivariate analysis conducted in order to detect possible preoperative clinical variables that effect patient's survival demonstrated that: (a) patients with a high preoperative Karnofsky score (80-100) exhibited a highly significant chance of having a prolonged survival (30-60)-(80-100) $p = 0.0001$, (60-80)-(80-100) $p = 0.016$ (b) patients with lower preoperative ASA score exhibited a highly significant chance of having a prolonged survival ASA1: ASA3 $p = 0.0088$, ASA2: ASA3 $p = 0.0211$ and ASA2: ASA4: $p = 0.0135$. Asymptomatic patients, patients with non-pathologic laboratory findings, patients who underwent a curative operation and patients with a lower tumor stage exhibited a highly significant chance of having a prolonged survival $p = 0.0058$, $p = 0.0072$, $p = 0.0014$ and $p = 0.0028$ respectively. There was no significant difference in survival of patients with inflammatory disease when compared to patients with malignant disease (Table-2).

As far as the subjective opinion of patients or patient's relatives regarding the operation, 88.5% were satisfied with their decision to undergo the operation, 91.4% would undergo the operation once more if needed and 91.4% would advise such an operation to a patient their age.

COMMENTS

Elderly patients have traditionally been viewed as poor candidates for urologic surgery. However, a review of the literature regarding renal, prostate, and bladder cancer supports what most urologists know intuitively: properly selected elderly patients can safely undergo surgery and can, thereby, potentially gain survival benefits (4).

Patients over 80 years old present with unique health-care challenges, since they suffer from a higher incidence of comorbid medical conditions, which make them less tolerant to perioperative anesthetic, surgical stress, blood loss and postoperative complications (5,6). Despite the risk of major surgery in these patients, radical nephrectomy still remains the treatment of choice in many cases. Under inflammatory conditions, surgical resection of the involved tissue and systemic antibiotic administration are the primary mainstays of therapy regardless of age. In advanced malignant disease nephrectomy is not only of palliative benefit, to overcome pain, hemorrhage and paraneoplastic syndromes, but also has the potential to increase overall survival (7).

The basic question is if radical nephrectomy can be used as a curative treatment for malignant

Table 2 – Chi-square test. Preoperative clinical variables that effect patient's survival are shown in bold letters.

Comparison	Test	Significance
Pre-op Karnofsky index- Survival	Chi-square test	(30-60)-(60-80) $p = 0.2763$ (30-60)-(80-100) $p = 0.0001$ (60-80)-(80-100) $p = 0.016$
ASA– Survival	Chi-square test	ASA1: ASA3 $p = 0.0088$ ASA1: ASA4 $p = 0.053$ ASA2: ASA3 $p = 0.0211$ ASA2: ASA4 $p = 0.0135$ ASA3: ASA4 $p = 1$
No Symptoms - Survival	Chi-square test	$p = 0.0058$
Curative - Survival	Chi-square test	$p = 0.0014$
Non-pathologic Laboratory - Survival	Chi-square test	$p = 0.0072$

ASA score = American Society of Anesthesiologists score.

conditions in asymptomatic patients over 80 years old. Considering the fair life expectancy of the elderly and the excellent 5-year survival rates for local-stage RCC and upper tract TCC, patients are likely to benefit from surgical treatment regardless of their age (8). Lamb et al. (9), demonstrated the natural history of RCC in the elderly by reporting on 36 patients medically unsuitable for nephrectomy, with a median age of 76 years and a median tumor size of 6.0 cm. None of the 13 patients who died during follow-up had deterioration of the RCC, but in most cases the cause of death remained unclear. In our patient group the median size of the renal mass was 5.2 cm, and the average age was of 83.5 years. During a median follow-up of 31 months only 20% (n = 7 patients) passed away and despite their tumor stage (T3-T4), high ASA score (3-4) and low Karnofsky score (30-70) demonstrated a median survival of 25 months.

Several recent studies showed that complications of cancer surgery are no more common in the elderly than in younger patients (10-16). Indeed, as demonstrated, postoperative complications were encountered in 14.3% of patients with an operative mortality (14 days postoperative due to a stroke) encountered in n = 1 patient (2.9%). Therefore, despite the advanced age of the patients and high median ASA score (median score 3), the study group tolerated the procedure just as well as younger patients.

A critical consideration when contemplating major cancer surgery in the elderly patient is often the length of time it would take for the patient to resume usual physical activities (8). Valid concerns about the possible adverse sequel of a prolonged period of convalescence and physical inactivity on the suboptimal cardiovascular and musculoskeletal status of the elderly are often arguments against performing major open cancer surgery in this patient population (1). This was as well noted in the aforementioned patients. The median length of time required in order for them to resume their usual physical activities was 13 weeks (3-48 weeks). Interestingly, there were no preoperative clinical variables that significantly influenced the length of time required in order for patients to resume to their usual physical activities. This can be partly explained due to the fact that 40% of patients presented with symptoms and 22.8% underwent a palliative operation.

Although recovery time is a notable end point, it should not minimize the importance of certain other needs of elderly patients, including those who psychologically need to have their cancers surgically removed. Most of the patients, even those who were asymptomatic and demonstrated small lesions, had a strong desire to have their tumors removed, as they did not wish to wait until progression that might lead to a clinically significant disease.

The importance of age and comorbidity in treatment decisions and survival outcomes has long been recognized in oncology. However, tumor stage and grade remain the only variables on which treatment decisions and outcome research are based. The aging process is not uniform and patients show variable declines in organ function. Some people at 75 years old might be as fit, if not more so, than others at age 60 years (17). Although changes in some physiologic variables are predictable, it is well recognized that there is more heterogeneity in the elderly than in younger individuals (18). Thus, age is highly heterogeneous from a clinical perspective and poorly reflected by chronological age. Consequently, it is important to distinguish between fit and frail elderly patients and not to judge solely based on chronological age when considering suitability for cancer therapy (19). Indeed, the multivariate analysis conducted in order to detect possible preoperative clinical variables that effect patient's survival demonstrated that patients with a high preoperative Karnofsky score and a low preoperative ASA score exhibited a highly significant chance of having a prolonged survival despite the fact that their median age was 83.5 years old. This could somewhat justify the fact that there was no significant difference of the survival of patients with inflammatory disease when compared to patients with malignant disease. Conservative management such as monitoring is of course an accepted treatment alternative that has often been chosen for the elderly patient with associated significant comorbidity. However, conservative treatments not infrequently result in progressive local and systemic symptoms, which require repeated hospitalization and ancillary procedures for palliation. Such a management strategy may significantly compromise the quality of life of an 80-year-old patient who could reasonably be expected to have 5 to 8 years of an active lifestyle.

CONCLUSIONS

Radical nephrectomy and nephroureterectomy are safe and effective in well-selected patients over 80 years old. Although the delayed recovery time is an end point, it should not minimize the importance that patients themselves believe that they truly benefit from surgery since most of them are satisfied with their decision to have undergone the operation, would repeat it if necessary and would advise it to a patient their age.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

In the paper by Labanaris et al., the authors evaluate the peri-operative morbidity of radical nephrectomy and nephroureterectomy in a cohort of 35 patients over the age of 80. On multivariate analysis, the authors noted that patients with a pre-operative Karnofsky index of 30 to 60, patients with an ASA score > 3, and symptomatic patients exhibited a slight but insignificant tendency to prolonged recovery time. On multivariate analysis of predictors of survival, pre-operative Karnofsky index, ASA score, absence of symptoms, curative surgical resection, and normal (i.e. non-pathologic) laboratory parameters predicted patient survival. Although this study addresses an important clinical question, which is: should age and of itself preclude surgical resection? This study is not sufficiently powered to address this clinical question and the heterogeneity of the study population (including varied indications for surgery including 4 patients having nephrectomy for non-cancer related

etiologies) is a significant limitation to the present study. My clinical impression is that patient specific co-morbidities, complexity of the surgical resection, and pre-operative medical optimization may be more reflective of expected peri-operative morbidity. Clinicians have at their disposal many clinical tools such as ASA score, ECOG (or Karnofsky) performance status, and Charleston index to evaluate patient surgical risk. The ultimate question in my view is how do these tools specifically predict outcome in the specific patient population undergoing renal extirpation surgery? To date, this question remains unanswered.

In conclusion, I caution clinicians using the numerical value of age as a means of selecting patients suited for surgical resection. A more comprehensive review of patient, disease, and surgery specific parameters is required in assessing expected surgical risk and outcome.

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EDITORIAL COMMENT

The authors are to be commended for examining this issue of extirpative radical surgery on patients over the age of 80 years.

One has to be cautioned regarding the inevitable selection bias for this type of single-center retrospective experience reporting, (as this was not a prospective series of consecutive patients presenting with renal cell carcinoma, but rather, this is a series of patients who had already decided on surgery).

Patients with intractable pain, significant hemorrhage or manifestations of para-neoplastic syndromes are more likely to be justified for surgery.

Although the authors are to be congratulated for their surgical skills and efficiency, a routine ex-

tended lymphadenectomy in this age group and clinical setting would not be recommended, in view of the controversial issue of therapeutic or even diagnostic benefit of the lymphadenectomy.

The conclusion of “survival benefit” cannot be made in the absence of a randomized trial of “surveillance” versus “intervention”. In addition to “survival”, one needs to consider subsequent post-operative “functionality”, physical and nephrologic. The questionnaire attempts to address the former issue. However, a study involving patients reporting on their experience needs to be interpreted carefully because of reporting bias, albeit often inadvertent. Prolonged recuperation, or exacerbation of any preexisting con-

ditions because of the surgery and anesthetic, would render radical surgery in this population much less attractive and perhaps unjustified.

The authors rightly pointed out physiologic age rather than chronologic age is more important. In addition to patient preference, the decision to proceed

with surgery in this elderly cohort (especially those who are relatively asymptomatic), needs to take into account medical co-morbidities, performance status and severity of symptoms.

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Epidemiologic Characteristics of Renal Cell Carcinoma in Brazil

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Brazilian Society of Urology

ABSTRACT

Purpose: In Brazil, National data regarding the epidemiology of renal cell carcinoma (RCC) are scarce. The aim of this study was to describe the demographic, clinical, and pathologic characteristics of RCC diagnosed and treated by members of the SBU - Brazilian Society of Urology.

Materials and Methods: For this cross-sectional study, data were collected through an on line questionnaire available to the members of the Brazilian Society of Urology (SBU). Between May 2007 and May 2008, voluntary participant urologists collected data on demographic, clinical and pathological characteristics from patients diagnosed with RCC in their practice.

Results: Fifty SBU affiliated institutions contributed with patient information to the study. Of the 508 patients, 58.9% were male, 78.9% were white, and the mean age was 59.8 years. Smoking history, high blood pressure and a body mass index above 30 kg/m² were present in 14.8%, 46.1% and 17.9% of the patients, respectively. Abdominal ultrasound and computed tomography were the main diagnostic methods. The majority of the cases were localized tumors and metastasis were presented in 9.5% of the patients; 98.4% underwent nephrectomy. Clear cell carcinoma was the most common histological type. In comparison with private institutions, stage IV disease was less frequent among patients treated at public health services (P = 0.033).

Conclusions: RCC in Brazil is more common in white men in their sixth decade of life. Ultrasound is the main diagnostic tool for the diagnosis of clear cell carcinoma and we found that localized disease was predominant. A national registry of RCC is feasible and may provide valuable information.

Key words: carcinoma; renal cell carcinoma; cross sectional studies; epidemiology; kidney neoplasms

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INTRODUCTION

The incidence of renal cell carcinoma (RCC) is increasing globally (1,2). Currently, the disease represents approximately 2.0% of all new cases of cancer and over 100.000 deaths worldwide (3). Improvements in imaging diagnosis may have contributed to the rising incidence of RCC over the past three

decades, since this rise in incidence is mainly a result of the increasing detection of small tumors (4). However, at least in the United States, both incidence of late-stage RCC and mortality rates due to the disease have also been rising, implying that improvements in the ability to diagnose RCC are being outweighed by the increasing prevalence of some of the risk factors for this tumor (5).

In Brazil, data regarding the epidemiology of RCC on a national scale are currently scarce, since the disease is not among the 10 most frequent tumor types annually reported by the National Cancer Institute (6). Data from regional surveys suggest that RCC represents approximately 1.2% of all cases of cancer in the country (7). Recognizing the need for better information about the burden of RCC in Brazil, the Brazilian Urological Society (SBU) led the effort to produce this first-ever survey on a national scale describing the epidemiology of RCC in Brazil.

The aim of this study was to describe the demographic, clinical, and pathologic characteristics of RCC diagnosed and treated by urologists associated to SBU in Brazil.

MATERIALS AND METHODS

Data Collection

To perform a cross-sectional study, a web-based survey containing 75 questions was made available to approximately 3,700 physicians affiliated to SBU, who were invited to participate in the study through mailed announcements and frequent advertising of the study on the SBU website. The questionnaire was available on the website for the duration of the study, and could also be sent by regular mail or fax upon request (www.sbu.org.br). Participant physicians were instructed to collect data from patients seeking medical attention between May 2007 and May 2008. All completed questionnaires were registered in a central database that was under the supervision of SBU. The study was approved by the institutional review boards affiliated with the centers where participants were enrolled. An informed consent was offered for all patients and signed by them. The study was sponsored by Pfizer Brazil.

Data collected from each patient included age, gender, race, state of origin, weight, height, tumor-node-metastases (TNM) stage, histological subtype, the presence of known risk factor for RCC (history of smoking, hypertension, obesity, diabetes, hypercholesterolemia, end-stage renal disease, and Von Hippel-Lindau disease), signs and symptoms present at diagnosis (hematuria, palpable mass, flank

pain, weight loss, fever, and night sweats), the exam leading to diagnosis (clinical findings, laboratory tests, or imaging studies), and type of medical assistance (public health care, private care, or third-party payment by insurance companies; the latter two were combined for analysis under the category “private institutions”).

Body-mass index (BMI), the weight in kilograms divided by the square of the height in meters, was calculated for each patient. TNM stage was determined according to the 2002 classification of renal tumors (8). Tumor histology was classified according to the Heidelberg classification (9). Five subtypes of RCC were reported in the study: clear-cell, papillary, chromophobe, collecting-duct, and unclassified carcinomas.

Statistical Analysis

In addition to descriptive statistics of the demographic, clinical, and pathologic variables, exploratory analyses were conducted for comparisons between groups of patients. The chi-square or Fisher’s exact tests were used to compare the frequency of categorical variables between groups, and Student’s-t-test or analysis of variance were used to compare continuous variables. All P values are two sided, and $P < 0.05$ was considered significant. All data analysis was conducted using the MedCalc software, version 9.6.0.0 (MedCalc, Mariakerke, Belgium).

RESULTS

Patient and Disease Profile

Fifty SBU affiliated institutions from 14 Brazilian States contributed with patient data for this study. Each institution was represented by at least one physician and a total of 508 patients were enrolled. Approximately three-quarters of patients were seen at institutions from the State of São Paulo. Table-1 shows the distribution of patients according to State. Patient demographics and tumor characteristics are given in Table-2. Slightly more patients were male, nearly 80% were white and 83.5% were assisted by

Table 1 – Distribution of patients according to Federation States.

State of Enrollment	Number	Percent
Bahia	1	0.2
Paraíba	1	0.2
Paraná	2	0.4
Goiás	3	0.6
Mato Grosso do Sul	4	0.8
Distrito Federal	6	1.2
Pará	6	1.2
Rio Grande do Sul	8	1.6
Sergipe	9	1.8
Piauí	12	2.4
Minas Gerais	18	3.5
Rio de Janeiro	19	3.7
Pernambuco	24	4.7
Espírito Santo	26	5.1
São Paulo	369	2.6
Total	508	100.0

public health services. The mean age was close to 60 years, and the most prevalent risk factor for RCC was hypertension. With regard to symptoms and signs upon presentation, hematuria (42.9%) and flank pain

(41.3%) were the most frequent, whereas the classic triad of hematuria, flank pain and palpable flank mass was present in only 4.5% of the cases (Figure-1). The most common procedure leading to the diagnosis of RCC was an abdominal ultrasound (73.4%), followed by computed tomography (CT) scan of the abdomen (19.1%) and physical exam (3%). Diagnosis through intravenous urography was anecdotal (0.6%). Three-quarters of patients had localized disease (i.e., TNM stage I and II) and the most common histological type was clear cell carcinoma; virtually all patients underwent nephrectomy (radical or partial) for management of their RCC. Other patient and disease characteristics are shown in Table-2.

Exploratory Analyses

The presence of most risk factors for RCC varied little according to age. However, there were significantly higher proportion of patients with a history of hypertension ($P < 0.0001$) or diabetes ($P = 0.0011$) among subjects aged 60 years or older, in comparison with younger patients. The proportion of cases diagnosed by ultrasound or by CT scan did not differ among patients seen at public health services or in private institutions ($P = 0.631$). Metastatic disease

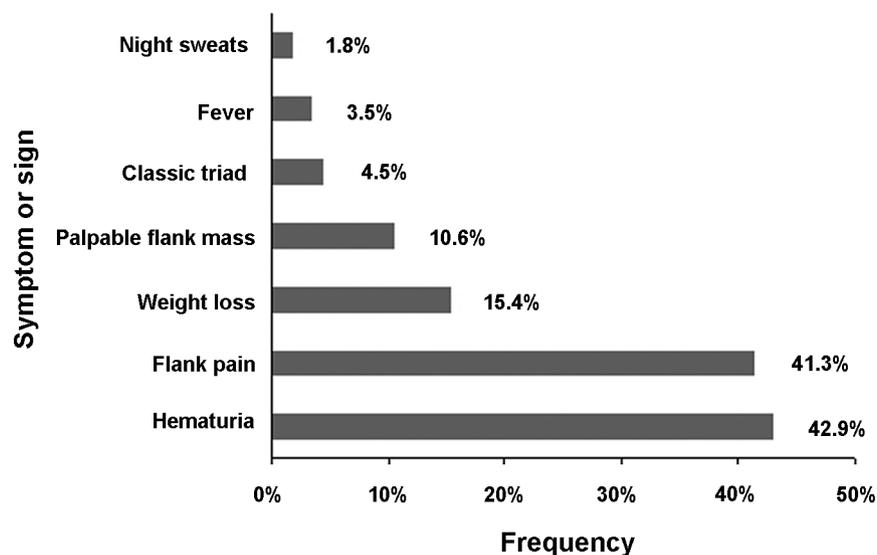
**Figure 1** – Frequency of signs and symptoms at presentation of renal cell carcinoma.

Table 2 – Patient and tumor characteristics.

Characteristic	Number	Percent
Age, years		
Mean (\pm SD), range	59.8 (\pm 12.3), 24.6 to 96.8	
Sex		
Female	209	41.1
Male	299	58.9
Race		
White	401	78.9
Black	33	6.5
Asian	3	0.6
Mixed race	71	14.0
Body mass index (BMI), kg/m ²		
Mean (\pm SD)	26.8 (\pm 5.2)	
History of smoking	75	14.8
Hypertension	234	46.1
BMI > 30 kg/m ²	91	17.9
End-stage renal disease	11	2.2
Von Hippel-Lindau disease	1	0.2
TNM stage		
I	189	37.2
II	124	24.4
III	61	12
IV	48	9.5
Unknown	86	16.9
Histological subtype		
Clear-cell carcinoma	374	73.6
Papillary carcinoma	33	6.5
Chromophobe carcinoma	46	9.1
Collecting-duct carcinoma	2	0.4
Unclassified	52	10.2
Unknown	1	0.2
Radical or partial nephrectomy	500	98.4
Type of medical assistance		
Public health	424	83.5
Private	14	2.8
Insurance company	69	13.6
Unknown	1	0.2

SD = standard deviation.

Table 3 – Exploratory analyses of TNM stage distribution according to clinical characteristics, presence of risk factors, histological subtype, and type of medical assistance.

Factors	TNM Stage (%)				p Value
	I	II	III	IV	
Age, mean (years)	58.9	59.6	61.3	60.6	0.578
Sex (%)					
Female	45.1	33.1	11.4	10.3	0.302
Male	44.5	26.7	16.6	12.1	
History of smoking (%)	24.4	23.0	35.3	27.0	0.089
Hypertension (%)	43.8	49.2	42.4	37.8	0.563
BMI > 30 kg/m ² (%)	18.1	21.1	11.7	17.0	0.478
End-stage renal disease (%)	2.1	1.7	1.7	0	0.799
Histological subtype (%)					
Clear-cell	42.4	29.1	16.1	12.3	0.1626
Others	51.9	30.2	9.4	8.5	
Medical assistance (%)					
Public health	83.6	92.7	83.6	22.9	0.033
Private institution	16.4	7.3	16.4	77.1	

BMI = body mass index.

was less frequent among patients seen at public health services ($P = 0.033$), in comparison with those seen in private institutions. On the other hand, TNM stage was not associated with any of the other patient demographic characteristics, tumor histological subtype or risk factors (Table-3).

COMMENTS

This study provides a cross-sectional view of RCC in Brazil, a country where no national incidence rates for the disease are currently available (6,7). In an attempt to overcome the paucity of data in our country, SBU carried out a nationwide study on the epidemiologic and clinical features of RCC in Brazil. As a result, a total of 508 patients were enrolled by physicians from 50 different institutions. Most demographic characteristics of the study cohort were quite similar to those in the existing literature (5), since male patients predominated, the majority was white, and the mean age was close to 60 years. Also, similar to what occurs in developed countries, most

of the patients presented with localized disease (37% with stage I RCC). The predominance of early-stage disease is corroborated by the fact that abdominal ultrasound (73.4%) or abdominal CT scans (19.1%) were main diagnostic methods in contrast to physical examination (3.0%) and intravenous urography (0.6%).

Tumor stage is considered one of the most important prognostic factors in RCC (10,11). In our study, the proportion of patients with metastatic disease (9.5%) was similar to that reported in other clinical series (12,13). On the other hand, this proportion is lower than expected from population-based studies, in which patients with metastatic disease comprise between 25% and 30% of cases upon presentation (14). We did not find an association between TNM stage and patient or tumor-related characteristics. It is generally acknowledged that men present with more advanced disease at diagnosis. Aron et al., analyzing 35,336 cases of RCC from the Surveillance, Epidemiology, and End Results (SEER) registries database from 1973 to 2004, reported that male gender was associated with higher stage at presentation and

poorer overall survival, compared with women (15). However, we did not find the same association in our sample. Similarly, there was no association between stage and the presence of risk factors for RCC in the present study. Smoking, hypertension and obesity are the most frequently recognized risk factors for RCC (16-18). Yet, the presence of risk factors did not seem to correlate with stage at presentation in the present series.

Several studies have evaluated the prognostic value of histological subtype in RCC. Although some studies have suggested that clear-cell histology is associated with a poorer survival (19), Patard et al. reported that in a multivariate analysis including TNM stage, Fuhrman nuclear grade and Eastern Cooperative Oncology Group performance status (PS), histological subtypes of RCC did not have an independent prognostic significance (12). Although we did not collect data on Fuhrman nuclear grade and PS, we did not find an association between the presence of clear-cell histology and more advanced disease. An obvious limitation of our study design is the lack of central pathologic review; therefore, we cannot exclude the possibility of histological subtype misclassification in some cases.

We found an association between TNM stage and type of medical assistance. Surprisingly, there was a higher proportion of early stage disease, especially stage II, among patients seen in public health care facilities, whereas patients seen at private institutions were more likely to present with metastatic disease ($P = 0.033$). Such findings are in contrast to those obtained in another epidemiologic study conducted by SBU. In that cross-sectional survey of prostate cancer in the State of São Paulo, 30% of the patients seen in public institutions were diagnosed with locally advanced or metastatic disease, compared with 21% of patients treated in the private sector (20). The reasons for these findings are not clear, and we may only speculate as to possible explanations. One reason for the higher frequency of metastatic disease in the private sector could be referral bias, leading to more patients with advanced disease in the public institutions being referred to medical oncologists or palliative care. Another explanation could be the migration of patients diagnosed with metastatic disease to the private sector seeking for faster assistance. Alterna-

tively, patients in the private sector could have undergone more extensive imaging assessment, leading to stage migration in this health care sector. The latter hypothesis, however, does not seem to be supported by our own finding of no significant difference in the proportion of cases diagnosed by ultrasound or by CT scan in the two sectors. Finally, the discrepancies in the proportions of patients with metastatic disease may have resulted from the play of chance or from the lack of data for complete classification of nearly 17% of patients.

The major drawback of the study was that participation of the urologists was on a volunteer basis and it did not include all the cases seen during the period. All SBU members were invited by mail to participate in this epidemiological survey. From the 76 institutions affiliated with the SBU, 50 (65.8%) took part in this study. Although we had the participation of institutions from 14 Brazilian States, 72.6% of patients that were enrolled in the study were from one single State, São Paulo. Probably due the fact that São Paulo has the majority (31.6%) of total SBU affiliated Institutions (24 of 76 institutions).

Although it could be filled out in a relative short period of time, the questionnaire used in this survey was rather long and required the review of medical charts, laboratory findings, imaging studies and pathology reports. Perhaps the use of shorter questionnaires aiming at more specific questions will be better accepted. Other strategies to increase participation of Brazilian urologists of the whole country in epidemiological surveys should be discussed.

Medical associations may provide many opportunities for productive research, especially for physicians not currently affiliated to academic institutions. Despite the limitations of the method, this study represents the largest collection of RCC cases in Brazil to date and shows that a registry is feasible and may provide valuable information regarding RCC in Brazil. We hope the present work will stimulate further participation of Brazilian urologists in future projects.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

Our approach to kidney cancer has changed considerably in recent years. More and more tumors are now diagnosed at earlier stages. For example, smaller masses are often benign justifying the use of needle biopsy to confirm the diagnosis. This procedure was unthinkable in previous eras when most tumors were considered malignant until proved otherwise after the analysis of abdominal ultrasound or CT scans. Similarly, this increased the indications for partial nephrectomy, as well as less aggressive methods, such as cryoablation. The authors presented an epidemiologic study on renal cell carcinoma in Brazil. It is very important that we can consult these data to plan a strategy to treat our patients. Three-quarters of patients had localized disease (i.e., TNM stage I and II) and the most common histological type was

clear cell carcinoma; virtually all patients underwent nephrectomy (radical or partial) for management of their RCC. The predominance of early-stage disease is corroborated by the fact that abdominal ultrasound (73.4%) or abdominal CT scans (19.1%) were main diagnostic methods in contrast to physical examination (3.0%) and intravenous urography (0.6%). Unfortunately, 85% of the patients in the study were from the southeast region of the country. Another obvious limitation of the study design is also the lack of a central pathologic review. A possible reason for the higher frequency of metastatic disease in private sector could be a referral bias, leading patients with more advanced disease to look for other specialists in private health care sector.

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REPLY BY THE AUTHORS

Although the vast majority of the cases were from the southwest region, it reflects the participation rates of our urological community. The opportunities for study participation were rigorously the same for all members of the Brazilian Society of Urology (SBU). We must remember that more than half of SBU members are in the Brazil southeast states. Based on this inedited data, the SBU must develop new approaches

to attract more Brazilian urologists for National trials and surveys.

Although the lack of central pathologic review be a limitation of the study design, as already discussed in the paper, it may represents a new opportunity to SBU to promote an approach with other National medical societies, specially the Brazilian Society of Pathology.

The Authors

The Role of Nephrectomy of the Atrophic Kidney in Bearers of Renovascular Hypertension

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ABSTRACT

Purpose: Evaluation of the beneficial effect of nephrectomy of the atrophic kidney on blood pressure (BP) and renal function.

Materials and Methods: A retrospective study of 51 patients with renovascular hypertension (RVH), bearers of atrophic kidney due to severe stenosis or occlusion of the renal artery. Average age was 47.1 ± 15 years, the median creatinine clearance was 54 mL/min, average systolic BP (SBP) 149.6 ± 22.5 mm Hg, average diastolic BP (DBP) 90.8 ± 17 mm Hg and the median number of hypotensors 3 (1 to 5) per patient per day. Blood pressure and serum creatinine were analyzed from 12 to 60 months after the nephrectomy.

Results: There was a significant improvement in the average SBP in the periods from 12 to 36 months ($p \leq 0.028$) and for the average DBP from 12 to 48 months after the nephrectomy ($p \leq 0.045$), accompanied by a significant reduction in the use of hypotensors from 12 to 48 months ($p < 0.05$). One year after the nephrectomy, there was a 69% improvement in blood pressure and 63.8% improvement in renal function of patients.

Conclusion: The removal of atrophic kidney in patients with RVH is a safe procedure which presents benefits for the control of arterial hypertension and renal function in bearers of renovascular hypertension.

Key words: nephrectomy; atrophic; kidney renovascular; hypertension

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INTRODUCTION

Among the causes of secondary hypertension, we emphasize renovascular hypertension resulting from renal ischemia caused by the total or partial stenosis of the renal artery, presenting an atherosclerotic etiology in 90% of the cases and fibrodysplasia of the artery in 10% (1,2). It is the second most common cause of secondary hypertension, only after parenchymal renal diseases. It occurs in from 1 to 5% of the adult hypertensive population, but increases in the elderly, diabetics and bearers of systemic atheroscle-

rotic lesions (1,3). It has growing participation as a cause of dialytic renal insufficiency (4,5).

Ischemic nephropathy is caused by the chronic and hemodynamically significant occlusion of the renal artery which results in a considerable reduction in the blood flow, a diminution in the glomerular filtration rate and leads to the progressive damage of the renal parenchyma (1,3,6). The renal hypoflow results in the activation of the renin-angiotensin-aldosterone (RAA) system, responsible in the final analysis for vascular alterations, damage to the dependent endothelial vasodilation and an increase in oxidative stress,

mainly in the etiology of atherosclerotic patients (7).

Renovascular hypertension (RVH) can be cured in special cases. The revascularization of the ischemic kidney, whether surgical or by percutaneous angioplasty (PTA), is the best means of treatment and should be considered when pharmacological treatment is insufficient for the adequate control of the blood pressure or when inexplicable renal insufficiency appears. We analyzed the nephrectomy of the atrophic kidney (less than 8 cm) in those patients with refractory blood pressure or a deterioration of the renal function, when the revascularization of the artery was no longer possible.

MATERIALS AND METHODS

This was a retrospective observational study of 61 patients with a diagnosis of RVH who underwent nephrectomy during the period from January 1989 to January 2007. Ten patients were lost to follow-up. The general data of the patients is found in Table-1. The average age of the patients was 47.1 ± 15 years with a predominance of the female sex and

white. The average pre-operative SBP was 149.6 ± 22 mm Hg and the average pre-operative diastolic blood pressure (DBP) was 90.8 ± 16.7 mm Hg with 2.8 ± 1 hypotensors per patient per day. The median pre-operative serum creatinine was 1.3 mg /dL (0.8 to 4.5 mg/dL) analyzed by the colorimetric method (8). Hypercholesterolemia and smoking were the most frequent risk factors.

The average renal size of the atrophic kidney was 7.1 ± 1.1 cm (10 to 5.2 cm) and the contralateral kidney was 10.9 ± 0.9 cm (9.3 to 13.5 cm), measured by ultrasonography. On echo-Doppler examination of the renal arteries the stenosis which made up $\geq 70\%$ of the diameter of the blood vessel were considered as hemodynamically significant lesions. The function of the atrophic kidney measured by renal scintigraphy with the radioisotope DTPA and captopril was 8% (0-49%).

The measurement of the plasma rennin activity (PRA) was performed by radioimmunoassay Gamma Coat PRA I125 Ria Kit, by the collection of blood by selective catheterization of the renal veins and cava inferior.

Of the 35% (18/51) of patients who were bearers of significant bilateral lesion, 17.6% (9/51)

Table 1 – General data of the 51 patients with renovascular hypertension who underwent nephrectomy.

Average age (years \pm SD, minimum - maximum)	47 ± 15 (13 - 77)
Sex: female / male	67% / 33%
Color: white / non-white	71% / 29%
Period of arterial hypertension (years - median)	11.5 (1 month - 30 years)
Average systolic blood pressure in mm Hg	149.6 ± 22.5
Average diastolic blood pressure in mm Hg	90.8 ± 16.7
No. of hypotensor drugs / patient / day	2.8 ± 1.0
Pre-operative (median) serum creatinine mg/dL	1.3 (0.8-4.4)
Hypercholesterolemia	67%
Smoker and ex-smoker	53%
Diabetes mellitus	18%
Previous cardiac disease	31%
Previous cerebrovascular disease	21%
Peripheral vascular disease / aortic aneurism	19%

required revascularization by percutaneous transluminal angioplasty (PTA) of the contralateral artery. The previous surgical revascularization by means of an autotransplant of the contralateral kidney was carried-out in 9.8% (5/51) of the patients, 4% (2/51) of whom no longer required dialysis. Eight percent (4/51) did not undergo any procedure.

The arteriography, performed by means of selective catheterization of the renal arteries, was performed in 74% (38/51) of the cases. The magnetic resonance angiography of the renal arteries was performed in 16% (8/51) of the patients and its principal indicator was the presence of creatinine equal to or greater than 2 mg/dL.

The recommendation for the nephrectomy of the atrophic kidney was made only after total or significant occlusion of the renal artery, associated with the absence of renal function, had been demonstrated. In 70.5% of the patients nephrectomies by video laparoscopy were performed and in the remaining 29.5% nephrectomies by lumbotomy.

The postoperative measurements of blood pressure were made in accordance with the recommendations of the WHO. and were completed each 12 months for five years, with the same period for the collection of serum creatinine. Patients were regarded as cured who had DBP < 90 mm Hg and systolic (SBP) < 140 mm Hg with no hypotensor medication and with an improvement in blood pressure with DBP < 90 mm Hg and /or SBP < 140 mm Hg with the same or a reduction in hypotensor medication or with a reduction in DBP of at least 15 mm Hg with the same number or a reduction in hypotensor medication (9). We considered therapeutic failures those cases in which there was a worsening of blood pressure or an increase in the number of hypotensors for the same pressure levels; all the other cases benefited from the treatment, in accordance with the criteria cited above (9).

In the assessment of renal function, we used the estimated creatinine clearance, obtained on the basis of the MDRD equation (modification of diet in renal disease study prediction equation) (9,10). The numbers obtained were transferred to the creatinine clearance graph where each line represents a patient throughout the period of observation, the horizontal and ascending lines indicating an improving and the descending ones, a worsening renal function.

Statistical Analysis

The data have been summarized as numbers and percentages for the qualitative variables and as averages \pm standard deviations where the supposition of normality of the data has been satisfied and in those cases for which this supposition could not be made, the median was used (minimum - maximum).

The assessment of the pressure levels over the study period was performed by means of a variance analysis model (ANOVA) and the measurements repeated, the multiple comparisons were submitted to the construction of contrasts.

The comparison between the groups (R x NR) (Responders x Non-Responders) or Improvement x Worsening) was made by means of the Chi-squared test when the variable was qualitative and in those cases in which the value expected was less than five, the Fisher's Exact Test was used. For the quantitative variables Student's-t-test or Mann's test was used for those cases in which the supposition of normality could not be made.

A significance level of 5% was considered significant. SAS (Statistical Analysis System V. 9.0) software was used for the analysis of the data.

RESULTS

There was statistically significant variation both for the SBP ($p < 0.001$) and for the DBP ($p = 0.005$) over time (Figure-1). The decrease observed at 12 months post nephrectomy was 14.5 ± 2.8 mm Hg ($p < 0.001$) for the SBP and 9.7 ± 2.4 mm Hg ($p < 0.001$) for DBP. From 12 months to 60 months postoperatively there was no statistically significant variation whether in SBP ($p > 0.05$) or DBP ($p > 0.05$), shown in the respective Tables-2 and 3. It was observed that the average decrease in SBP from the pre-nephrectomy period to each of the periods assessed was significant until 36 months post-nephrectomy, while the average decrease in the DBP presented statistical significance until 48 months as compared with that of the pre-nephritic period (Table-4).

The average number of hypotensors used in the pre-operative period of 2.8 hypotensors/day diminished significantly ($p < 0.05$) for the period

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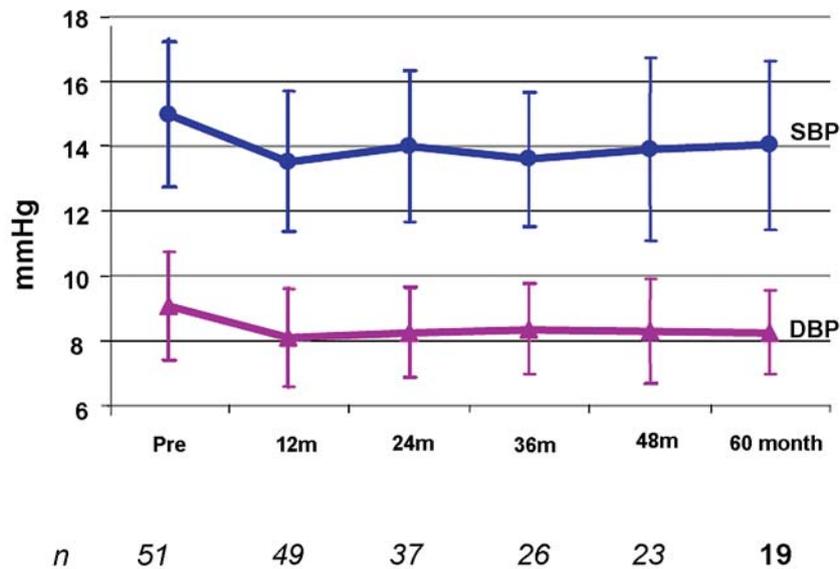


Figure 1 – Average SBP and DBP pre - and post-nephrectomy in patients with RVH.

of 12 months and remained constant until 48m (2.0 hypotensors/day) after the nephrectomy.

One year after the nephrectomy 49 patients were still being followed-up and the BP of 69% of them had improved, in accordance with the criteria previously mentioned (9). There was one death and one dialytic renal insufficiency (2/51), which were excluded from the sample. The value of the variations of the DBP and SBP at 12 months for each patient are shown in Figures-2 and 3 respectively, where in the lower part of each figure are shown the patients whose pressure levels improved. There was an 8% (4/51)

cure rate of RVH, 3 of the patients had fibromuscular dysplasia of the renal artery.

Sixty-nine percent (34/49) of the patients were considered responders as they had shown an improvement in blood pressure and 30.6% (15/49) of the patients as non-responders as their blood pressure had worsened. There was no significant difference ($p > 0.05$) between the groups for any of the factors analyzed: age, sex, color, initial blood pressure, initial creatinine, bilateral disease, risk factors and co-morbidities (Table-5). The renal function of the patients was checked by the measurement of serum

Table 2 – Averages of the systolic blood pressures from the pre-operative period until 60 months post-nephrectomy.

mm Hg	Pre	12 m	24 m	36 m	48 m	60 m
Average	149.6	135.2	140.0	136.0	139.0	140.4
DP	22.5	21.8	23.3	20.6	28.3	26.1
Median	140.0	136.0	134.0	132.5	132.0	130.0
Minimum	110.0	100.0	100.0	100.0	105.0	110.0
Maximum	210.0	190.0	186.0	176.0	220.0	200.0
No. observed	51	49	37	26	23	19

Nephrectomy of Atrophic Kidney in Renovascular Hypertension

Table 3 – Averages of the diastolic blood pressures (DBP) from the pre-operative period until 60 months post-nephrectomy.

mm Hg	Pre	12 m	24 m	36 m	48 m	60 m
Average	90.8	81.1	82.7	83.6	83.0	82.6
DBP	16.7	15.0	14.1	14.0	16.0	13.1
Median	90.0	80.0	81.0	83.5	81.0	80.0
Minimum	50.0	47.0	50.0	65.0	60.0	66.0
Maximum	140.0	130.0	110.0	120.0	130.0	120.0
No. observed	51	49	37	26	23	19

creatinine taken every 12 months up to 60 months post-nephrectomy and the estimated creatinine clearance (MDRD) was calculated. There was a follow-up loss of 7.8% (4/51) of the patients.

Figure-4 shows the progress in renal function over the 60 months of observation. Twelve months post-nephrectomy 64% (30/47) of the patients presented an improvement in creatinine clearance (MDRD), represented by the ascending curves.

Figure-5 shows the progress in renal function over 60 months. One can observe the 36% (17/47) of patients whose renal function worsened (falling curves). Worthy of note among this group are the 23% of patients who initially lost renal function, but who demonstrated recovery of this function during the follow-up period. Dialysis was necessary in 8% (4/51) of the patients over the 60-month period.

When the characteristics of the patients divided into groups according to the improvement or

worsening of their renal function were studied, they were found to be homogeneous, that is to say, without any statistically significant difference among the variables studied ($p > 0.05$), i.e., these same factors as were analyzed for the blood pressure (Table-6).

Sixty percent of the cases (31/49) of this study had levels of serum rennin activity. Lateralization of the rennin was found in 85% of the patients divided among the different groups, with no statistical significance.

In eleven patients (21.5%) there was no segmental stenosis of the vessel. In the histopathological analysis of the renal artery of the remaining patients we found atherosclerosis of the renal artery in 63% of the cases, fibromuscular dysplasia in 26% and Takayasu arteritis in 6%. The histological data obtained from the renal parenchyma are: ischemic atrophy of the renal parenchyma in 72% of the cases, benign nephrosclerosis in 38%; malignant nephro-

Table 4 – Differences in systolic and diastolic pressures as between the pre-operative period and each of the instants assessed in patients with RVH (in mm Hg).

Months	Δ SAP (SAP post less SAP prev)	Δ DAP (DAP post less DAP prev)
12 m	14.5 \pm 2.8 ($p < 0.001$)	9.7 \pm 2.4 ($p < 0.001$) g
24 m	8.5 \pm 3.9 ($p = 0.028$)	6.9 \pm 3.0 ($p = 0.023$)
36 m	10.9 \pm 4.7 ($p = 0.022$)	7.1 \pm 3.5 ($p = 0.045$)
48 m	10.1 \pm 5.2 ($p = 0.055$)	7.9 \pm 3.7 ($p = 0.035$)
60 m	9.1 \pm 5.8 ($p = 0.117$)	7.6 \pm (4.0) ($p = 0.062$)

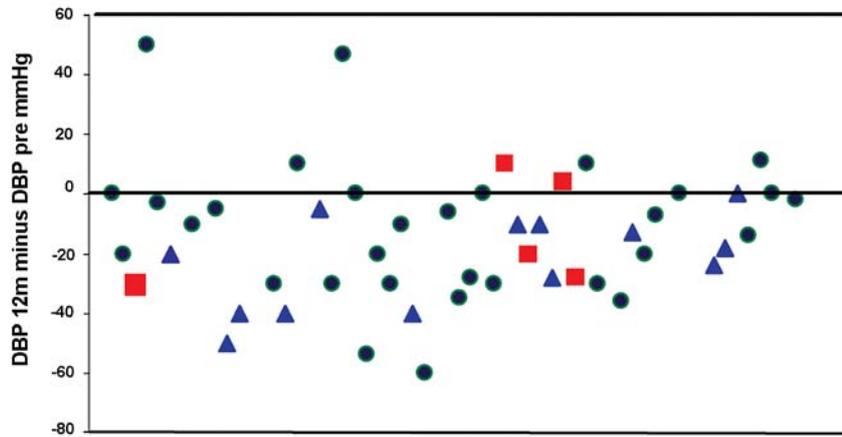


Figure 2 – Variation of SBP of each patient 12m after nephrectomy (n = 49). ● reduction , ▲ same and ■ increased number of hypotensors.

sclerosis in 10%, ischemic infarction of the renal parenchyma in 4% of the patients, interstitial nephritis in 6%, chronic pyelonephritis in 12 % and malignant renal neoplasms (of less than 1 cm) in 4% of the cases studied.

In the group with improvement of the renal function, 54.2% of the patients had a diagnosis of fibromuscular dysplasia and 29.2% of the cases had atherosclerosis and by means of the application of the generalization of Fisher’s Exact Test, a statisti-

cally significant association was observed ($p = 0.003$) between this histological type and the improvement in renal function. No embolic complications were identified in this series.

COMMENTS

RVH treatment has changed over recent years. The use of nephrectomy has declined as a result of the

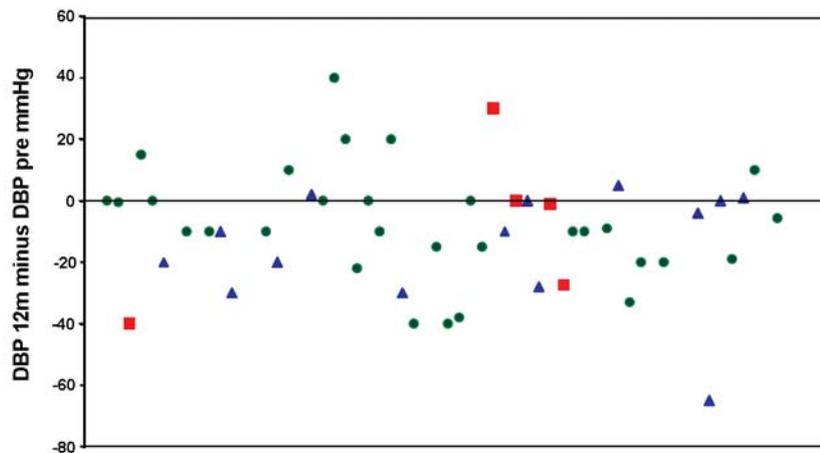


Figure 3 – Variation of the DBP of each patient 12 months after nephrectomy (n = 49). ● reduction, ▲ same and ■ increase in the number of hypotensors.

Nephrectomy of Atrophic Kidney in Renovascular Hypertension

Table 5 – Characteristics of the patients with renovascular hypertension, in accordance with the pressure response to nephrectomy.

	Responders (N = 34)	Non Responders (N = 15)	p Value
Age (years)	46.2 ± 13.7	45.5 ± 15.8	0.891
Sex: Male / Female	35.3% / 64.7	33.3% / 66.7%	0.894
Color: White / Non-white	73.5% / 26.5%	60.0% / 40.0%	0.502
Time of hypertension in years	12 (0.10 - 25)	9 (0.75 - 30)	0.585
Systolic Blood Pressure prev mm Hg	149.1 ± 23.0	150.9 ± 22.6	0.800
Diastolic Blood Pressure prev mm Hg	92.7 ± 14.7	86.5 ± 21.4	0.247
No. hypotensors	2.9 ± 0.9	2.5 ± 1.2	0.267
Serum Creatinine (mg/dL)	1.1 (0.8 - 4.5)	1.5 (0.8 - 4.4)	0.116
Clearance of Creatinine (mL/min)*	60.5 (15 - 100)	44.0 (17 - 83)	0.095
US atrophic kidney (cm)†	7.3 ± 1.2	6.6 ± 1.0	0.061
Lesion > 70% of contralateral renal artery on Doppler	35.3%	40.0%	0.753
Scintigraphy com DTPA atrophic kidney %	9.6 (0 - 49)	5.0 (0 - 17)	0.115
Contralateral kidney %	90.4 (59 - 100)	95.0 (83 - 100)	0.099
Lateralization of serum rennin: Yes / No	75.0% / 25%	88.9% / 11.9%	0.633
Hypercholesterolemia: Yes / No	61.8% / 38.2%	73.3% / 26.7%	0.433
Smoking: Yes / No	50.0% / 50.0%	60.0% / 40.0%	0.518
Heart Disease: Yes / No	29.4% / 70.6%	33.3% / 66.7%	> 0.999
Stroke: Yes / No	20.6% / 79.4%	20.0% / 80.0%	> 0.999
Diabetes Mellitus :Yes / No	17.6% / 82.4%	13.3% / 86.7%	> 0.999
Peripheral Arterial Disease			
Yes / No	17.6% / 82.4%	20.0% / 80.0%	> 0.999
Aortic Aneurism: Yes / No	11.8% / 88.2%	13.3% / 86.7%	> 0.999

† US = renal ultrasound.

rise of new hypotensor drugs, developed on the basis of the knowledge the aldosterone angiotensin rennin system and the development of angioplasty techniques (PTA) with the implanting of “stents” (3,11). More recently, the improved understanding of the mechanisms which harm dependent endothelial dilation and oxidative stress, especially as related to high levels of angiotensin II, particularly in the atherosclerotic lesion, herald new forms of treatment for the future (12).

The removal of the atrophic kidney caused by the severe stenosis of the renal artery was carried-out

in patients with refractory arterial hypertension with no possibility of revascularization.

Various studies have been reported in the literature comparing percutaneous revascularization and conservative clinical treatment in the treatment of RVH (13), but there are few series regarding the nephrectomy of the atrophic kidney as an alternative form of treatment for the bearer of renovascular hypertension with blood pressure of difficult control (14-16).

This study analyzed 51 nephrectomies of the atrophic kidney for complete obstruction of the

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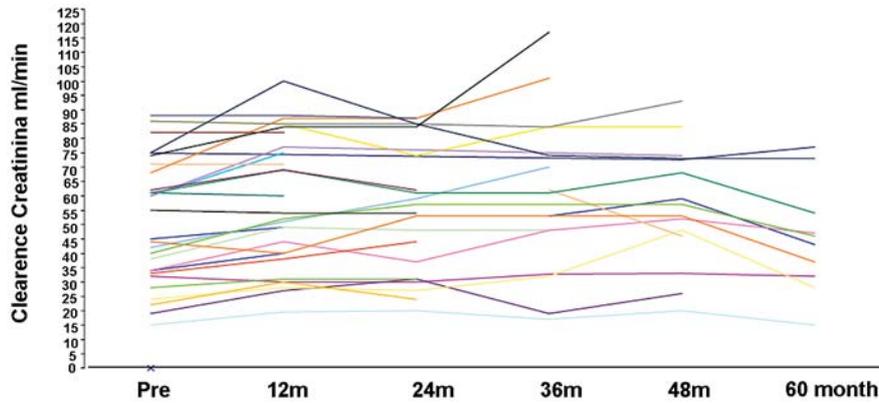


Figure 4 – Patients with improved creatinine clearance ($n = 30$).

renal artery. There was a predominance of the video laparoscopic technique, which was used in 70.5% of the cases. A year after nephrectomy, SBP was 135 ± 21 mm Hg and DBP of 81 ± 15 mm Hg, significantly lower than the initial levels, and they were thus maintained for 36 months and 48 months, respectively, together with a significant reduction in the number of hypotensors.

The division into groups on the basis of response in terms of blood pressure and renal function one year after nephrectomy, was performed to identify those characteristics which determined the response. Sixty-eight percent of the cases which

presented an improvement in arterial hypertension were included in the group (R), 8% of them being cured after one year, 75% (3/4) of them being patients with RHV due to fibromuscular dysplasia of the renal artery and 32% of the remaining cases belonging to the NR group (Table-5). The creatinine clearance (MDRD) curve (9,10,13) was used to enable us to classify the patients by group into those which presented either improvement or worsening of the renal function at 12 months. There was an improvement in creatinine clearance one year after nephrectomy in 64% of the cases (Figure-4) and a worsening in 36% (Figure-5). Twelve percent of the

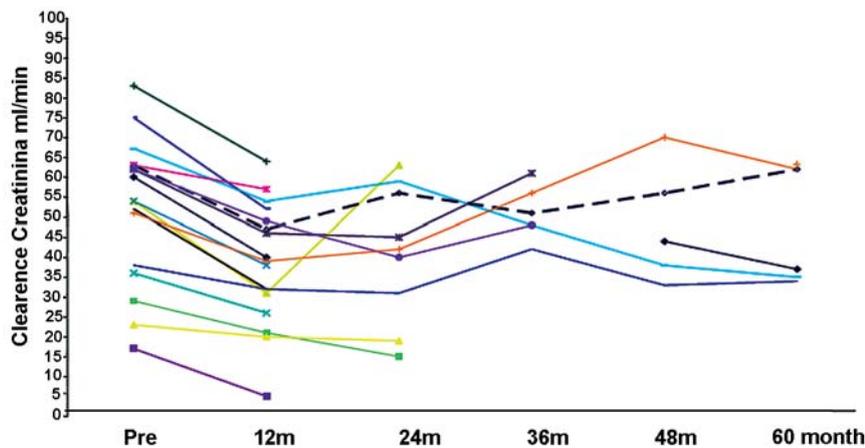


Figure 5 – Patients with a worsening of creatinine clearance ($n = 17$).

Nephrectomy of Atrophic Kidney in Renovascular Hypertension

Table 6 – Characteristics of the patients in accordance with the response of their renal function to nephrectomy.

Improvement (N = 30)	Worsening (N = 17)	p Value	
Age (years)	47.1 ± 15.3	46.1 ± 14.3	0.825
Sex: Male / Female	33.3% / 66.7%	35.3% / 64.7%	0.892
Color: White / Non-white	80.0% / 20.0%	52.9% / 47.1%	0.051
Time of hypertension years	8.5 (0.10 - 30)	13.0 (0.75 - 30)	0.337
SBP previous mmHg	148.2 ± 23.3	148.5 ± 23.2	0.963
DBP previous mm Hg	90.7 ± 16.4	91.8 ± 15.9	0.824
Nº. hypotensors	2.8 ± 1	2.8 ± 1	0.939
Serum Creatinine mg/dL	1.3 (0.8 - 4.5)	1.3 (0.8 - 4.4)	0.991
Clearance Creatinine mL/min*	57 (15 - 100)	54 (17 - 83)	0.903
US atrophic kidney cm†	7.1 ± 1.0	7.1 ± 1.3	0.929
Lesion >70% of contra-lat. renal artery on Doppler	43.3%	17.6%	0.074
Scintigraphy with DTPA atrophic kidney %	9 (0 - 49)	7 (0 - 28)	0.649
Contralateral kidney %	91 (59 - 100)	93 (72 - 100)	0.600
Lateralization of serum rennin: Yes / No	78.9% / 21.1%	70.0% / 30.0%	0.665
Hypercholesterolemia: Yes / No	60.0% / 40.0%	82.4% / 17.6%	0.114
Smoking: Yes / No	43.3% / 56.7%	64.7% / 35.3%	0.159
Heart disease: Yes / No	33.3% / 66.7%	29.4% / 70.6%	0.782
Diabetes Mellitus: Yes / No	13.3% / 86.7%	17.6% / 82.4%	0.692
Stroke: Yes / No	13.3% / 86.7%	29.4% / 70.6%	0.252
Aortic Aneurism: Yes / No	6.7% / 93.3%	17.6% / 82.4%	0.336

† US = renal ultrasound.

patients with creatinine clearance < 30 mL/min at surgery, continued not to need dialysis during the period of 60 months analyzed (Figure-4) and 8.5% of the patients whose renal function worsened at 12 months, showed recovery of the function over the 60 months (Figure-5). There was no statistically significant lesion present (Table-6). Moderate renal insufficiency, which might be an important factor leading to a final need for dialysis, was not significant in this patient population, possibly because of the small number of cases involved.

In the four groups, the characteristics studied, such as sex, color, age, smoking, hypercholesterolemia and co-morbidities presented similar distribution with no significant statistical difference ($p > 0.095$).

No lateralization of the rennin was found as a predictive factor of results, similar data are described by Hasbak et al. (17). The factors which would explain the absence of the lateralization of rennin are bilateral stenosis of the renal artery, states of volemic depletion, chronic use of inhibitors of the conversion enzyme of angiotensin I to II (IECA) and renal insufficiency. Rossi et al. (18) found a correlation of the lateralization of serum rennin activity only in bearers of RVH with unilateral atrophic kidney by complete occlusion of the renal artery that underwent nephrectomy, but there was no lateralization of the rennin plasma in patients treated with angioplasty.

The presence of significant lesion (> 70%) of the contra-lateral renal artery made no statistically

significant difference ($p = 0.753$) to the results of this study. Bilateral lesion was treated by nephrectomy after revascularization of the contra-lateral renal artery in 27% (14 patients).

Kane et al. (14) also found an improvement in blood pressure in patients who had undergone nephrectomy of the atrophic kidney (59%) for the treatment of RVH. In the comparison, in nephrectomy with the revascularization of the ischemic kidney undertaken by Oskin et al. (13) to evaluate blood pressure and renal function, nephrectomy was as effective as revascularization for the control of arterial hypertension, but was inferior to revascularization for the preservation of the renal function.

The average age of 47 years in this series is inferior to the 65 years of other reported series (3,13,14). Of the 34 (67%) women in this study, 38% were of childbearing age, at risk of becoming pregnant. The prevalence of renovascular hypertension during pregnancy is unknown, whereas the significantly greater risk of pre-eclampsia in the woman with chronic arterial hypertension is known. Nephrectomy of the atrophic kidney before a new pregnancy after a failure, can improve the maternal and fetal prognosis (19).

The relationship between stenosis of the renal artery and other systemic lesions is well known (20-22). The significant prevalence of stenosis of the renal artery (greater than 75%) in patients who died from stroke was 10.4% of the cases, 4.6% of whom with complete occlusion of the vessel (20). In the literature, patients with peripheral vascular disease associated with stenosis of the atherosclerotic renal artery suffered higher mortality from cardiac causes during the two-year follow-up (21) and the severity of the lesion of the renal artery was directly proportional to the worst cardiac prognosis (22).

The exact relationship between the degree of stenosis and the loss of mass is unknown. As the Doppler is not an invasive examination it has been used for the follow-up of stenotic lesions. Significant stenosis (> 60%) and severe arterial hypertension, progressed with 36% of renal atrophy over two years, followed-up using Doppler examination(23).

Arteriography was the examination primarily used to determine the presence of the obstruction and the viability of the atrophic kidney. Presently, magnetic resonance angiography and angiotomography

of the renal arteries may be used as alternatives to arteriography with the advantage of avoiding arterial catheterization (24,25). However, when there is a suspicion of fibrodysplasia of the renal artery, where the lesions are more distal, magnetic resonance angiography is not appropriate, as it has greater sensitivity to the lesions of the artery located up to 3 cm from the ostium (24,25).

In this series, among the causes of the renal atrophy which led to nephrectomy, we found atherosclerosis of the renal artery, fibromuscular dysplasia, trauma of the renal artery, thrombosis of the renal artery in patients submitted to renal autotransplant and failure of endovascular revascularization. In another series, the nephrectomy of the atrophic kidney cured the RVH caused by a fall which occurred when removing the traumatic lesion from the renal artery (26). The high incidence of thrombosis is due to the fact that the renal arteries in these cases are small, difficult to manipulate and possess lesions aggravated by previous procedures (16).

The diagnosis of fibromuscular dysplasia of the renal artery was associated with better results as regards both pressure and renal function, renal dialytic insufficiency being a rare cause (27).

From the physiological point of view, the reduction in the levels of angiotensin II after the nephrectomy of the atrophic kidney would cause lesser oxidative stress and could lead to the restoration of the dependent endothelial dilation, responsible in the final analysis for the vascular lesions (renal, coronary and cerebral), mainly those of atherosclerotic etiology. It is known that high levels of angiotensin II are related to an increase in the pro-fibrotic factors, with the consequent replacement of the functioning glomerulus by fibrosis, leading to a loss of renal mass and the advance of renal insufficiency. Hypercholesterolemia, especially the increase in the oxidized LDL, associated with stenosis of the renal artery, speeds up the development of fibrosis in the ischemic kidney by the spread of pro-fibrotic mechanisms (NF- β , TGF- β , oxidative stress among others) and suppression of the remodeling of the tissues (28).

In the future, we should have more options for the treatment of arterial hypertension and vascular obstruction. New therapies such as gene therapy and cell therapy, which do not call for the use of drugs, are

appearing. The implantation of embryonic cells (stem cells) or of genes which codify angiogenic factors may be used as alternative therapies for the inoperable vascular obstructions. Gene therapy takes endothelial growth factors or blocks the harmful genes involved in the pathogenesis of the disease. The endothelial dysfunction caused by oxidative stress, an important mechanism of the atherosclerotic vascular lesion, may be treated in the future either by cell therapy or by gene therapy in association with pharmacological therapy (29,30).

CONCLUSION

In patients with renovascular hypertension, nephrectomy of the atrophic kidney is a procedure which results in improvement of the arterial hypertension and of the renal function in two-thirds of patients.

CONFLICT OF INTEREST

None declared.

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Supracostal Access: Does it affect Tubeless Percutaneous Nephrolithotomy Efficacy and Safety?

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ABSTRACT

Introduction: Tubeless percutaneous nephrolithotomy (PCNL) in selected patients has been found to be safe and can reduce postoperative discomfort without increasing complications. The challenges of tubeless PCNL via supracostal access are inadequate drainage and postoperative bleeding, conditions that may increase pulmonary complications. We compare the efficacy and safety of the tubeless supracostal versus the standard supracostal PCNL.

Materials and Methods: Supracostal PCNL with one percutaneous renal access, no significant bleeding, extravasation and residual stone was performed in 95 patients. Of these, 43 were tubeless PCNL (Group-I) and 52 were PCNL with standard routine postoperative nephrostomy tube (Group-II). In group-I, PCNL was done by the standard supracostal technique with the placement of a postoperative external ureteral catheter for 48 hours. The operative time, success rate, hospital stay and ensuing complications were compared between group-I and group-II.

Results: Patients in the tubeless PCNL group (Group-I) were 90.7% stone -free while those with standard routine postoperative nephrostomy tube (Group-II) were 84.6% stone -free. Additionally, stone fragments of less than 4 mm in diameter were found in 9.3% of patients in group-I and 25.4% in group-II. The success rate, hematocrit change and complication were not significantly different between both groups. The analgesic requirement, operative time and hospital stay were all significantly less in the tubeless supracostal group (Group-I). None of group I and only one patient of group II needed intercostal drainage.

Conclusion: Tubeless supracostal percutaneous nephrolithotomy in selected patients is effective with acceptable complications. This technique offers the advantage of lower analgesic requirement, shorter operative time and hospital stay. The pulmonary complication is the same as the standard supracostal percutaneous nephrolithotomy.

Key words: *percutaneous nephrolithotomy; efficacy; complications*

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INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the accepted treatment for large renal and upper ureteral stones. The four stages of PCNL are: (1) renal access, (2) tract dilatation, (3) nephroscopy and stone disintegration, and (4) nephrostomy tube placement. In uncomplicated PCNL where there is no significant

extravasation, significant bleeding, or any need for a second nephroscopy, the placement of the nephrostomy tube may not be necessary (tubeless PCNL) (1-4). In specific situations of PCNL, a supracostal renal approach is necessary (5-8). Pulmonary complication is more common with this approach due to the anatomy of the kidney. Extravasation and bleeding may be more commonly found in tubeless PCNL and

may increase the incidence of postoperative pulmonary complications in supracostal access. The efficacy and complication of tubeless PCNL via the supracostal route were compared to those of supracostal PCNL with routine nephrostomy tube placement.

MATERIALS AND METHODS

Patients

A total of 95 patients underwent PCNL via supracostal. The patients were divided into two groups, 43 receiving tubeless supracostal PCNL (Group-I) and 52 receiving supracostal PCNL with routine nephrostomy tube placement (Group-II). Four criteria were established for PCNL of both groups in this study regardless of the stone burden, namely, (1) a single access site, (2) non obstructive renal unit, (3) no significant perforation or bleeding, and (4) a second look would not be required. The mean age of group-I and II was 51.49 ± 12.77 years (range 30-83 years) and 50.63 ± 12.18 years (range 23-76 years), respectively. The mean stone size of group I and II was 3.83 ± 1.45 cm (range 1.8-8.0 cm) and 4.11 ± 1.57 cm (range 2.3-9.5 cm), respectively. Ten patients (23.8%) in group I and 12 patients (23.1%) in group II had previous open nephrolithotomy. Patient profiles are shown in Table-1. The positions of the calculi are shown in Table-2. All patients were operated by a single surgeon.

Methods

Single stage percutaneous nephrolithotomy was done in all patients. Intravenous antibiotic was given before the operation in all cases. After the induction of general anesthesia, an open-end 6F ureteral catheter was placed via a transurethral approach into the ureter with the patient in a supine position. The tip of the ureteral catheter was placed at the ureteropelvic junction or at the renal pelvis. The percutaneous access was created by a single urologist (BL) in all cases. Under fluoroscopic guidance in the prone position and after injection of contrast media via ureteral catheter, 95 sites were supracostal upper pole access. The needle was pushed through the diaphragm and retroperitoneum in full expiration, whereas the needle was passed through the kidney during deep inspiration. The working and safety guide-wires were inserted after the tip of the needle was in the collecting system. Tract dilatations were performed by Amplatz fascial dilators (Cook Urological Spencer, Indiana, USA) or telescopic metal dilators sizes from 8F-30F, with an inserted 30F Amplatz sheath. Using a standard nephroscope (26F), stone disintegration was obtained with ultrasonic and/or pneumatic lithotripsy. Fluoroscopy and contrast nephrostogram with systematic nephroscopy were performed to evaluate the stone-free status.

As regards tubeless PCNL, the ureteral catheter (the same 6F ureteral catheter that was placed at the beginning of the operation) was adjusted neph-

Table 1 – Profiles of patients.

	Group I (Supracostal Tubeless PCNL)	Group II (Supracostal Standard PCNL)	p Value
Patients	43	52	
Side (R:L)	19:24	23:29	
Gender (M:F)	20:23	38:14	
Age (years)	51.49 ± 12.77 (range 30-83)	50.63 ± 12.18 (range 23-76)	0.740
Stone size (cm)	3.83 ± 1.45 (range 1.8-8.0)	4.11 ± 1.57 (range 2.3-9.5)	0.363
Previous open nephrolithotomy	10 (23.8%)	12 (23.1%)	0.934

Table 2 – Stone positions.

	Group I (Supracostal tubeless PCNL)	Group II (Standard supracostal PCNL)	p Value
Staghorn stone (%)	14 (32.5)	15 (28.8)	0.227
Calyceal stone (%)	12 (27.9)	9 (17.3)	
Pelvic + Calyceal stone (%)	13 (30.2)	25 (48.1)	
Upper ureteral stone (%)	2 (4.7)	3 (5.8)	
Upper ureteral stone + calyceal stone (%)	2 (4.7)	0	

roscopically, the tip being placed at the renal pelvis. The working sheath was removed with the safety guide wire still in place. The nephrostomy site was examined and, if there was no evidence of active bleeding for 5 minutes, the wound was closed with sutures. The guide wire was then removed and the ureteral catheter was left attached to the Foley catheter for 48 hours. The nephrostomy tube sized 20F was routinely inserted in the remaining cases (Group-II). The prolonged placement of the ureteral catheter and nephrostomy tube depended on postoperative fever, bleeding or other complications.

Before and on the first day of the surgery, all patients were tested for complete blood count to determine any change in the hematocrit level. Postoperative chest x-ray (CXR) was routinely done in all cases. The patient's symptoms and CXRs were used to evaluate pulmonary complications. If the patients developed shortness of breath, chest pain and desaturation in the recovery room and CXR revealed pleural effusion, the intercostal drainages were done immediately. Postoperative plain film KUB at day 1 was done for evaluation of the stone free status. Meperidine injection was given when the patients complained of pain. Statistical analysis with Chi-square for qualitative variables and Student's-t-tests for quantitative variables with $p < 0.05$ was considered statistically significant.

RESULTS

The stone-free rate was 90.7% in group I and 84.6% in group II, and fragments ≤ 4 mm occurred 9.3% and 15.4% in groups I and II, respectively. The

operative time was 47.38 ± 16.93 min (range 25-90 min) in group I and 58.85 ± 18.46 (range 30-105 min) in group II, which was significantly different ($p = 0.03$). The hospital stay was 3.45 ± 1.01 (range 2-7 days) and 4.83 ± 1.44 (range 3-10 days) in group I and group II, respectively. Meperidine usage was 37 ± 31 (0-150) mg in group I and 70 ± 36 (0-150) in group II which was significantly different ($p < 0.001$). Decrease in the hematocrit level was 2.65 ± 2.59 mg% in group I and 2.31 ± 2.46 mg% which was not statistically different ($p = 0.522$). There were 4 patients (9.30 %) in group I and 5 patients (9.62 %) in group II who had hydrothorax as indicated by respiratory symptoms or postoperative CXRs. Only 1 patient (1.92 %) of group II needed intercostal drainage (Table-3).

COMMENTS

Percutaneous nephrolithotomy has replaced open stone surgery for large renal or upper ureteral calculi because it is a less minimally invasive technique. The last stage after completion of PCNL is the placement of the nephrostomy tube. The purpose of the nephrostomy tube is to provide hemostasis along the tract, avoid urinary extravasation and maintain adequate drainage of the kidney. In selected patients, tubeless percutaneous nephrolithotomy, with only an externalized ureteral catheter or double J stent, is safe, economical and provides reduced postoperative discomfort with the same outcome (1-4). Inclusion criteria of tubeless PCNL are the use of a single access site where the renal unit is not obstructive, no significant perforation, bleeding and no need for a

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Table 3 – Results and complications.

	Group I (Supracostal tubeless PCNL)	Group II (Standard supracostal PCNL)	p Value
Stone free (%)	39 (90.7)	44 (84.6)	0.131
Stone fragment \leq 4 mm (%)	4 (9.30)	7(15.4)	
Operative time (min)	47.38 \pm 16.93 (range 25-90)	58.85 \pm 18.46 (range 30-105)	0.030
Hospital stay (days)	3.45 \pm 1.01 (range 2-7)	4.83 \pm 1.44 (range 3-10)	< 0.001
Meperidine usage (mg)	37.00 \pm 31.00 (range 0-150)	70.00 \pm 36.00 (range 0-150)	< 0.001
Hematocrit change (mg%)	2.65 \pm 2.59	2.3 \pm 2.46	0.522
Pleural complication (%)	4 (9.30)	5 (9.62)	0.492
Intercostal drainage	-	1 (1.92)	

second look (1-4). The stone burden may not necessarily to be taken into account.

Winfield and associates reported significant complications after premature removal of nephrostomy tube after PCNL (9). Bellman and colleagues reported tubeless PCNL with only a double-J stent for one week without compromising efficacy and safety (1). We previously reported tubeless PCNL in 37 patients with only the placement of an externalized ureteral catheter for 48 hours to provide adequate drainage for the upper tract without increasing complications and blood transfusion (2). Due to the selected patients in tubeless PCNL, the stone free status had to be assessed during the operation. The systematic nephroscopy, intraoperative fluoroscopy with contrast nephrostogram were used for evaluation of the stone free status. Karami and Gholamrezaie (10) and Aghamir et al. (11) reported the technique of tubeless PCNL without any externalized ureteral catheter or double J stent. They found that the totally tubeless PCNL technique was safe and effective, requires less hospital stay and analgesics and led to a fast recovery time. No urinoma was found on postoperative ultrasound with an average length of hospital stay of 1.6 days.

Under specific conditions, access to the kidney may require the upper pole approach. The

indications for the upper pole approach are staghorn calculi, large or multiple upper calyceal stones, renal calculi associated with ureteropelvic junction or upper ureteral pathology, large upper ureteral calculi and calculi in specific anatomy (8,12,13). The upper pole approach provides a straight tract along the long axis of the kidney and ensures reaching most of the collecting system, which provides easier manipulation of the rigid nephroscope and other rigid instruments. This approach can achieve a better stone clearance (12,13). Upper pole access can be achieved via the supracostal and infracostal approaches. Due to the anatomy of the kidney, pulmonary complications are more common with the supracostal approach (8,13). We previously reported 170 supracostal PCNL compared with 294 infracostal PCNL. We found that both approaches provide the same effective results, but pulmonary complications are higher when using the supracostal approach as compared with the subcostal approach. The pulmonary complications that needed intercostal drainage were 5% and 0.3% in supracostal and subcostal approach, respectively. There was a 17-fold greater possibility of pulmonary complication in the supracostal when compared to the subcostal approach (12).

Postoperative pulmonary complications after PCNL can be detected by postoperative symptoms and

postoperative CXRs. The symptoms of pulmonary complications are poor oxygen saturation, dyspnea and tachypnea postoperatively. The abnormality of postoperative CXRs depends on the volume of pleural effusion (14). The treatment of hydrothorax depends on the amount of hydrothorax and the patients symptoms. Conservative treatment is preferentially for those with no or mild symptoms and minimal effusion. Patients with significant symptoms and a large amount of pleural effusion need intercostal drainage. The incidence of pulmonary complications after 12th supracostal approach that need surgical intervention was from 0% to 23% (range 5-8).

The techniques of supracostal approach require coordination with the anesthetist to control respiration. To avoid injuring the intercostal vessels, the intercostal puncture is made in the lower half of the intercostal space. During full expiration, the needle is passed through the retroperitoneum and diaphragm to prevent injury to the lung. The needle insertion, which is passed through the parenchyma to the collecting system, is done during deep inspiration for downward displacement of the kidney. An Amplatz sheath is used in all patients during the percutaneous supracostal approach to maintain low pressure irrigation that can reduce the risk of pleural effusion and extravasation. After supracostal access, postoperative CXRs were routinely used in all cases for evaluation of pulmonary complications (12).

One concern with the tubeless PCNL technique is to ensure adequate drainage and no significant bleeding postoperatively. Extravasation and bleeding can be significant problems of this technique after supracostal approach and may lead to pulmonary complications. There is limited published data in the literature to date on tubeless PCNL in percutaneous nephrolithotomy via supracostal access. Shah and colleagues (15) reported 72 patients of tubeless PCNL via supracostal access compared with 72 patients with routine standard supracostal PCNL. Only a single 6F double J stent was placed in the tubeless group, whereas both the 6F double J stent and a 28F nephrostomy tube were placed in control group. The double J stent was removed at 1-2 weeks after the surgery and nephrostomy tube was removed in 12-24 hours. Stone free at 1 to 2 weeks was 99.44% and 91.66% in tubeless and in control group, respec-

tively. Blood transfusion was required in 3 patients of the tubeless group and in 4 of the control group with only 1 patient in control group had hydrothorax that needed intervention. They concluded that tubeless PCNL via supracostal is safe and effective with lower analgesic requirement and shorter hospital stay without increasing thoracic complication. Shah and associates (16) reported 30 bilateral simultaneous supracostal tubeless accesses in 51 urinary tracts of 45 renal units. As regards the supracostal access tracts, no urine leakage or major chest complication were found, and patients were stone free or had residual stone fragment of less than 5 mm in 39 and 4 renal units, respectively. Gonen et al. reported 10 tubeless and stentless supracostal PCNL. These authors found that this technique is safe and offers advantages of a lower analgesia and shorter hospital stay without increasing of pulmonary complication (17).

In our series, all patients in the present study had the same criteria for the tubeless PCNL. We found that the incidence of pulmonary complications in tubeless supracostal PCNL was not different from the standard supracostal PCNL. The pleural complication was 9.30% in tubeless supracostal PCNL and 9.62% in standard PCNL. Almost all of these patients were resolved after conservative treatment. Only one standard PCNL patient needed intercostal drainage. The results of the treatment, as justified by stone free and insignificant residual fragment condition, were the same in both groups. The analgesic requirement, operating time and hospital stay were less in tubeless group compared to the standard supracostal PCNL. All patients in both groups, who had previous open nephrolithotomy (10 of group I and 12 of group II) were found to be safe with the same outcome. The longer hospital stay in our series compared to the other studies was obviously related to our tubeless PCNL technique which was different from the other patients where we routinely left a ureteral catheter indwelling for 48 hours after the surgery (2).

CONCLUSIONS

Tubeless supracostal percutaneous nephrolithotomy in selected patients with externalized ureteral catheter is safe and effective with lower analgesic re-

quirement, shorter operative time and shorter hospital stay. This technique does not increase hemorrhage or pulmonary complications when compared with the standard supracostal percutaneous nephrolithotomy.

CONFLICT OF INTEREST

None declared.

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Total Prostatectomy within 6 Weeks of a Prostate Biopsy: Is it Safe?

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ABSTRACT

Purpose: Many urologists recommend a six-week time interval between a prostate biopsy and a total prostatectomy (TP) to allow the biopsy induced inflammation to subside. Our aim was to assess whether the time interval between prostate biopsy and TP has an impact on the surgical outcome.

Materials and Methods: A retrospective analysis was performed on data from patients who underwent a TP by a single surgeon from 1992 to 2008. The patients were divided into two groups according to the time interval between biopsy and TP, Group 1 ≤ 6 weeks and Group 2 > 6 weeks. Relevant perioperative variables and outcome were analyzed.

Results: 923 patients were included. There was a significant difference between the two groups in the surgeons' ability to perform a bilateral nerve sparing procedure. Those who had a TP within six weeks of the biopsy were less likely to have a bilateral nerve sparing procedure. No significant difference was noted in the other variables, which included Gleason score, surgical margin status, estimated blood loss, post-operative infection, incontinence, erectile function, and biochemical recurrence.

Conclusions: TP can be safely performed without any increase in complications within 6 weeks of a prostate biopsy. However, a TP within six weeks of a biopsy significantly reduced the surgeon's perception of whether a bilateral nerve sparing procedure was performed.

Key words: *prostatic neoplasms; biopsy; prostatectomy; outcomes*

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INTRODUCTION

In the United States, it is estimated that 192,280 men will be diagnosed with prostate cancer in 2009 (1). Total prostatectomy (TP) is the most common treatment for organ confined prostate cancer (2). We prefer the term "Total prostatectomy" instead of "radical prostatectomy" as we find it a more appropriate term to describe the procedure (3). Transrectal ultrasound (TRUS) guided biopsy with peri-prostatic nerve block has been the preferred

modality for diagnosing prostate cancer (3). TP is typically deferred for six to eight weeks following a biopsy (4). The hypothesis is that there is an inflammatory response to the biopsy and administration of local anesthesia (4). This inflammation may take several weeks to subside (4). However, under several circumstances the TP may be performed earlier without this waiting period. The objective of this study was to assess whether the time interval between prostate biopsy and total prostatectomy has an impact on the surgical outcome.

MATERIALS AND METHODS

We performed a retrospective analysis of 1,943 patients who underwent TP at our institution by one surgeon between 1992 and 2008. The clinical, operative and pathological details were entered into an Institutional Review Board approved database and analyzed. The patients were divided into two groups according to the time interval between biopsy and TP, Group 1 ≤ 6 weeks and Group 2 > 6 weeks. We excluded patients who received neoadjuvant androgen ablation therapy, salvage TP and where the date of biopsy was unavailable. The groups were compared for preoperative and pathological parameters. Outcome variables analyzed included estimated blood loss, nerve sparing procedure, surgical margin status, Gleason score, infection, continence, erectile function (EF), biochemical recurrence and mean follow-up. The ability to perform a nerve sparing procedure was assessed based on the surgeon's operative report. At the conclusion of the TP, the surgeon indicated whether or not one or both neurovascular bundles appeared intact. This was based on the appearance of prostatic bed and operative site. A comment was always made as to whether one or more neurovascular bundles were spared. Patients were followed-up at 6 weeks, 3 months and every 6 months thereafter. EF and continence were evaluated at 3 and 6 months and 6-monthly by the surgeon or by using an annual questionnaire mailed to the patient. During the interview, all patients were asked the same questions to evaluate EF. Potency was defined as "EF sufficient for intercourse with or without a phosphodiesterase-5 inhibitor". Continence was defined as "never wearing a pad". More recently, assessment of EF was done by using the Sexual Health Inventory for Men questionnaire and continence was assessed by the International Consultation on Incontinence questionnaire (5,6). EF and continence at completion of second year follow-up was used to code the status of each patient for analyzing continence and EF. In addition, EF was assessed only in patients who were potent before surgery and had a nerve sparing procedure. Biochemical recurrence was defined as a PSA ≥ 0.2 ng/mL.

Statistical analysis was performed using SPSS Version 16.0. Student's-t-test was used to compare continuous variables. Cross tabulation with Chi square

test and Fisher's exact test were used to compare categorical variables. The significance value was set at a two-sided $p \leq 0.05$.

RESULTS

Out of 1,943 patients 336 (17.5%) had neoadjuvant hormonal therapy, 23 (1.2%) had radiotherapy and in 661 (34%) patients the date of biopsy was not available in the database. After excluding these patients, 923 patients met the inclusion criteria. A total of 123 (13%) were in Group 1 and 800 (87%) in Group 2. The mean time to surgery following biopsy in Group 1 and 2 was 30 ± 9 and 91 ± 39 days respectively. The median time interval in Group 1 was 32 days and in Group 2 was 82 days. No significant difference was noted between the groups when comparing age, clinical stage and preoperative biopsy findings (Table-1). There was a significant difference between the groups in the surgeon's report as to whether a nerve sparing procedure was performed ($P = 0.009$) (Table-2). Those who had TP earlier than six weeks of a prostate biopsy were considered less likely to have a bilateral nerve sparing procedure. No significant difference was found in the other variables, which included estimated blood loss, wound infection, Gleason score, a positive surgical margin, continence, erectile function and clinical/biochemical recurrence.

COMMENTS

The vast majority of men with clinically localized prostate cancer do not have any symptoms (7). Many, if not most are overwhelmed emotionally following the diagnosis of prostate cancer. Patients are confronted by the prospect of changes in their life span, body image, and personal relationships (8,9). Prostate cancer is usually diagnosed by a transrectal ultrasound guided biopsy (10) and typically the results are obtained within 72 hours. The diagnostic process is stressful and has been shown to be associated with an increase in serum cortisol (11). Patients who have been newly diagnosed with a cancer often have numerous short term problems which must be confronted (12,13). Apprehensions encountered by patients are

Table 1 – Comparison of preoperative variables.

	I (≤ 6 weeks)	II (> 6 weeks)	p Value
No. patients (%)	123 (13)	800 (87)	
Mean Age	61 ± 7	60 ± 8	0.3*
Mean total PSA at diagnosis	6.8 ± 3.5	7 ± 5	0.65*
Mean biopsy Gleason score (± SD)	6.45 (± 1)	6.36 (± 0.9)	0.37*
Biopsy Gleason group N (%)			0.13
6 or less	65 (53%)	496 (62%)	
7	46 (37.5%)	231 (29%)	
8 or more	12 (9.5%)	71 (9%)	
Mean number of biopsy cores	9.5 ± 3	9 ± 3	0.35*
Clinical T-Stage N (%)			0.45
T1	80 (65%)	539 (67.5%)	
T2	41 (33%)	241 (30)	
T3	2 (1.5%)	20 (2.5%)	

SD = standard deviation, *Student-t-test.

described as the “7 D’s”: death, dependency, disfigurement, disruption of social relationships, disability (interference with educational, work, or leisure roles), discomfort (pain), and disengagement (returning to a normal lifestyle from the patient role) (14). According to the present standard of practice, patients are generally requested to wait for at least 6 weeks following a prostate biopsy before proceeding with TP. In the modern era most patients have easy access to virtually limitless health and medical information thus enabling them to understand their disease and decide amongst various treatment modalities. In these circumstances, a waiting period of 6 weeks can lead to considerable mental anguish. This could be considered a drawback of surgery compared to other modalities. Garsson et al. have demonstrated the effect of psychological intervention on a positive outcome in cancer patients (15). In this context, a reduction in the waiting interval might affect the outcome with regard to patients’ quality of life.

Traditionally, surgery is performed 6 to 8 weeks following a needle biopsy of the prostate and a minimum of 12 weeks following a transurethral resection of the prostate (4). It is hypothesized that this delay enables inflammatory adhesions or hematoma to resolve thereby maintaining anatomic relationships between the prostate and the surrounding structures

(4). The tissue reaction subsequent to the peri-prostatic nerve block and biopsies may make preservation of the neurovascular bundles more difficult. It might also lead to a potentially serious complication such as rectal injury. When surgery was performed within 6 weeks of biopsy, we have occasionally noted that the apical dissection of the neurovascular bundles is more difficult. Whether this is related to the biopsies or the peri-prostatic nerve blockade is unclear. Although the local anesthetic is generally placed near the base of prostate it tends to diffuse in the peri-prostatic space and involve the apex and this inflammatory reaction is variable.

Lee et al. reported that the interval between biopsy and TP did not have an effect on the immediate post operative outcome (16). In our study we did not find an additional increase in blood loss when the surgery was performed within 6 weeks of a prostate biopsy. The perioperative complications were similar in both groups. There was no significant difference in biochemical recurrence between Group 1 (14%) and Group 2 (11%) (P = 0.28). However, a significant difference was noted between the groups (P = 0.009) in ability to perform a bilateral nerve sparing procedure. A bilateral nerve sparing procedure was performed in only 49% of patients in Group 1 compared to 61 % of patients in Group 2. In their study on 2,996 patients,

Table 2 – Comparison of surgical, functional and oncologic outcome.

	I (≤ 6 weeks)	II (> 6 weeks)	p Value
Mean EBL (± SD) in mL	493 (± 288)	477 (± 300)	0.6
Mean wet weight of prostate (± SD)	47 (± 18)	46 (± 21)	0.76
Pathologic Gleason	6.5(± 1.2)	6.9 (± 0.8)	0.08
Bilateral nerve sparing (%) (n = 847)			
Bilateral	59 (49)	441 (61)	0.009
Unilateral	21 (17)	119 (16.5)	0.44
None	41(34)	166 (22.5)	0.007
No. infections (%)	1(0.8)	7 (0.9)	0.7
No. of positive margin (%)	45 (35)	229 (28.5)	0.09
Continence at 2 years(%) (n = 785)			
Continent	90 (92)	654 (95)	0.12
Incontinent*	18 (8)	33 (5)	
Potency (%) at 2 years (n = 458)#			
Potent	38 (68)	293 (73)	0.43
Impotent	18 (32)	109 (27)	
No. of biochemical recurrence (%)	17 (14)	93 (11.5)	0.284
Mean follow-up in months (± SD)	53.5 (± 49)	40 (± 39)	< 0.05

* wearing a pad, #potency was calculated for those patients who had nerve sparing surgery; EBL = estimated blood loss; SD = standard deviation.

Eggner et al. concluded that a shorter interval between biopsy and TP did not adversely affect surgical outcome (17). They analyzed radical prostatectomy conducted before 4 and 6 weeks after a prostate biopsy and did not find a difference in operating time, estimated blood loss, surgical margin status, urinary incontinence or EF (17). Similar to our study, they noted a significant reduction in the proportion of patients who had a nerve sparing procedure in the early surgery group (17). Although the specific explanation for this finding is still unknown, the data from both the studies indicates that a cautious approach is needed. Further, prospective studies are needed to confirm and analyze factors leading to this finding.

Our study has some limitations. It is a retrospective study spanning fifteen years. The biopsy date was unavailable for a significant number of patients and hence they were excluded. The reason for operating within 6 weeks could not be precisely documented.

However, at our institution we do not follow a rigid timeline for advising TP, and typically other factors such as availability of the operating room, patient anxiety weigh in when scheduling the surgery.

CONCLUSIONS

It is feasible to perform a TP within 6 weeks after a prostate biopsy without an increase in complications. In our experience, TP within 6 weeks of a biopsy limits the ability to perform a bilateral nerve sparing procedure. However, early surgery did not affect the potency rate in men who had a nerve sparing procedure. In this context it would be prudent to perform early TP only in carefully selected cases when there is a high risk of progression and potency is not of concern. When surgery is performed before six weeks patients should be counseled about the

decreased chances of preserving the neurovascular bundles.

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CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

The purpose of this study was to assess the impact of time interval, ≤ 6 weeks (Group I) compared to > 6 weeks (Group II), between prostate biopsy and total prostatectomy (TP) on the surgical outcome including the ability to perform nerve sparing procedure in patients with organ confined prostate cancer.

In the PSA era, most of patients were diagnosed by transrectal ultrasound guided biopsy. The number of core biopsy was increased from 6 cores to average of 10 to 12 cores and peri-prostatic local anesthesia become more popular. These procedures will give an impact such as more inflammation around the prostate which will hamper the subsequent surgical procedure.

This study concluded that it is safe to perform TP within 6 weeks after biopsy. However, there was a significant reduction of the surgeons' ability to perform bilateral nerve sparing procedure in this setting. These findings are supported by other studies. Lee DK et al. (reference 16 in article) reported no significant difference in peri-operative parameters as well as immediate post-operative outcome in patients with biopsy to TP intervals above and below the median which was 8 weeks. Eggener et al. (reference 17 in article) reported similar findings and also found significant less nerve sparing procedures

in early TP group. Therefore, it is better to wait for 6 weeks after biopsy before doing the surgery especially if potency is of paramount important for the patient.

However, problems like fear of negative impact on disease-free progression could arise in the waiting period which might make the patients choose another treatment modality. Recently, there were 2 studies with totally more than 2600 TP performed two or more months after biopsy without any neo-adjuvant treatment (1,2). These studies concluded that delays up to several months from biopsy to TP have no influence on biochemical recurrence. Hence, we could reassure the patients that this procedure has a low risk.

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Transurethral Resection of Prostate: A Comparison of Standard Monopolar versus Bipolar Saline Resection

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ABSTRACT

Introduction: Transurethral resection syndrome is an uncommon but potentially life threatening complication. Various irrigating solutions have been used, normal saline being the most physiological. The recent availability of bipolar cautery has permitted the use of normal saline irrigation.

Material and Methods: In a randomized prospective study, we compared the safety and efficacy of bipolar cautery (using 0.9% normal saline irrigation) versus conventional monopolar cautery (using 1.5% glycine irrigation). Pre and post-operative hemoglobin (Hb) and hematocrit values were compared. Hemodynamics and arterial oxygen saturation were monitored throughout the study. Safety end points were changes in serum electrolytes, osmolarity and Hb/PCV (packed cell volume). Efficacy parameters were the International Prostate Symptom Score (IPSS) and Qmax (maximum flow rate in mL/sec) values.

Results: Mean preoperative prostate size on ultrasound was 60 ± 20 cc. Mean resected weight was 17.6 ± 10.8 g (glycine) and 18.66 ± 12.1 g (saline). Mean resection time was 56.76 ± 14.51 min (glycine) and 55.1 ± 13.3 min (saline). The monopolar glycine group showed a greater decline in serum sodium and osmolarity (4.12 meq/L and 5.14 mosmol/L) compared to the bipolar saline group (1.25 meq/L and 0.43 mosmol/L). However, this was not considered statistically significant. The monopolar glycine group showed a statistically significant decline in Hb and PCV (0.97 gm %, 2.83, $p < 0.005$) as compared to the bipolar saline group (0.55 gm % and 1.62, $p < 0.05$). Patient follow-up (1,3,6 and 12 months postoperatively) demonstrated an improvement in IPSS and Qmax in both the groups.

Conclusion: We concluded that bipolar transurethral resection of prostate is clinically comparable to monopolar transurethral resection of prostate with an improved safety profile. However, larger number of patients with longer follow up is essential.

Key words: prostate; transurethral resection of prostate; saline; glycine

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INTRODUCTION

Transurethral resection of prostate (TURP) is a standard operative procedure for patients with benign prostrate hypertrophy. Irrigants used range from distilled water to a variety of non-hemolytic solutions like glycine, saline, sorbitol and mannitol.

Irrigant fluid absorption by the patient is a potentially serious complication of TURP, resulting in the TURP syndrome with appreciable morbidity and mortality (1,2).

As an isotonic electrolyte medium, normal saline is the most physiologic irrigant for TURP, but its electrical conducting properties prohibit its use

with conventional monopolar cautery. The development of bipolar resection systems now permits the use of normal saline as an irrigant. Use of bipolar cautery has been reported to be associated with less collateral and penetrative tissue damage, lower incidence of TURP syndrome, shorter catheter indwelling times and earlier hospital discharge (3-7). This study was undertaken to compare the safety and efficacy of bipolar cautery using saline as an irrigant with conventional monopolar cautery using glycine as an irrigant.

MATERIALS AND METHODS

Following Institutional Ethics Committee approval and informed consent from patients, we studied 60 patients with a diagnosis of benign enlargement of the prostate undergoing TURP. They were divided into two groups using standard randomization codes. Group I (n = 30) had TURP performed with monopolar cautery using 1.5% glycine as an irrigant. In Group II (n = 30), bipolar cautery was used with 0.9% saline as irrigant. Indications for surgery included failed medical therapy, acute urinary retention with failed voiding trial, recurrent urinary tract infection and hematuria. Patients with documented or suspected prostate cancer, neurogenic bladder, previous prostate surgery, urethral stricture, associated bladder stones and renal impairment were excluded from the study.

Preoperative International Prostate Symptom Score (IPSS), Qmax (maximum flow rate in mL/second) and prostate volume by ultrasound were recorded, as well as patient age, weight and height. Preoperative blood investigations included complete hemogram, liver and renal function tests, chest X-ray and electrocardiogram. Surgery was performed by trainees and consultants (4 surgeons).

Surgery was performed under spinal anesthesia in all patients. Patients received 10 mL/kg of normal saline intravenously prior to administration of spinal block. Normal saline infusion was continued in the intraoperative period. External jugular vein was cannulated and a baseline sample (2 mL) sent for estimation of serum sodium, potassium and osmolarity. These tests were repeated every 15 minutes until the end of the procedure. Baseline and post procedure

hemoglobin and hematocrit values were also studied. Resection time, volume of irrigant used, weight of the resected gland and duration of surgery in both the groups were recorded. The patients vital parameters (pulse, blood pressure, oxygen saturation monitoring by pulse oximeter) were monitored and clinical signs of transurethral resection (TUR) syndrome were watched for.

Bipolar resection was performed using the Gyrus PK bipolar resection system. Generator settings for cutting and coagulation were 160-180 W and 100-120 W respectively. Monopolar resection was performed using Erbee cautery with cutting and coagulation setting of 100 and 60 W respectively.

Barnes method of resection was used in all our patients. The resectoscope used was 26 Fr Modified Iglesias double sheath continuous irrigation resectoscope with thumb operating working element. The height of the irrigation fluid was 60 cm in all cases. To prevent thermal damage to the urethra, we used copious amounts of jelly around the sheath in the urethra and always carefully monitored any early exchange of worn loops and discarding of loops with distortion or insulation faults.

Postoperative irrigation was used to ensure clear catheter drainage. Catheter removal was done on postoperative Day 2 in all cases.

Patients were followed-up at 1, 3, 6 and 12 months with the IPSS reassessment and Qmax obtained using rotating disc type uroflowmeter.

The Student-t- test was used to compare the parametric data between the groups i.e.; age, weight, height, volume of the irrigant, resection time and weight of resected gland. ANOVA test was used to compare hemoglobin (Hb), packed cell volume (PCV), osmolarity, serum electrolyte changes, IPSS and Qmax in the groups p value < 0.05 was considered significant and a value < 0.005 highly significant.

RESULTS

Demographic profiles in both the groups were comparable (Table-1). Also comparable were preoperative Hb, hematocrit, osmolarity and serum electrolytes (Table-2). Prostate size on ultrasound

TURP: Comparison of Monopolar vs. Bipolar Resection

Table 1 – Age, height and weight profile.

Variable	Monopolar Mean (SD)	Bipolar Mean (SD)	Significance
Age (year)	65.96 (6.6)	63.86 (6.1)	p > 0.05 not significant
Height (cm)	171.33 (5.99)	170.93 (5.4)	p > 0.05 not significant
Weight (kg)	55.86 (5.7)	59.23 (7.3)	p > 0.05 not significant

SD = standard deviation.

Table 2 – Comparison of electrolytes, osmolarity, hemoglobin and hematocrit between bipolar and monopolar groups.

Variable	Preoperative		Postoperative		p Value	
	Glycine (variance)	Saline (variance)	Glycine (variance)	Saline (variance)	Glycine	Saline
Sodium (mEq/L)	132.59 40.75	132.93 68.72	128.47 70	131.68 39.57	NS	NS
Potassium (mEq/L)	4.036 0.38	4.217 0.42	3.843 0.51	3.789 0.45	NS	NS
Osmolarity (mMol/L)	294.54 128.27	285.85 59.47	289.36 67.25	285.42 63.61	NS	NS
Hemoglobin (g/dL)	12.35 3.17	12.26 1.72	11.38 2.18	11.71 2.05	3.27 x 10 ⁻⁷ S	0.014 S
Hematocrit (%)	38.15 25.91	38.60 17.64	35.32 12.48	36.98 18.54	1.81 x 10 ⁻⁵ S	0.008 S

NS = not significant.

ranged from 40-80 cc. Weight of resected gland, resection time and volumes of irrigant used were comparable (Table-3).

The monopolar glycine group showed a greater decline in serum sodium (4.12 meq/L) compared to the bipolar saline group (1.3 meq/L). However, this was not statistically significant between the groups (p = 0.93 for bipolar and p = 0.2 for monopolar group respectively). Serum osmolarity declined in the monopolar glycine group by 5.14 mosm/L as compared to 0.43 mosm/L in the bipolar glycine group. This decline in osmolarity from the preoperative value

was not significant in either group, p > 0.05. Serum potassium values showed no significant change in either group (p > 0.05). The monopolar glycine group showed a statistically highly significant decline in Hb (0.97 gm %, p < 0.005) from the preoperative value. In comparison, the bipolar group showed a smaller drop in hemoglobin (0.55 gm %, p = 0.014). Hematocrit values showed a similar trend with the glycine monopolar group recording a more significant fall from the preoperative value as compared to the bipolar saline group (2.83, p < 0.005 and 1.62, p < 0.05 respectively) (Table-2).

Table 3 – Comparison of intraoperative variables between bipolar and monopolar groups.

Variable	Glycine mean (SD)	Saline mean (SD)	Significance
Volume of irrigant (L)	19.8 (5.4)	18.76 (8.1)	p > 0.05 not significant
Resection time (min)	56.76 (14.51)	55.1 (13.3)	p > 0.05 not significant
Resected weight (g)	17.60 (10.8)	18.66 (12.1)	p > 0.05 not significant

SD = standard deviation.

Table 4 – Comparison of IPSS between bipolar and monopolar groups.

Time	BIPOLAR IPSS mean (SD)	MONOPOLAR IPSS mean (SD)	p Value
Pre-op	24.07 (3.68)	23.43 (4.04)	0.539 NS
Post-op 1 mo	7.73 (0.83)	7.47 (0.90)	0.237 NS
Post-op 3 mo	6.77 (1.04)	6.60 (1.04)	0.537 NS
Post-op 6 mo	6.30 (0.95)	6.40 (0.97)	0.688 NS
Post-op 12 mo	6.13 (0.94)	6.23 (0.94)	0.681 NS

IPSS = International Prostate Symptoms Score; SD = standard deviation.

The surgeons reported better coagulation and a clearer operative field with the bipolar resectoscope. None of our patients had any ureteric orifice injury and no procedure was abandoned due to capsular perforation. None of our patients required blood transfusion or recatheterisation for clot retention. Also, none of our patients required any intervention in the postoperative follow-up, i.e. reoperation, treatment of strictures or bladder neck contractures. None of our patients had any documented urinary tract infection, epididymitis or myocardial infarction in the postoperative follow-up.

Patient follow-up (1,3,6 and 12 months post-operatively) demonstrated an improvement in IPSS

and Qmax in both the groups. The improvement in IPSS was comparable in both groups (Table-4). The Qmax at follow-up was significantly higher in the bipolar group as compared to the monopolar group ($p < 0.05$, Table-5).

COMMENTS

Our understanding of the pathophysiology leading to TURP syndrome has improved in recent years. Recent technological advances have led to the development of new bipolar resection systems that permit normal saline to be used as irrigant.

Table 5 – Comparison of *Q*_{max} between bipolar and monopolar groups.

Time	Bipolar <i>Q</i> _{max} (mL/s) mean (SD)	Monopolar <i>Q</i> _{max} (mL/s) mean (SD)	p Value
Pre-op	6.59 (2.51)	6.44 (2.28)	0.827 NS
Post-op 1 months	17.92 (2.16)	14.04 (2.59)	< 0.05 S
Post-op 3 months	18.44 (1.93)	14.91 (2.29)	< 0.05 S
Post-op 6 months	18.42 (2.76)	15.30 (2.33)	< 0.05 S
Post-op 12 months	18.52 (2.07)	15.42 (2.31)	< 0.05 S

*Q*_{max} = maximum flow rate; SD = standard deviation.

Recent trials evaluating the safety and efficacy of bipolar resectoscopes have claimed advantages over standard monopolar resection (3-7). By using physiologic saline (0.9% NaCl) as irrigation fluid, it eliminates any danger of TUR syndrome and thus eliminates the conventional time limit of resection. The bipolar system can be used as safely and effectively in the resection of the large gland (> 60 g) as reported in the resection of small and medium-sized glands (8). Collateral and penetrative tissue damage is reduced, there is less tissue charring, better identification of the surgical capsule and less granulation tissue formation.

Our study showed a fall of 1.3 mEq/L in the serum sodium concentration in the saline bipolar group. In a small pilot study by Issa et al., it was observed that despite a prolonged resection time, the mean drop in serum sodium concentration was only 1.6 mEq/L (9). In comparison, the glycine monopolar group showed an appreciable decline in sodium levels (4.12 mEq/L). However, the drop in sodium was not statistically significant.

The crucial physiological derangement of the central nervous system functions during TURP syndrome is not hyponatremia per se but acute hypoosmolarity. Only a few studies correlate a patient outcome after TURP with both serum sodium concentration and osmolarity. In a series of 72 patients undergoing TURP, serum sodium concentration decreased by 10 to 54 mmol/L in 19 (26%) while osmolarity changed in only two (3%). The two patients who had both hyponatremia and hypoosmolarity developed

pulmonary edema and encephalopathy. The 5 patients in this series with the largest decreases in serum Na concentration had no changes in serum osmolarity and no signs of TURP syndrome. As serum Na concentration does not necessarily reflect serum osmolarity, the recommendation is that serum Na concentration should be reported together with osmolarity when the irrigant solution contains osmotically active solutes such as glycine (1).

Our study showed a drop in osmolarity of 5.14 mosmol/L in the glycine group compared to a drop of 0.43 mosmol/L in the saline group. This drop, however, was not statistically significant.

Plasma potassium fluctuations have also been studied during endourological procedures. Norlen et al. (10) reported dilutional hypokalemia when distilled water was used as an irrigant. In contrast, Krishna Moorthy et al. (11) reported significant hyperkalemia in patients undergoing TURP and percutaneous nephrostolithotomy with glycine and sterile water, probably due to hemolysis during absorption of fluid into the circulation. There was no alteration in potassium levels when normal saline was used as irrigating fluid. Hyperkalemic cardiotoxicity is increased by hyponatremia and acidosis. It is possible that the cardiovascular changes occurring in TURP syndrome can be a combination of both hyponatremia and hyperkalemia. Our study, however, showed no significant changes in potassium levels in either group.

Issa and coworkers report their experience with large prostate resections and only a minimal fall in hematocrit with the bipolar resectoscope (9).

Our study results showed a highly significant drop in hematocrit and Hb in the monopolar-glycine group (2.83%, 0.97gm% respectively). There was however a significant drop in hematocrit (1.62%) and Hb (0.55 gm%) in the bipolar-saline group also. However, no patient from either group required blood transfusion.

In our study, the resection was done by trainee residents who were at different stages of their learning curves. This may explain comparable operating time in both groups. Michielsen et al. have reported significantly longer operating times with bipolar resection (12). Recent studies have shown shorter operating times, less blood loss and shorter periods of irrigation and catheterization with bipolar resection (13,14). Improvement in Qmax in our study was significantly higher with the bipolar group although IPSS was comparable in both the groups.

CONCLUSION

Our study results indicate that bipolar TURP is clinically comparable to monopolar TURP with an improved safety profile. Bipolar saline TURP may prove safer in patients with large prostates where longer resection time and greater absorption of irrigating fluid is a concern. However, larger numbers of patients with longer follow-up is essential.

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CONFLICT OF INTEREST

None declared.

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Photoselective Vaporization of the Prostate in Men with a History of Chronic Oral Anti-Coagulation

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ABSTRACT

Purpose: A considerable percentage of patients with benign prostatic hyperplasia (BPH) also have additional cardiac pathologies, which often require anticoagulant therapy. The aim of this study was to evaluate the efficacy and safety of photoselective vaporization of the prostate (PVP) for BPH in cardiac patients receiving anticoagulant therapy.

Materials and Methods: A total of 67 patients suffering from BPH and high risk cardiac pathologies were operated on using laser prostatectomy. All patients had cardiac pathologies with bleeding disorders requiring anticoagulant use, and underwent standard urologic evaluation for BPH. Patients were treated with laser prostatectomy for relief of the obstruction using the KTP/532 laser energy at 80 W.

Results: The mean patient age was 71.4 years (range 55-80). Mean prostate volume on transrectal ultrasonography was 73.2 mL (range 44-120). Operation time ranged from 40 to 90 min, with an average value of 55 min. The average hospital stay was 48 hours (range 12-72) and the Foley catheters were removed within 48 hours, with a mean catheterization time of 34.2 ± 5.9 hours (0-48). No patient required an additional procedure due to severe bleeding necessitating intervention during the early postoperative phase. Mean International symptoms scoring system (IPSS) values and post voiding residual volume decreased and peak urinary flow rate increased ($p < 0.001$). Our results showed that the mean prostate volume had decreased by 53% at 6 months.

Conclusions: High-power photo selective laser vaporization prostatectomy is a feasible, safe, and effective alternative for the minimal invasive management of BPH, particularly in cardiac patients receiving anticoagulant therapy.

Key words: prostate; prostatic hyperplasia; bladder outlet obstruction; laser surgery; anticoagulants

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INTRODUCTION

Both medical and surgical options for the treatment of benign prostatic hyperplasia (BPH) have expanded in recent years (1). Concerning the surgical treatment of this pathology, despite its effective and successful results, transurethral resection of the prostate (TURP) has been found to be associated with significant risks for the patient. While intraoperative

mortality rates have been reported to be from 0% to 0.8%, morbidity (especially bleeding and perforation) rates were 6.9% to 14% (range 2-5). Morbidity in the month after surgery varied from 9.5% to 18% (range 2-5) and consisted mainly of bleeding with or without clot retention, which can necessitate re-operation or transfusion. Moreover, an increase in the risk of deep venous thrombosis of 6.8% to 10% in normal patients undergoing TURP has previously been reported (6).

Regarding the management alternatives in patients receiving oral anticoagulant, studies have clearly demonstrated that instead of temporarily ceasing anticoagulant drugs (which may increase the risk of thromboembolic processes) physicians tended to stop anticoagulant agents for a certain period preoperatively and to use heparin intravenously during this phase (7).

Oral anticoagulant therapy is commonly used in atrial fibrillation, recurrent thromboembolic disorders, and prosthetic heart valves. TURP adds an additional risk in these patients with an additional BPH pathology (6). Therefore, an alternative surgical technique to TURP is needed.

Concerning the various potential therapeutic strategies for minimally invasive treatment of BPH that could be associated with less morbidity than TURP, various types of laser prostatectomy have been used in the last 10-15 years (8,9). Although several alternatives have been used to reduce the known perioperative morbidity, perioperative hemorrhage remains the major complication of this specific intervention (10). Previous studies have shown that visual ablation of the prostate with the neodymium : yttrium–aluminium–garnet (Nd: YAG) and holmium laser could be performed in patients under anticoagulant treatment with satisfactory hemostatic results (11-13). In particular, holmium laser enucleation of the prostate is a safe and effective therapeutic modality in patients on anticoagulation with symptomatic BPH refractory to medical therapy.

As regards this procedure, the 80 W KTP (potassium titanyl phosphate) laser vaporization of the

prostate combines the tissue-debulking properties of transurethral resection of the prostate with the known good hemostatic properties of other laser techniques. It is a safe procedure for the patient and provides a virtually bloodless operation and immediate improvement of voiding (14-18).

In the present prospective clinical study we aimed to evaluate the efficacy of high-power photoselective laser vaporization prostatectomy for the minimal invasive management of BPH in cardiac patients receiving anticoagulant therapy.

MATERIALS AND METHODS

Between May 2004 and September 2005, a total of 67 patients (referred with complaints of infra-vesical obstruction and high risk cardiac pathologies) were retrospectively included in the study program. While the majority of the patients had had bypass surgery (58/67, 86.5%) due to ischemic heart disease, the remaining had valvular pathology and had undergone replacement surgery. Conservative management along with the use of alpha blockers had failed to alleviate the symptoms in these patients.

All patients underwent standard urologic evaluation for BPH with the International symptom scoring system (IPSS) symptom score, peak urinary flow rate (Q_{max}), ultrasound prostate volume estimation, prostate-specific antigen, and digital rectal examination. In addition, blood loss and serum sodium levels were determined preoperatively and on day 1 postoperatively in patients during intervention and observed in all patients. Patients included in the study program were on anticoagulant therapy for various indications (Table-1). Forty-six patients were on acetyl salicylic acid, 12 patients were on clopidrogel bisulfate, and 9 patients were on warfarin sodium medication.

Anticoagulant medication was stopped 2 days before the surgery in all patients. Subcutaneous Low molecular weight heparin (LMWH) was started 24 hours after the discontinuation of oral anticoagulant (warfarin sodium) in 9 patients due to the coagulation risk and stopped 12 hours before surgery when the International Normalized Ratio (INR) decreased to less than 1.4. LMWH was restarted 12 hours after

Table 1 – Indications for oral anticoagulant therapy.

Indications*	N. Pts
Myocardial infarction	36
Prosthetic heart valves	9
Congestive heart failure	3
Pacemaker	13
Aortic aneurysm	1
Chronic atrial fibrillation	21
Total	83

* More than 1 pathology in some patients.

surgery and oral warfarin sodium was resumed after the patients were able to receive medication (24 hours after the last LMWH application). After INR increases to greater than 2, LMWH can be discontinued. No significant complication occurred in any patient due to the cessation of the medication; in 9 patients, however, anticoagulant therapy was maintained using enoxaparin. Furthermore, the 58 patients on acetyl salicylic acid or clopidogrel bisulfate medication did not receive any anticoagulant therapy during the surgery and these agents were restarted 3 days after photoselective vaporization of the prostate surgery. All patients presented with an American Society of Anesthesiologists score of 2 or lower and, thus, were considered to be at low surgical risk.

All patients were treated with laser prostatectomy for relief of the obstruction. Indications for surgery were the same as previously described in detail (18). During the laser procedure, KTP/532 laser energy at 80 W was delivered by a 6F side-firing fiber through a 24F continuous-flow cystoscope (KTP/532 laser; Nigara PV trade mark laser system; Laserscope, San Jose, CA). PVP using saline irrigation was performed under spinal or general anesthesia. The prostatic lobes were readily vaporized to within capsular fibers. The mean duration ranged from 40 to 90 minutes with an average time of 55 minutes, during which a mean of 122.7 ± 24 kJ (range 30-280) of energy was delivered. A urethral catheter was inserted postoperatively. On rare occasions, if hematuria persisted despite intermittent irrigation, continuous irrigation was begun using a 3-way catheter and bladder washouts required were recorded. The catheter was routinely removed within 48 hours of the operation. Details of adverse events were noted, including any pyrexia greater than 38 degrees C, hypotension episodes (systolic blood pressure less than 100 mmHg), and blood transfusion or clot retention episodes. When patients were able to void adequately, they were discharged from the hospital. Postoperative efficacy parameters were mean and percentage changes from baseline in hemoglobin, sodium level (12 hours after the operation), IPSS, peak urinary flow rate (Qmax), post-void residual urine volume, and transrectal ultrasound prostate volume measurement.

The patients were reassessed at 3 and 6 months postoperatively with respect to any changes in

these parameters. The Mann-Whitney U and Friedman test was used to assess statistical significance.

RESULTS

A total of 67 patients on anticoagulation were included in this study, of whom 54 (81%) presented with symptomatic BPH refractory to medical treatment. Table-2 lists the main characteristics of all patients. Before surgery, mean preoperative INR was 1.32 (0.9-2.5) in those receiving warfarin treatment. These values for the patients on warfarin anticoagulation and LMWH substitution were 2 ± 0.22 and 1.20 ± 0.15 , respectively. Applied energy (kJ) was 226 ± 56 and we used only one fiber for each patient.

No patient required an additional procedure due to severe bleeding necessitating intervention during the early postoperative phase and no blood transfusion was required before, during, or after the procedure. In 5 patients (7.4%) receiving LMWH treatment, however, prolonged bleeding (mean 2.4 days) was observed and continuous bladder irrigation and washout were necessary in these patients. Two other patients receiving LMWH (2.9%) were referred with bleeding 7-10 days after the procedure, which was treated conservatively. Thus, a total of 7 patients (10.4%) experienced bleeding after laser surgery and were subsequently treated appropriately with no major consequences. On the other hand, in 5 (55.5%, 5/9) patients receiving LMWH, prolonged bleeding was observed. Similarly, of the 2 patients with delayed bleeding this represented 2/9 (22.2%) of those on LMWH. Therefore, 7/9 patients (77.7%) on LMWH experienced bleeding, which represented 10.4% of patients in the entire series. Immediately after the procedure, 8 patients (11.9%) experienced 1 to 7 days of mild irritative symptoms requiring no specific treatment, and 5 patients (7.4%) had urgency for 10-14 days but none had incontinence, newly developed impotence, or required re-operation. Five patients (7.4%) required re-catheterization for about 3 days due to transient urinary retention following the removal of the urethral catheter. Mean preoperative and postoperative hemoglobin was 12.6 g/dL (range 8.9 to 14.8) and 11.7 g/dL (range 8.0 to 13.2), respectively ($p < 0.62$). Mean preoperative and postoperative

Table 2 – Baseline characteristics and preoperative parameters in patients who underwent photoselective vaporization of the prostate surgery.

	Mean (range)
Age (years)	71.4 ± 9 (55-80)
Prostate vol. (cc)	73.2 ± 33 (44-120)
Surgery indications (%):	
LUTS refractory to medical treatment	54 (81%)
Urinary retention	12 (18%)
Hematuria	1 (1%)
Qmax (mL/sec)	6.8 ± 2.9
Residual urine (mL)	123.6 ± 108.6
IPSS	24.3 ± 5.9
PSA level (ng/mL)	4.52 ± 3.7

IPSS = International symptom scoring system; LUTS = lower urinary tract symptoms; Qmax = maximum flow.

serum sodium was 138.7 (range 131 to 145) and 138.0 (range 128 to 142), respectively ($p < 0.82$). Evaluation of the pre- and postoperative hemoglobin and plasma sodium levels did not show any significant difference. Despite the significant change with respect to hemoglobin values after the procedure, this change was not clinically significant. Saline solution (0.9%) was used for irrigation intraoperatively and fluid absorption was not observed in any of the patients.

The perioperative and postoperative data of those who underwent LMWH and those that did not are presented (Table-3). Of the sexually active patients 62% had retrograde ejaculation at 3 and 6 months. No other significant complications were observed. Again no patient required admission to the intensive care unit for severe cardiac problems (such as myocardial infarction) during the study.

The voiding parameters showed improvement during the early phase of follow-up. The mean prostate volume had decreased by 53% after 6 months (Table-4).

At the end of the 6 months, no postoperative complications developed in any patients, i.e. urinary tract infection, stress incontinence, cloth retention, bladder neck contracture, or urethral stricture.

COMMENTS

BPH is the most common cause of bladder outlet obstruction in the elderly and it is the most frequent pathology requiring surgical treatment in men. Concerning the treatment of this condition, medical and surgical options for the treatment of infravesical obstruction have expanded in recent years (1). Among the surgical techniques, the gold standard treatment, TURP, has been applied with significant success rates for years and it significantly improves urinary symptoms and urinary flow. However, it is well known that, despite its common acceptance and widespread application, complications can be seen in up to 20% of cases following a successful intervention (10,19-21). Currently, there are a number of minimally invasive procedures that may be safe and effective alternatives to TURP. Among these, one promising surgical technique is laser prostatectomy (8,9,22).

Over the past 10-15 years a variety of endoscopic laser techniques have evolved for the treatment of BPH that have been associated with less morbidity than TURP with a shorter hospital stay. The initial type of laser in this field, the Nd: YAG laser, has allowed the performance of prostatectomy in an almost

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Table 3 – Perioperative and postoperative outcomes and follow-up results (LMWH (+) the patients who had low molecular weight heparin before the PVP surgery and LMWH (-) those who did not.)

	LMWH (+)	LMWH (-)	p Value*
No. of patients	9 (13%)	58 (87%)	
Mean perioperative ± SD			
Resection time (min)	52.5 ± 14.8	48.7 ± 12.6	0.07
Serum hemoglobin change (gm/dL)	-0.4 ± 0.6	-0.3 ± 0.5	0.72
% Serum hematocrit change	-0.4 ± 1.1	-0.5 ± 2.1	0.66
Serum sodium change (mmol/dL)	-0.5 ± 1.8	-0.2 ± 2.2	0.81
Postoperative			
No. bladder washouts	5 (7%)	7 (10%)	0.01
Mean postoperative stay ± SD (days)	1.9 ± 1.2	1.8 ± 1.3	0.97
Mean catheterization time ± SD (days)	2.2 ± 1.4	2.1 ± 1.7	0.83
No. of complications			
No. pts with prolonged bleeding	4 (6%)	1 (1%)	0.01
Re-hospitalization for secondary hemorrhage	2 (3%)	-	-
Re-hospitalization for acute urinary retention	5 (7%)	0	0.01

* Mann Whitney U test; PVP = photoselective vaporization of the prostate; LMWH = Low molecular weight heparin; PSA = prostate-specific antigen; Qmax = maximum flow; SD = standard deviation.

bloodless field and without absorption of irrigant, but long-term follow-up data have demonstrated that sloughing of the remaining necrotic tissue may cause bladder outlet obstruction and related symptoms for a definite period of time after treatment. Moreover, patients undergoing these types of laser treatment required a longer period for maximum improvement, which probably reflects the lack of tissue debunking at the time of surgery.

Another type of laser used for obstruction relief in BPH patients is the holmium laser application and this type of laser has been reported to be an effective alternative to the “gold standard” for large prostates, entailing significantly less blood loss and a much shorter catheter time and hospital stay (1,2,15).

Several studies of high risk cases with different laser types have been performed in the past. In

Table 4 – Comparative evaluation of all parameters before and after photoselective KTP laser prostatectomy.

Parameter	Before treatment	3 months	6 months	p Value*
Q-max (mL/sec)	6.8 ± 2.9	21.5 ± 8.8	24.5 ± 9.6	< 0.001
IPSS symptom score	24.3 ± 5.9	8.2 ± 2.3	7.9 ± 2.6	< 0.001
Mean prostate vol. (mL)	73.2	29.7 (-59%)	24.8 (-53%)	< 0.01
Residual urine (mL)	123.6 ± 108.6	43.1 ± 32.9	26.2 ± 18.9	< 0.001
Mean PSA level (ng/mL)	4.52	4.18	4.64	< 0.01

* Friedman test; KTP = potassium titanyl phosphate; IPSS = International symptom scoring system.

contrast to laser types previously used, the potassium titanyl phosphate (KTP) laser has been shown to vaporize prostatic tissue with minimal coagulation of the underlying structures. With use of the KTP laser, heat has been found to be concentrated into a small volume, which causes the ablation of the tissue by rapid vaporization of cellular water by leaving a 2-mm rim of coagulated tissue. After favorable results were obtained in studies of animal models and human cadavers, the clinical use of 60-80 W KTP laser prostatectomy began in selected patients (4,6,7,9,10). Again *ex vivo* studies have demonstrated that larger coagulation zones during 80 W KTP laser vaporization make this technique a relatively bloodless ablative procedure, giving rise to hemostasis, that is highly superior to conventional TURP-like tissue resection (17). Decreased morbidity (bleeding or other cardiac high risk disorders) and shorter hospital stay have been reported as the factors resulting in the rapid acceptance of photoselective vaporization of the prostatic tissue.

Yuan et al. have reported 12 months' results from a prospective clinical trial in 128 high-risk men with benign prostatic hyperplasia who underwent photoselective vaporization of the prostate (23). According to their results, the mean operation time was 51.6 (22.8) min, the mean catheterization time was 2.8 (1.6) days, IPSS decreased from 19.2 (6.1) before surgery to 6.1 (4.6), Q(max) increased from 7.0 (2.8) mL/s to 24.8 (8.0) mL/s, and residual urine decreased from 168 (89) mL to 23 (34) mL, 12 months later. All these results were similar to our clinical outcomes.

On the other hand, Ruszat et al. and Woo et al. reported that there was no perioperative discontinuation in drug administration since withdrawal would have posed a considerable risk for thromboembolic events (24,25). We stopped anticoagulant medication 2 days before surgery in all patients but started LMWH, 24 hours after the discontinuation of oral anticoagulant because of the coagulation risk. We did not observe any complications linked to the discontinuation of anticoagulant treatment after the surgery.

New-generation, high-power potassium titanyl phosphate lasers can be used in the day-care setting, with minimal risk of complications and without the need for postoperative catheter drainage (10,11,17).

Furthermore, the ability to use this technology in the management of relatively large prostates, in a safe and effective manner, represents another advantage of this technique that makes it preferable to the other surgical alternatives including open prostatectomy or TURP.

Based on our relatively short follow-up data, we suggest that high-power KTP lasers represent a very significant challenge to the 'gold standard' status of TURP. KTP laser prostatectomy has been found to be sufficiently effective in our patients receiving anticoagulant therapy due to certain cardiac problems. Successful results similar to those produced by TURP including significant improvements both in IPSS symptom scores as well as maximum flow rates were observed in the majority of patients. Again residual urine volume decreased significantly after laser vaporization. Limited complications were observed and apart from the mild dysuria and urgency no major complication that really affects the quality of life in the treated patients was observed in our series. The urethral catheter was removed within 48 h in all patients and most of the patients were discharged the following day. More importantly, although mild hematuria lasting a couple of days after the procedure was observed in some patients, severe hemorrhage requiring intervention was not observed in any patient.

Thus, our data confirmed the hemostatic efficacy of KTP laser vaporization during its TURP-like resection with highly effective tissue removal especially in high-risk patients by giving rise to hemostasis. On the other hand, 7/9 patients on LMWH experienced minor bleeding complications in our study and so this subgroup had a particular risk although none required intervention or transfusion. Despite all these successful results, we must emphasize that the relatively small number of patients and short follow-up period, the absence of a control group (TURP group), and the small number of patients who used LMWH during the procedure could be considered the drawbacks of our study.

CONCLUSION

Our results demonstrate that high-power photoselective laser vaporization prostatectomy is feasible

and appears to be safe and effective for quickly relieving bladder outlet obstruction due to BPH in a day-care setting with minimal risk of complications and minimal need for postoperative catheterization. Although several factors limit the interpretation of the results of this study, the procedure could be considered as a promising alternative in the treatment of BPH in all but especially in high-risk patients receiving anticoagulant therapy. However, we suggest that larger randomized clinical trials to compare this technique with standard TURP and long-term follow-up data are needed to determine its efficacy, safety, and durability.

CONFLICT OF INTEREST

None declared.

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Parachute Technique for Partial Penectomy

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ABSTRACT

Purpose: Penile carcinoma is a rare but mutilating malignancy. In this context, partial penectomy is the most commonly applied approach for best oncological results. We herein propose a simple modification of the classic technique of partial penectomy, for better cosmetic and functional results.

Technique: If partial penectomy is indicated, the present technique can bring additional benefits. Different from classical technique, the urethra is spatulated only ventrally. An inverted "V" skin flap with 0.5 cm of extension is sectioned ventrally. The suture is performed with vicryl 4-0 in a "parachute" fashion, beginning from the ventral portion of the urethra and the "V" flap, followed by the "V" flap angles and then by the dorsal portion of the penis. After completion of the suture, a Foley catheter and light dressing are placed for 24 hours.

Conclusions: Several complex reconstructive techniques have been previously proposed, but normally require specific surgical abilities, adequate patient selection and staged procedures. We believe that these reconstructive techniques are very useful in some specific subsets of patients. However, the technique herein proposed is a simple alternative that can be applied to all men after a partial penectomy, and takes the same amount of time as that in the classic technique. In conclusion, the "parachute" technique for penile reconstruction after partial amputation not only improves the appearance of the penis, but also maintains an adequate function.

Key words: *penis; penile cancer; surgery; surgical procedures; reconstructive surgical procedures*

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INTRODUCTION

Penile carcinoma is a rare but mutilating malignancy. Tumors are often localized in the penis at the time of diagnosis, and they may be better controlled by surgical excision (1-6). In this context, partial penectomy is the most commonly applied approach for best oncological results (7,8). We herein propose a simple modification of the classic technique of partial penectomy, for better cosmetic and functional results.

SURGICAL TECHNIQUE

After diagnosis of penile carcinoma confirmed by incision biopsy, patients are elected for surgical treatment. When possible, more conservative procedures such as postectomy or glansectomy are performed. If partial penectomy is indicated, the present technique can bring additional benefits. Our Institutional Review Board approved the present study.

Patients are generally operated in the supine position, under spinal anesthetic block. After proper

asepsis, a surgical glove or condom secured distally to the proposed line of amputation excludes the lesion. A tourniquet is applied at the base of the penis. The skin is incised circumferentially around the penis, deepening to Buck's fascia. The urethra is isolated from the corpora cavernosa and divided, aiming to obtain at least 1 cm distal redundancy, but without oncological compromise (at least 1-2 cm margin). Dorsal vein complex is ligated, corpora are divided, and the surgical specimen is sent to the laboratory for frozen-section analysis. Corpora are secured with continuous sutures with vicryl 2-0, opposing the margins

of Buck's fascia. Tourniquet is removed and adequate hemostasia is obtained.

Different from classical technique, the urethra is spatulated only ventrally. An inverted "V" skin flap with 0.5 cm of extension is sectioned ventrally. The suture is performed with vicryl 4-0 in a "parachute" fashion, beginning from the ventral portion of the urethra and the "V" flap, followed by the "V" flap angles and then by the dorsal portion of the penis (Figures 1 and 2). After completion of the suture, a Foley catheter and light dressing are placed for 24 hours.

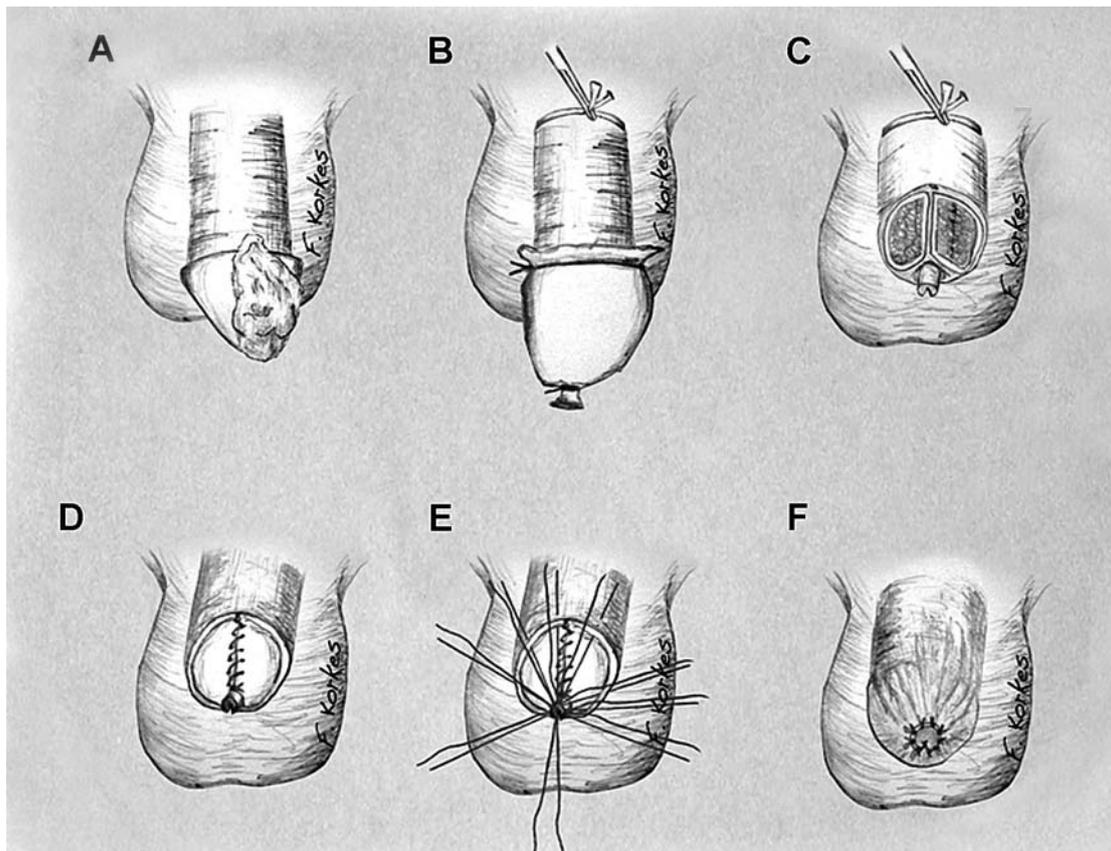


Figure 1 – Schematic drawing of parachute technique for partial penectomy. A) Penile tumor elective for partial penectomy. B) A surgical glove is secured distally to the proposed line of amputation and a tourniquet is applied at the base of the penis. C) Skin is incised circumferentially around the penis, deepening to Buck's fascia, the urethra is isolated from the corpora cavernosa, divided and spatulated only ventrally. D) Corpora cavernosa are closed with continuous sutures with Vicryl 2-0, the tourniquet is removed and adequate hemostasis is obtained. E) Final suture is performed with Vicryl 4.0 in a "parachute" fashion, beginning from the ventral portion of the urethra and the "V" flap, followed by the "V" flap angles and then by the dorsal portion of the penis. F) Final aspect.



Figure 2 – Final aspect of parachute technique for partial penectomy.

COMMENTS

After partial penectomy, sexual intercourse and adequate micturition are aims possible to be achieved in most settings. A few authors have evaluated psychological, social and sexual consequences after these procedures (9-11).

The purpose of the present technique is to preserve the morphologic aspect of the penis closer to a normal situation and additionally a permeable meatus. Several complex reconstructive techniques have been previously proposed, but normally require specific surgical abilities, adequate patient selection and staged procedures. We believe that these reconstructive techniques are very useful in some specific subsets of patients. However, the technique herein proposed is a simple alternative that can be applied to all men after a partial penectomy, and takes the same amount of time as the classic technique. We have performed four of such procedures, with good cosmetic aspect after a mean of 8 months of follow-up. All patients had distal pT2 tumors, two underwent inguinal lymphadenectomy, had positive lymph nodes and died of disease progression after 6 and 15 months; one underwent open inguinal lymphadenectomy without evidence of disease and was lost to follow up after 8 months, and the other underwent laparoscopic

inguinal lymphadenectomy also without evidence of disease. No cases of meatal stenosis were observed, and patients were satisfied with the final result, resembling the aspect of a patient with phimosis. Although the present technique has been applied only to a few patients, we are begging a prospective study to evaluate long-term outcomes.

In conclusion, the “parachute” technique for penile reconstruction after partial amputation not only improves the appearance of the penis, but also maintains an adequate function.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

In this manuscript, the authors describe a novel approach to the surgical management of penile cancer. In this surgical technical report, the cosmetic and functional outcomes of partial penectomy using a ventral spatulation of the urethra and “V” flap technique have been reported. I applaud the authors for their innovative surgical approach, which appears highly reproducible and technically feasible in most cases of penile carcinoma. Although the authors have discussed briefly the four cases in which the “parachute” technique of partial penectomy was utilized, the authors will need to validate their outcomes in a prospective trial in a larger cohort of patients prior to being considered a “superior” surgical approach. Similarly, the authors should obtain an index of erectile function (e.g. IIEF-5) before and following partial penectomy using the standard and “parachute” technique whereby ultimately validating the superior functional outcomes of this reported technique.

Recent advances in the primary management of penile cancer have highlighted that penile preserving approaches can be employed in select patients whereby offering the potential of improved quality of

life and erectile function preservation. Several clinical parameters must be considered when contemplating such penile preserving approaches including the primary tumor stage, grade, location of the penile lesion, and ability to maintain a “functional” penis whereby maintaining the ability to direct a urinary stream and potentially preserve sexual function. As a urologic oncologist, one principle which must never be compromised nevertheless is complete tumor excision with negative surgical margins at the primary tumor site whereby eliminating the nidus for cancer dissemination as well as a potential site of local symptomatic recurrence. As new surgical and technical advances being readily available in our treatment armamentarium, we must ensure that cancer-specific outcomes of these approaches meet the benchmark we have established in the management of this highly aggressive tumor phenotype.

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Determination of the Association of Urine Prostate Specific Antigen Levels with Anthropometric Variables in Children Aged 5-14 Years

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ABSTRACT

Purpose: Calculation of PSA is possible in human fluids even if it presents in very low concentrations with the help of hypersensitive immunodiagnostic methods. The periurethral glands represent one of the potential sources of urine prostate specific antigen (uPSA) in both sexes but the purpose of studying PSA levels in children is still unclear in the literature. In this pilot study we studied uPSA in a small cohort of normal, pre and post pubertal children, in relation to standard anthropometric variables.

Materials and Methods: The study cohort consisted of 58 children 5-14 years old (42 boys/16 girls). Height, weight, body mass index (BMI) and the respective stature-for-age, weight-for-age and BMI-for-age percentiles of the sample were determined. uPSA levels were measured using a third generation immunodiagnostic method (DPC Immulite®) that has a lower limit of detection of 3 ng/L. When levels of PSA were above the upper limit of detection, uPSA levels were assessed using the ROCHE technique.

Results: uPSA levels tend to be higher in male than female children ($p = 0.091$, linear regression analysis). uPSA was measurable only in 3/16 girls (18.75%). Measurable uPSA was found in 18/42 boys (42.8%). The range of urine PSA in boys was 0-161000 ng/L (mean 10561.9 ± 31830.48 ng/L). Statistical analysis with linear regression showed correlation with height and age in boys.

Conclusions: The use of hypersensitive assays allows calculation of uPSA in childhood. The values of this variable are measurable in both sexes and related with gender. In boys, uPSA was correlated with age and height but not with other variables tested. Further studies are required to clarify this field.

Key words: prostate-specific antigen; child; urine

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INTRODUCTION

Prostate specific antigen (PSA) was discovered initially in seminal fluid as γ -seminoglobulin in

the late 1960s (1). Since then there has been a great number of discoveries and developments in the field of this marker. It is now clear that PSA is not tissue or gender specific. Studies have shown its presence in

other tissues and especially in female tissues, such as periurethral glands, breast, endometrium and ovarian tissue (2, 3).

Advances in clinical biochemistry in the last decade have made possible measurement of PSA using highly sensitive assays in body fluids with extremely low concentrations. One of these methods, the third generation DPC Immulite® method (Diagnostics Products Corp., Los Angeles, CA) has a detection limit of 3 ng/L and a calibration range up to 20000 ng/L (4).

Previous studies have shown that serum PSA can be calculated not only in boys in the different stages of puberty but also in girls, although in the latter it is encountered in lower concentrations and with lower frequency (5,6). Recently PSA was measured in the urine of children of both sexes (7). The role of uPSA in children has not been investigated yet. Prostate development in childhood is related with testosterone activity, androgen receptor and 5-alpha reductase activity in the target organ (8-10). Diseases that affect the levels and activity of the above substances such as disorders of sexual differentiation and hypospadias (11) could potentially decrease PSA production in urine. uPSA could be used as a non-invasive marker for these diseases.

In the present study, we collected urine sample from healthy boys and girls aged 5-14 years, calculated uPSA levels and investigated the association of PSA with standard anthropometric variables.

MATERIALS AND METHODS

We studied 58 healthy children (42 boys and 16 girls) aged 5-14 years, not displaying any endocrine, neurological, nephrological or urogenital disorders. Children taking any kind of medication or with a fever at the time of collection of urine specimen were excluded from the study. Samples were collected from children who visited the outpatient department for minor health problems and from normal children of the hospital staff. Subjects were natives of Greece. This research study was approved by the Research Ethics Committee and local school authorities.

Each sample was collected according to the following protocol: Written consent was first ob-

tained from the parents of each child who were fully informed about the study design. Then the first 5 mL of urine was collected from the first morning urination between 7.00-9.00 hours. The sample was centrifuged at 3000 s/min for 2 minutes and the top 2 mL of supernatant was stored at -30°C. In addition, height and body weight was recorded in order to calculate the respective stature-for-age, weight-for-age and body mass index (BMI)-for-age percentiles of the sample. uPSA was calculated using the DPC Immulite method, which has a lower limit of detection of 0.003 µg/L. Samples that had PSA levels outside of the measurable range of the DPC Immulite were measured using the ROCHE technique. Bio-statistical analysis was performed using the Stata 9.0 software suite. We used the Pearson correlation to study correlations between continuous variables, the ANOVA or linear regression analysis to study continuous over categorical variables and Pearson's chi square test was utilized to study categorical variables. For all statistical tests a significance level of 0.05 was used. As far as the age of the subjects was concerned, we examined it not only as a continuous variable, but also as a binomial categorical variable as well in two groups: a childhood group (26 boys, ≤ 12 years old) and adolescent group (16 boys, > 12 years old).

RESULTS

PSA was detected in the urine of 18 of 42 boys (42.8%) and in three of 16 girls (18.75%). uPSA levels tend to be higher in male than female children ($p = 0.091$, linear regression analysis). Two girls 6 and 11 years old respectively had a uPSA value of 10 ng/L and another one 13.5 years old had uPSA of 316 ng/L. The range of uPSA in boys presented greater variability. Especially in boys 5-8 years old, uPSA activity was detected in 5 of 14 specimens (35.7 %). In 4 cases the range was 3-10 ng/L and in one case the activity was < 3 ng/L. In the group of boys aged 8-12 years old it was detected in 2/12 (16.6%) specimens with values 20 and 79 ng/L. In boys older than 12 years, uPSA was detected in 11/16 (68.75%) specimens with a range of 200 ng/L-161000 ng/L. Statistical analysis of uPSA in

PSA Levels and Anthropometric Variables in Children

boys showed a moderate strong positive relation with age ($p: 0.043$, $\rho: 0.317$) and height ($p: 0.043$, $\rho: 0.318$). The relationship of uPSA to age and height

is shown Figures-1 and 2 respectively. Pearson's correlation coefficients for uPSA showed no correlation with weight, BMI, stature-for-age, weight-

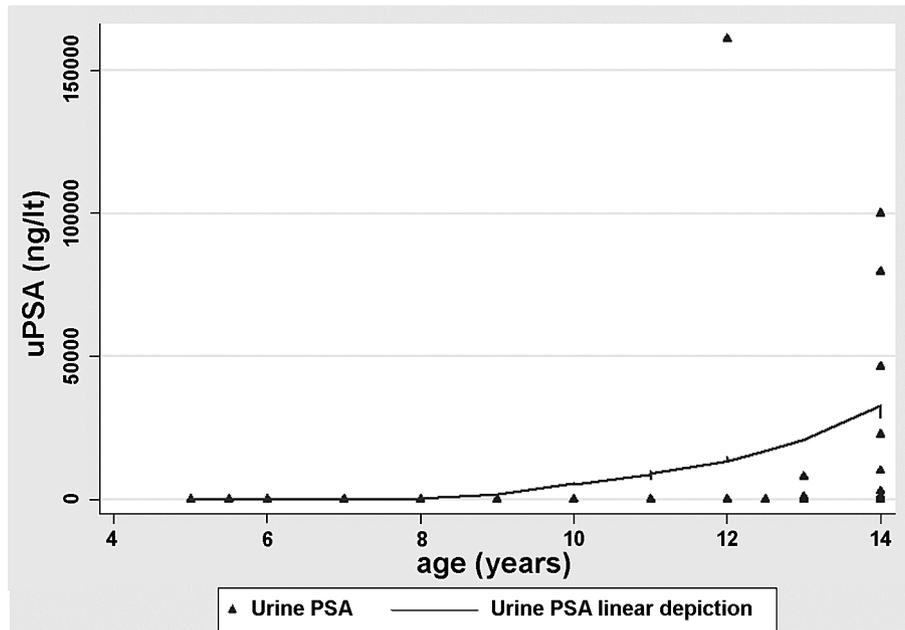


Figure 1 – Urine PSA in boys in relation to age. There is a sharply increase of uPSA in boys after the age of 12 years, when they come into adolescence.

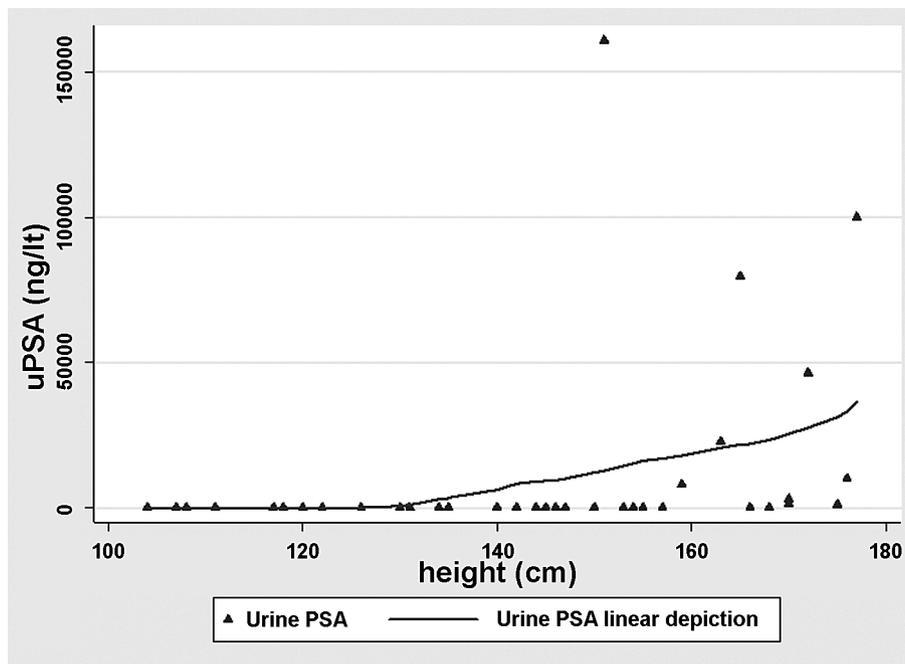


Figure 2 – Urine PSA in boys in relation to height. The slope is proportional to that of Figure-1 reflecting as a major contributor of increase entry of boys into adolescence.

Table 1 – Results of statistical analysis in boys.

Variable	rho	p Value *
Age	0.316	0.043
Weight	0.225	0.156
Weight-for-age	-0.046	0.773
Height	0.318	0.042
Height-for-age	0.142	0.376
BMI	0.014	0.93
BMI-for-age-percentile	-0.214	0.179

* For all statistical tests a significance level of 0.05 was used.
BMI = mass body weight.

for-age or BMI-for-age percentiles (Table-1). Boys were divided according to their age into two groups: childhood (26 boys, ≤ 12 years old) and adolescent group (16 boys, > 12 years old) in order to study if there was any relation of weight to uPSA. Sub-classification of each group according to BMI-for-age percentiles in normal, overweight and obese was also performed. We also investigated whether BMI-for-age percentiles classification correlates with age group using Pearson's chi square. No relation was found ($p = 0.69$). Linear regression analysis did not show any relation of uPSA with obesity in neither childhood nor in adolescence groups.

COMMENTS

It is well known that serum PSA levels rise sharply with increasing stage after males reach puberty and this rise has been shown to correlate with testosterone levels (6,12). A recent study from Antoniou et al. showed that serum PSA levels do not differ significantly between the two sexes until the age of 12 years, with median values of 38.41 ng/L (range: 1-2768) and 4.059 (1-287) ng/L for boys and girls respectively. After the age of 12, serum PSA levels in boys are seen to increase sharply (13). Another study by Sato et al. found that there is a gradual increase in uPSA activity from 1-4 month old infant males and boys older than 10 years of age. In boys 0.3-9 years there was no uPSA activity (7). These results reflect

the previous study by Goldfarb et al. who showed that PSA levels in prostatic tissue were high at birth and decreased after 6 months, and subsequently re-appeared by 10 years of age and increased during puberty (14).

In our study, we showed that uPSA was detectable in 26% of boys aged 5-12 years old within the range of 2-79 ng/L. In boys older than 12 years uPSA values increased up to 161000 ng/L. There was a statistically significant correlation between uPSA levels and height. Taller boys had higher levels of uPSA. This correlation disappeared when it was investigated in relation to stature for age percentiles because this variable is corrected for age. Statistical analysis of uPSA levels in boys with weight, BMI and the respective stature-for-age, weight-for-age and BMI-for-age percentiles of the population did not reveal any correlation.

uPSA was found only in a small percentage of girls in our sample (18.75% of girls). Other studies have shown that PSA is detectable in 11-38% of adult females with mean values of 290 and 3.720 ng/L respectively (15,16). Periurethral glands or the "female prostate" are considered to be homologous to the prostate gland as these organs have the same embryological origin (17,18). Periurethral glands in females are considered to be the primary site of PSA secretion in urine and manifest active secretion in approximately 66.7-80% of women (2,17,18). These glands do not undergo developmental changes from fetal to adult age (17). Another possible source of female adult urine PSA is the reactive metaplastic changes of cystitis cystica and cystitis glandularis that occur in adult women (19). The presence of PSA in females is under regulation of steroid hormones especially androgens and progestin. Our results support the concept that periurethral glands do not (if at all) influence significantly the serum PSA in both sexes (20).

uPSA could be potentially used as a non-invasive marker of sexual development and abnormalities in boys. However, there are major disadvantages for its use. It requires hypersensitive PSA assays that are not always available in the biochemistry department. In addition values are not standardized and may fluctuate in the same subject from one urine sample to another (21).

Our study design has certain limitations as it has involved a relatively small cohort of children, a single urine specimen from each child and the Tanner stage of the individuals was not recorded. Better designed studies which consider the above limitations will help to better define uPSA levels and variation in this population.

CONCLUSION

The use of hypersensitive assays allows calculation of uPSA in childhood. The values of this variable are measurable in both sexes and related with gender. In boys, uPSA is correlated with age and height but not with other variables tested. Further studies are required to clarify this field.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

My concerns regarding the paper are more related to the limited relevance of the issue in clinical practice in pediatric urology. Despite the arguments of the authors that “-uPSA has an importance as a potentially noninvasive marker (in contrast with serum hormones like FSH and testosterone) which could be

used easier in that part of the population” the first task of the authors would be to define the sensitivity of the method, which was very poor in the series (26% boys 5-12 years and 18.75% of girls).

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EDITORIAL COMMENT

In this straightforward work, the authors evaluate the value of urinary PSA in children of both sexes aged 5-14 years. They found that urinary PSA (uPSA) values differ significantly between boys and girls, being measurable in only 18.75% of girls, against 42.8% of boys. Also they observed that in boys the uPSA values increased with age and height, but not with weight (obesity).

Although somewhat expected, this information is quite interesting, since in a previous work (ref. 13), the same group showed that the serum PSA (sPSA) does not differ significantly between boys and girls until 12 years of age (difference being observed in boys with the increase of sPSA due to prostatic development during puberty). Furthermore, another study (ref. 7) showed no detection of uPSA in children aged 0.3 to 9 years.

The simultaneous evaluation of both uPSA and sPSA, with the same hypersensitive assay, would certainly clarify these contradictory data and enhance the information presented in this work.

One also wonders why only the first 5 mL of the first morning urination were collected for analysis, since a midstream sample seems to more appropriate for biochemical evaluation.

Although easier to collect than blood samples, uPSA still seems to be less reliable for evaluation than sPSA in this age group, therefore its practical value is still to be determined.

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REPLY BY THE AUTHORS

We agree with the comments of Dr. Macedo and we feel that a larger and better designed study would solve the problem of low sensitivity.

We also agree with the comments of Dr. Denes and would like to emphasize that although in our previous work sPSA was measurable in both sexes in childhood (1); in our last work, uPSA was measurable in 42.8% of males and in only 18.75% of female children. One could conclude that peri-urethral glands do not influence significantly the serum PSA in both sexes. Furthermore, Sato et al. (2) did not find a measurable uPSA in children from 0.3 to 9 years old. The above studies have many methodological differences (method of statistical analysis, assay, sample size, etc) that could explain the divergence in their results. We are in agreement with the suggestion that simultaneous evaluation of both urine and serum PSA in the same sample population using the same hypersensitive assay would further clarify the subject.

Regarding the relation of height and uPSA we should emphasize that this moderate positive relation ($p: 0.043$, $\rho: 0.318$) was lost when the comparison was conducted between stature-for-age and uPSA. This practically means that we should be rather cautious to draw a definite conclusion between the two

variables, considering that comparison of uPSA with stature-for-age is more accurate when referring in children population.

Regarding the sampling method of urine collection in our protocol, the first voided urine sample better reflects local PSA production by the prostate and urethra than the midstream sample (3).

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Dynamic Evaluation of Pelvic Floor Reconstructive Surgery Using Radiopaque Meshes and Three-dimensional Helical CT

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ABSTRACT

Purpose: This prospective study was performed to achieve visualization of the reestablishment of anatomy after reconstructive surgery in the different pelvic compartments with non-absorbable radiopaque meshes, providing valuable anatomic information for surgeons implanting meshes.

Materials and Methods: A total of 30 female patients with stress urinary incontinence (SUI), anterior and posterior vaginal wall prolapse, or both underwent surgical repair using radiopaque meshes after written informed consent. Patients with SUI underwent five different surgeries. Patients with anterior vaginal prolapse underwent a procedure using a combined pre-pubic and transobturator mesh, and those with posterior vaginal prolapse underwent posterior slingplasty. Three-dimensional reconstruction using helical CT was performed four weeks postoperatively.

Results: In all cases, the mesh was clearly visualized. Transobturator slings were shown at the midurethra, and the anchoring tails perforated the obturator foramen at the safety region. Mini-slings were in the proper place, and computed angiography revealed that the anchoring system was away from the obturator vessels. In patients undergoing procedure for anterior vaginal prolapse, both pre-pubic armpit and obturator slings were clearly seen and the mesh was in the proper position, supporting the bladder base and occluding the distal part of the urogenital hiatus. Transcoccygeal sacropexy revealed indirectly a well-supported “neo rectovaginal fascia” and the anchoring tails at the level of ischial spines.

Conclusion: Three-dimensional helical tomography images of the female pelvis using radiopaque meshes have a potential role in improving our understanding of pelvic floor reconstructive surgeries. These radiopaque meshes might be the basis of a new investigative methodology.

Key words: *pelvic organ prolapse; prostheses and implants; surgical mesh; tomography, spiral computed*

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INTRODUCTION

The understanding of physiopathological concepts of stress urinary incontinence (SUI) and pelvic organ prolapse (POP) has changed over the last few years; this has led to the development of new therapies and surgical techniques.

Minimally invasive synthetic slings became the preferred technique in the last decade and several

factors have contributed to their rapid acceptance. There have been a number of conceptual changes in addition to the developments of biomaterials (1).

The integral theory according to Petros and Ulmsten emphasizes the need to “restore anatomy to restore the function” (2). The theory is based on the fact that organs are suspended by ligaments and pelvic muscles inserted into these ligaments. The muscles stretch the organs against the ligaments to give them

shape and support. By a sequence of coordinated contraction and relaxation, the organs are closed (continence) or are opened out actively (emptying). Lax ligamentous insertion points therefore may cause not only prolapse, but also, symptoms of incontinence and abnormal emptying. The Integral System of diagnosis and surgery is based on a 3 zones classification (anterior, mid and posterior). The anterior zone is the one addressed when treating SUI and the goal is to restore the anatomy involving the external urethral ligament, which attaches the external meatus to the anterior surface of the pubic bone; the suburethral vagina (or Hammock); and the pubo-urethral ligament (2).

However, the blind passage of long needles and the pull-through of the sling have remained the key stages of all sling techniques.

Sling use has also brought about a series of new complications related to the tape and to the techniques, some of which have even been proven to be potentially lethal (3,4). Most of the major complications are related to the blind nature of the needles passage (5).

On the other hand, recurrence of POP, especially at the anterior compartment, has led to the development of new meshes and kits for POP repair.

Live anatomy restoration, however, is very difficult to assess due to the limitation of available imaging procedures and because the type-I meshes are not radiopaque.

When surgery is performed, the anatomical results are estimated using prolapses grading systems that are often subjective (6). Ultrasound has been used to assess the results of these procedures, but it is usually operator-dependent and may produce low quality images. Therefore, a better tool would be helical computerized tomography using three-dimensional reconstruction techniques, because it provides a high quality image and gives a dynamic evaluation when performed during rest and straining. A 3D method of visualizing the pelvic floor could facilitate understanding of the anatomy and function of this complex part of the body (7).

This prospective study was carried out in order to visualize the anatomical reconstruction after stress urinary incontinence and prolapse surgery in different pelvic compartments with non-absorbable radiopaque meshes.

MATERIALS AND METHODS

Multi-slice computer tomography (MSCT) was used to obtain high-resolution computer tomography (CT) images of pelvic regions (dynamic pelvic CT) and multi-plane reformatted (MPR) images. Thirty patients underwent pelvic floor reconstructive surgery for stress urinary incontinence (SUI) and anterior or posterior vaginal wall prolapse using radiopaque meshes (Table-1). These special meshes were made with barium-impregnated borders.

Helical pelvic scanning was performed with 1 mm slice thickness during rest and during straining.

In patients with SUI and anterior vaginal prolapse (AVP), surgeries were performed with the aid of a cystography. Anterior meshes (NAZCA TC[®], Promedon, Argentina) were placed with positioning of posterior transobturator arms anchored to the arcus tendineus at each side and anterior arms were self anchored to the prepubic space. In patients who underwent posterior vaginal prolapse (PVP) repair, an enema and a vaginogram were performed to establish landmarks and facilitate comprehension of the anatomy. A posterior mesh (NAZCA R[®], Promedon, Argentina) was placed with arms fixed through the sacrospinous ligaments at each side. Puncture was carried out 3 cm lateral and below the anal orifice.

Using the volume data acquired, overlapped reconstruction was performed at a stand-alone workstation (General Electric Medical System, GE Healthcare) to generate the images.

All patients were evaluated four to six weeks after the surgical procedure.

RESULTS

We evaluated a total of 30 patients who underwent pelvic floor reconstructive surgeries.

The meshes were visualized accurately in all cases. Patients with SUI underwent Transobturator tape (TOT) or mini-sling (OPHIRA[®] - PROMEDON[™]) procedures. Transobturator slings were attached at the midurethra and throughout the obturator foramen, allowing for normal urethral mobility during

Table 1 – Demographic data from patients and procedures.

Condition	Procedure	N
SUI	Transobturator tape	5
	Prepubic sling	2
	Micro-sling	8
	Retropubic sling	1
Recurrent SUI	Crossover transobturator sling	2
AVP	Transobturator cystocele repair	5
PVP	Infra-coccygeal sacropexy	7
	Transcoccygeal sacropexy	
Total		30

AVP = anterior vaginal prolapse; PVP = posterior vaginal prolapse; SUI = stress urinary incontinence.

straining (Figure-1). Micro slings were attached with anchoring columns near the obturator foramen without passing through. The angiographic study showed that the sling was positioned away from the major pelvic vessels (Figure-2).

Pre-operative study of patients with anterior vaginal wall prolapse showed the bladder below the inferior border of the pubic bone. The NAZCA-TC® (Promedon, Argentina) mesh in both the prepubic and

transobturator approaches was clearly seen at the right position, supporting the bladder base and occluding the distal portion of urogenital hiatus. During stress maneuver, the bladder was maintained above the inferior border of pubic bone, indicating a successful treatment (Figure-3).

For placement of posterior meshes, transcoccygeal and NAZCA-R® (Promedon, Argentina) sacropexy was performed, showing De Lancey's

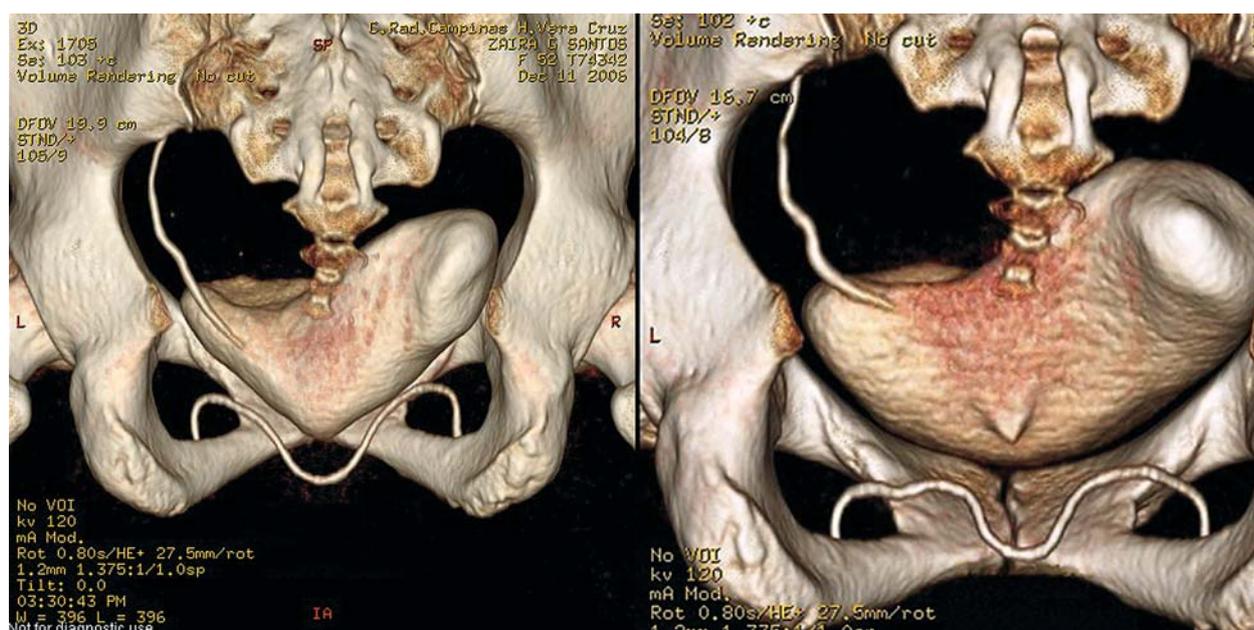


Figure 1 – Posterior views of a transobturator sling (Unitape® - Promedon™) during strain and relaxation.

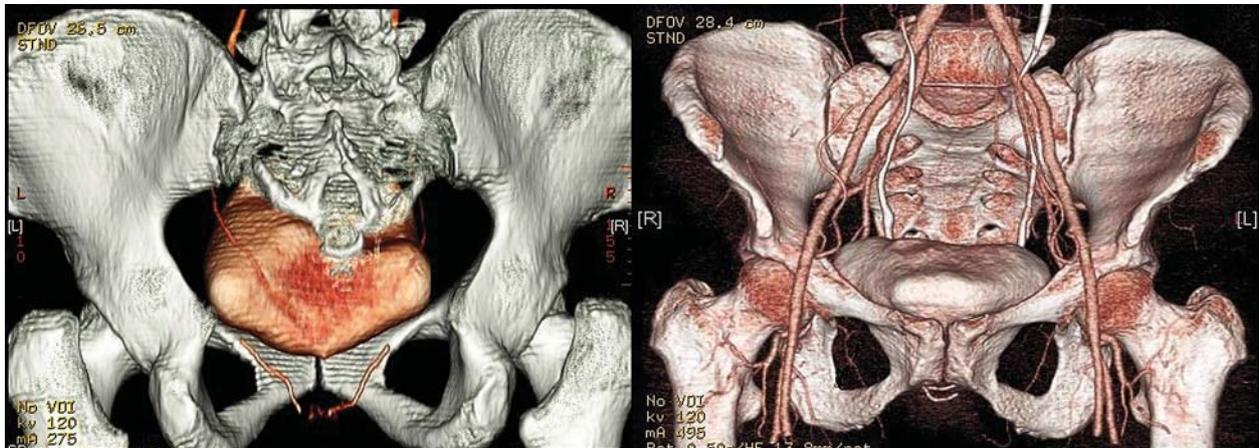


Figure 2 – Position of the Ophira® mini-sling and its distance from the obturator vessels.

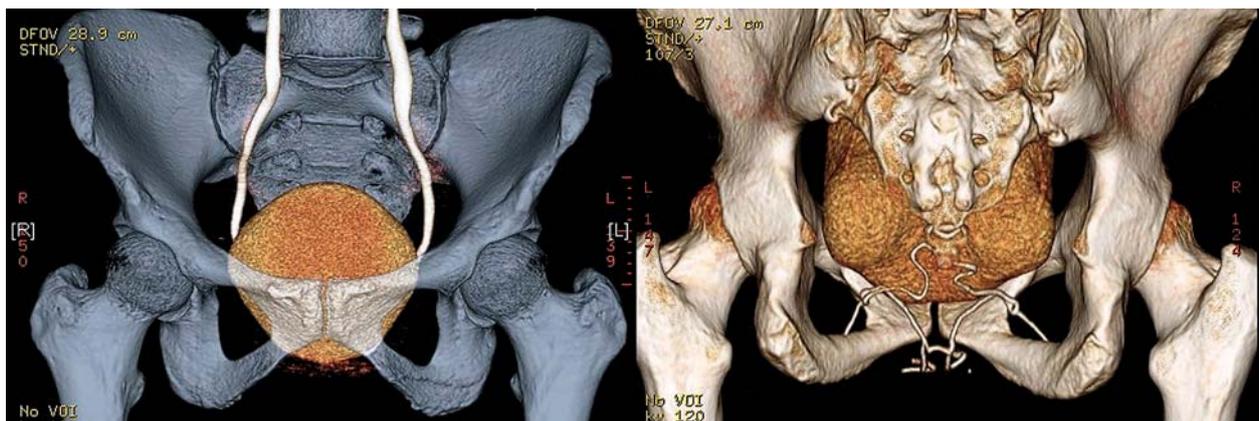


Figure 3 – Pre- and postoperative images of a cystocele corrected using Nazca-TC®.

level I correction at the level of ischial spines (Figure-4).

There were no complications related to radiation exposure or contrast medium hypersensitivity.

COMMENTS

Female POP is the result of vaginal wall protrusion, associated or not with descensus uteri. The world's female population is becoming older as life expectancy becomes longer, and therefore the prevalence of POP is increasing (8). Thus, the risk for an 80 year-old woman to undergo treatment for POP or urinary incontinence is approximately 11% (9).

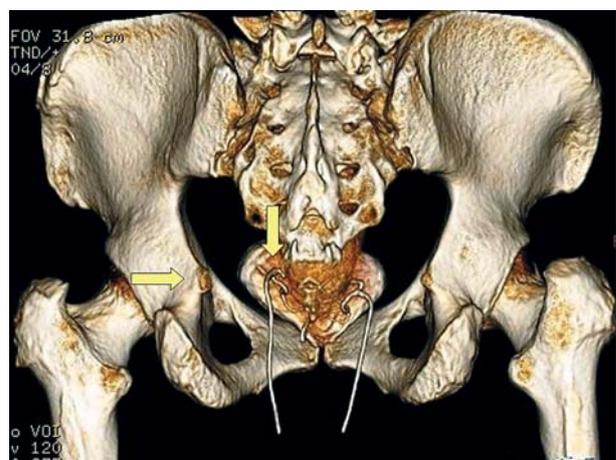


Figure 4 – Relationship between the Nazca-R® and the ischial spine.

The main techniques proposed to treat POP, levator ani myorrhaphy and pericervical ring repair, do not use synthetic materials such as polypropylene meshes. The high failure rate associated with these techniques could be explained by the poor tissue quality used in the surgical repair.

The use of synthetic meshes began in the last decade as an alternative to treat patients with high-grade prolapses and recurrent POP (10). Many attempts to demonstrate the live anatomy of these meshes have been made. Despite careful segmentation and verification by experts, limitations and some inaccuracies in ultrasound exist due to inherent technical limitations. The urethra and vagina, in particular, are small structures that are difficult to distinguish by transabdominal or transperineal ultrasound. Minor movement artifacts result in discrepancies in the quality of images (6).

In the present cases, dynamic pelvic CT and generation of MPR images allowed for direct observation of the pelvic floor adequate correction. Technologic advances in CT systems, including shorter scanning times with low radiation exposure and high quality images, allowed us to explore how the meshes work and how they behave under straining (11,12).

Patients with SUI underwent two different types of surgeries for incontinence. Contrast medium and sometimes a Foley catheter were used to provide better visualization of the urethra. The TOT sling was clearly demonstrated at the medial border of the obturator foramen (safety zone), and a kinking in the slings was noticed during rest, confirming the low-tension procedure. During straining, the bladder neck moved downward to the inferior margin of the pubic bone, stretching the tape to create the backboard support with no leakage (Figure-1). The transobturator cross-over sling was performed only as salvage procedure in patients with recurrent urinary incontinence due to severe intrinsic sphincter deficiency. In these cases, the slings assumed a helical shape around the midurethra, and the transobturator arms were observed (13). The detailed technique was described by Palma et al. and involves full dissection around the fixed urethra and placement of a "looping" sling anchored at each side through a transobturator arm (14). The Ophira mini-sling system[®], which supports the urethra in an arc-to-arc manner, was also displayed appropriately.

The tape was located at the midurethra, and the anchoring columns did not perforate the obturator foramen. The self anchoring short arms are placed through a minimal longitudinal incision underneath the mid urethra (15). During stress, normal mobility was preserved in accordance with the current concept of female stress incontinence.

A more detailed study using computed angiography showed the sling to be just below the pubis and the anchoring arms to be away from the obturator vessels (Figure-2). This confirms that the procedure may be performed in a safe manner, keeping the needle away from the neurovascular bundle.

Given the high recurrence rate of anterior vaginal prolapse with conventional repairs, synthetic meshes have been used in selected cases, such as high grade and recurrent prolapses (14-16).

CT scan was able to reveal pre-operatively a high-grade cystocele and post-operatively the body of the mesh supporting the bladder base and occluding the inferior part of the urogenital hiatus. During straining, the bladder neck remained above the inferior border of the pubic bone, confirming a good anatomical result (Figure-3).

Images obtained from the high-grade posterior vaginal wall prolapse correction showed the anchoring arm tips. The arrows point to the ischial spines, confirming the level I correction (Figure-4).

An enema was also performed in these patients, revealing a normal appearance of the rectum, which indicated proper correction of the rectocele.

CONCLUSION

The three dimensional helical tomography images of the female pelvis using radiopaque meshes have a potential role in improving our understanding of pelvic floor reconstructive surgeries. These radiopaque meshes might form the basis of a new investigative methodology.

CONFLICT OF INTEREST

Dr. Paulo Palma is a clinical investigator for Promedon, Argentina.

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EDITORIAL COMMENT

The authors report the use of helical CT to assess anatomical results following the surgical repair of stress urinary incontinence (SUI) and pelvic organ prolapse using a variety of mesh-based repairs. Accordingly, the authors radiographically confirm the expected post-operative site of these repair systems and demonstrate the correction of related pelvic floor defects. As described, previously used techniques have often provided images of limited quality and the authors succeed in providing high quality images following pelvic floor reconstruction. The added use of angiography and cystography, as well as the use of dynamic imaging during straining, adds to their visual findings.

Certainly, this study is of academic interest to those who specialize in the treatment of stress urinary incontinence and pelvic organ prolapse. Despite a significant body of research, I believe that many would characterize our understanding of the pathophysiology underlying stress urinary incontinence as limited. The authors describe two of the most notable anatomic theories of stress urinary incontinence. Indeed, such

theories provide the framework for much of our current understanding of SUI and guide the development of novel techniques for surgical repair. Related to this work, I believe that the radiographic confirmation of a suburethral tape that stretches with strain so as to provide a suburethral support to a descending bladder neck is of great interest. Nonetheless, the exact relationship between anatomy and function is not clearly defined. Indeed, recent research identifies differing anatomic locations and relationships when comparing the anatomic support focal to the integral theory and that seen with midurethral slings (1). Such findings underscore the importance of future study to forward our understanding of urinary incontinence.

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EDITORIAL COMMENT

From 1900 until the early 1990s, surgery for stress incontinence (SI) and prolapse remained basically unchanged, either some type of vaginal or abdominal sling or suspension. Both types of operation were painful, and required catheters and hospital stays of 7 to 10 days. Complicating surgical management of SI was the convention of not operating on patients who had urodynamically demonstrated “detrusor instability”, now known as “Overactive Bladder” (OAB) (1).

In 1990s the Integral Theory (2), and a method for creating artificial neoligaments were introduced (3). The theory stated that stress and urge symptoms in the female, both originated from lax suspensory ligaments of the vagina, and both were potentially curable surgically by creation of artificial ligaments. This method disregarded earlier urodynamically based conventions, and it has revolutionized the treatment of stress incontinence with minimal pain, short hospital

and high long-term cure rates. Though apparently benign, major complications have been reported with these operations, provoking calls for zero tolerance for such operations (4).

The same surgical principle, creation of artificial neoligaments, has been applied to prolapse surgery. Beginning in 1992, polypropylene tapes inserted via the perineal route (infra-coccygeal sacropexy) were used to cure prolapse of the uterus (5). These methods did not address large cystoceles. Delorme's transobturator route (2001) for a midurethral sling was harnessed for repair of large cystoceles, and meshes were attached to tapes inserted via the perineal route for repair of large rectoceles.

Though effective, major problems have been encountered with the use of large meshes. Since 2005, new mini-sling techniques have been introduced to treat incontinence and prolapse (6-8). This method seems to avoid most of the problems of large mesh, using small lengths of tape to strengthen the natural tissues, rather than replace them totally.

This is a short summary of the rapid new direction in pelvic floor surgery, which has overtaken the Urogynecology community, all in the space of 15 years. Even the report of life-threatening complications, and attempts at caution (4) has not slowed the momentum of change.

Trailing a long way behind this accelerated innovation has been a precise understanding of where these meshes go, and their effect on pelvic floor structure and function. It is well and good to apply a theory, and to use it justify a particular incontinence or prolapse technique. But that is not good science. Good science is when a convention or theory is challenged forensically for truth or falsity in an objective way. That is the only way for medicine to progress.

Professor Palma and his team at Campinas University have been at the forefront of scientific challenge. Their editorial "The Dark Side of Urodynamics" (9) reinforced the Cochrane Review's conclusions, that pre-operative urodynamics have no predictive value for incontinence surgery. Invalidating the convention that urodynamically diagnosed "OAB" was a contraindication for surgery, has potentially opened the door for surgical cure for millions of women who have urgency symptoms. It has also indirectly

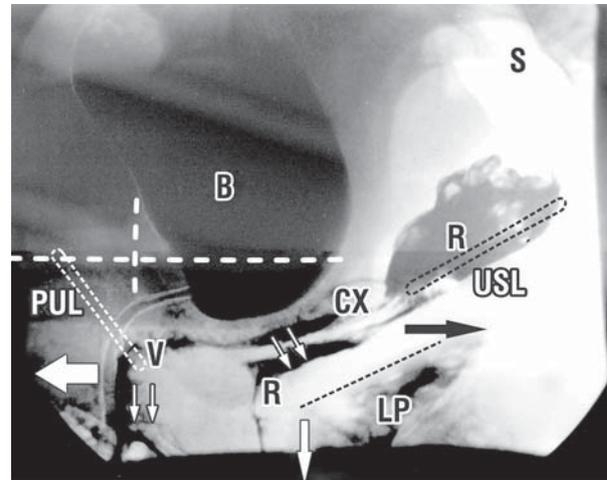


Figure 1 – A sitting X-ray taken in the straining position, with radio-opaque dye injected into the bladder (B), vagina (V), rectum (R), levator plate (LP). PUL and USL represent the pubourethral and uterosacral suspensory ligaments. The organs are tensioned like a trampoline by the muscle forces (arrows) contracting against the suspensory ligaments.

validated the Integral Theory's view that OAB is not a pathogenic condition per se. The Theory's view is that stress and urge both have anatomical origins, and urge and OAB are but different manifestations of a normal but prematurely activated micturition reflex caused by lax suspensory ligaments (10).

This forensic emphasis on functional anatomy is especially evident in the Palma team's teaching of diagnosis and surgery. They have widely taught the technique of "simulated" or "virtual" operations, a clinical challenge to the Theory (2), digitally anchoring specific ligaments during vaginal examination, and observing the effect. For example, pressing upwards to one side of the midurethra during coughing will control urine loss. Urge symptoms can also be reduced by pressing upwards in the position of other suspensory ligaments, uterosacral, and cardinal (gentle digital support of bladder base). They have constructed special teaching models for surgery, which mimic live pelvic floor anatomy (11).

Anatomical studies of tapes and implants in cadavers are not accurate, and are not validly transferable to the live patient. In the cadaver, all the muscles and organs are collapsed (12) while in the live patient (Figure-1), the organs are horizontal, suspended by

ligaments and stretched by muscle forces like a trampoline (13).

The three-dimensional helical tomography technique using radiopaque meshes (14) is a major contribution to pelvic floor science, as it provides accurate reference points in the live patient, where the anatomy is similar to what is seen in Figure-1. For the first time, we have a precise tool to help us understand how the pelvic floor and its organs function, what implants do, and what they should not do. This is where the real worth of the new technique lies, its relevance to the live patient.

Though only the technique was presented in this contribution (14), it is certain that this method will be applied to answer so many questions left hanging by the whirlwind advance in surgical innovation we have witnessed over the past 15 years. With this contribution, Professor Palma and his team have demonstrated the necessity of good science as the essential monitor for innovation.

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Urodynamics in a Community-dwelling Population of Females 80 Years or Older. Which Motive? Which Diagnosis?

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ABSTRACT

Purpose: To determine why community-dwelling women aged 80 years or over were referred for urodynamic evaluation despite their advanced age and which urodynamic diagnosis was made.

Materials and Methods: One hundred consecutive females (80-93 years) were referred to our urodynamics outpatient clinic for evaluation of lower urinary tract symptoms (LUTS) between 2005 and 2008. Clinical evaluation comprised of a previous history of LUTS, previous medical history of neurological disease or dementia, pelvic floor dysfunction or prior pelvic surgery. Exclusion criteria were complete retention and severe dementia involving failure to understand simple instructions. Assessed items were results of uroflows (free flow and intubated flow), cystometry and urethral pressure profilometry, and final urodynamic diagnosis.

Results: The main complaint evoked by the patients was incontinence (65.0%) of which 61.5% was “complicated” and urgency was reported by 70.0%.

Interpretable free flow at arrival was very low (44.0%). Prevalence of detrusor overactivity was high, found in 45 patients of whom 16 had detrusor hyperactivity with impaired detrusor contractility. Detrusor overactivity and urgency were strongly associated ($p = 0.004$). Twenty-five patients had intrinsic sphincteric deficiency alone and 15 detrusor underactivity.

Conclusion: In this particular community-dwelling with an elderly female population, urodynamics is easily feasible. Incontinence, mainly “complicated” is the more frequent complaint and urgency the more frequent symptom. Urodynamic diagnosis underlines the high incidence of detrusor overactivity as well as impaired detrusor function.

Key words: ageing; women; bladder outlet obstruction; urodynamics

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INTRODUCTION

Demographic trends indicate that the most rapidly growing adult population older than 65 years is the sub-group older than 85. Some troublesome problems are reported in the elderly primarily due to a change in lower urinary tract (LUT) function. The evaluation of LUT dysfunction is based

on urodynamic investigation which is considered the gold standard. In fact, the use of urodynamics remains debatable, as it is invasive, expensive, time consuming, and frequently it is unhelpful to achieve a final diagnosis. The place of urodynamics in the elderly has been mainly discussed concerning incontinent patients and in the frail and elderly living in a long term care residence (1,2) but less studied

in the community-dwelling elderly (3). Guidelines suggest to carry out urodynamics in the elderly after failure of conservative treatment or surgery, and do not recommend urodynamics for frail elders. Often, this procedure is not easy to put into practice as in the case of our urodynamics outpatients clinic where evaluations are performed only when requested by a general practitioner, gynecologist or urologist.

In recent years, more and more elderly females have been referred for evaluation of LUT dysfunction. The major part of this population consists of community-dwelling women who live at home, perform daily tasks, take an active part in society and play sports well into old age. Therefore, the remaining question is the diagnosis of frailty in order to take into account the guidelines. Distinction between ageing, disability and frailty is not clear and the objective measurement of frailty remains to be discussed (4,5). When considering research findings, the prevalence of frailty ranges from 33% to 88% according to the criteria employed (6). Multiple systems must be involved in the frailty definition: sarcopenia, osteopenia, nutritional changes, factors of illness. It has been suggested that older persons who retain the capacity to improve (even a small increase in their gait speed) are therefore not frail (5).

Prevalence of lower urinary tract symptoms (LUTS) and LUT dysfunction increases significantly with ageing. Most urinary problems are multifactorial in origin and are not only the result of the LUT changes with aging (7). Age related changes in the female LUT involve both bladder, impaired contractility or overactivity, and urethra, decreased urethral closure pressure and urogenital atrophy. Some studies have been conducted in order to evaluate the effect of age on the LUT function (8-12). In fact, these studies seldom concerned the oldest subgroup and were mainly devoted to the role and effects of detrusor overactivity (8,11,12). Taking into account these limitations, our objective was to assess a sizeable population of community-dwelling women, aged 80 years or more, referred for urodynamics in our outpatients' clinic in order to answer to the following questions: why is urodynamics prescribed, what are the patient complaints, what are the urodynamic findings and the urodynamic diagnosis and finally, is

urodynamics able to help the physician to achieve a better management of LUTS?

MATERIALS AND METHODS

This was a retrospective study. Among 848 women of all ages referred to our urodynamics outpatient clinic between January 2005 and March 2008, 100 (11.8%) aged 80 years or more (mean age 83.2 years; range 80-93 years) were community-dwelling and able to perform everyday tasks.

This study was conducted in accordance with the declaration of Helsinki. According to the local practice of our Ethics Committee, there is no formal Institutional Review Board approval required for retrospective studies.

Assessment by a physician included detailed medical history and usual medication, physical examination (including neurological and cognitive testing). All patients completed a 2- or 3-day bladder diary and had a urine dipstick test.

Specific evaluation comprised of a history of LUTS being the major complaint in cases of concomitant LUTS, previous medical history of neurological disease (stroke, multiple sclerosis, lumbar injury etc.) or dementia, pelvic floor dysfunction and previous pelvic surgery. Exclusion criteria were complete retention, severe dementia involving failure to understand simple orders or a Mini-Mental State score $<$ 20. One patient with spinal cord injury was excluded from the study.

Quality of life was assessed using the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) for incontinent patients and the visual analog scale (VAS) for continent patients.

Urodynamics was performed according to Good Urodynamic Practices (13) with a Laborie's Dorado[®] unit. Detailed urodynamic testing included: 1) an initial free uroflow (FF1), 2) a cystometry in the seated position at the medium filling rate of 50 mL/min with normal saline at room temperature (triple-lumen urethral catheter 10F for 67 patients and 7F for 33 patients) and intubated flow (IF), 3) urethral pressure profilometry (UPP) in supine position, empty bladder (before the cystometry) and 200-250 mL filling if incontinent, and 4) a second free uroflow (FF2) if bladder was filled for UPP.

No routine provocative maneuver for detrusor overactivity (DO) was performed during cystometry but coughs were used as quality control of pressure recordings (13).

Studied items were results from uroflows (FF1, FF2 and IF), filling cystometry and UPP, and final urodynamic diagnosis. To be interpretable, a uroflow had to have a urinated volume $>$ 100 mL.

Data are presented as mean \pm SD and range. The Wilcoxon signed-rank test was used for comparison of related samples and the Chi 2 test to compare unrelated samples with $p < 0.05$ considered significant. Statistical analyses were performed using SAS, version 5.0 (SAS Institute, Inc., Cary, NC).

RESULTS

Motive for Urodynamics

Patients' main complaints are summarized in Table-1. Incontinence was the main complaint: 22 urge, 32 mixed and 11 stress. Forty patients had previously received treatment (chemical or surgical) for incontinence in middle age or later as well as for recurrent incontinence or developed urgency. Among these patients, 12 had anticholinergic treatment failure for DO. Other complaints were 16 frequency (\geq 8 voids per 24 hours), 12 dysuria (low stream or hesitancy or straining) or incomplete retention and

1 cystitis (recurrent urinary tract infection and pain during voiding); 6 patients with pelvic organ prolapse had a pre-operative evaluation.

Incidence of incontinence (stress, urge and mixed) was 65.0% close to that of the symptom urgency (urge or mixed incontinence, and frequency) which was evoked by 70.0% of this elderly population.

ICIQ-SF score was 12 ± 4 (maximum 21) and VAS score 4.2 ± 2.5 (maximum 10).

Previous Medical History

Previous medical history of disease and/or pelvic surgery was obtained by detailed questioning which is summarized in Table-2.

Feasibility of FF and IF

A significant result was the low percentage (44.0%) of interpretable free flow (FF) on arrival (FF1) compared to the percentages of interpretable IF and FF2 (Table-3).

Maximum Cystometric Capacity (MCC)

Patients able to perform an IF (voided volume = 209 ± 135 mL) had a MCC of 337 ± 150 mL ($p < 0.001$).

Table 1 – Patient main complaint vs. urodynamic diagnosis.

Patient Main Complaint		Urodynamic Diagnosis					Number of Women
		DO	ISD	DU	LBC	N	
Incontinence	Stress	2	7	0	1	1	11
	Urge	16	4	0	0	2	22
	Mixed	15	10	2	2	3	32
Incomplete retention or dysuria		2	0	10	0	0	12
Preoperative for POP		3	1	1	0	1	6
Frequency		7	2	2	2	3	16
Cystitis		0	1	0	0	0	1
Number of women		45	25	15	5	10	100

DO = detrusor overactivity; ISD = intrinsic sphincteric deficiency; DU = detrusor underactivity; LBC = low bladder compliance; N = normal urodynamic data; POP = pelvic organ prolapse.

Table 2 – Previous medical history of the studied population.

Previous History	Number of Women
Neurological disease	23
Cognitive impairment (Mini-Mental State ≥ 20)	12
Pelvic surgery	
pelvic organ prolapse	16
hysterectomy	23
TVT	8
sling	6
others	4
Other diseases	
muscle-skeletal	29
cardio-vascular	57
depression	15
diabetes mellitus	9

TVT = Tension-free vaginal tape.

Cystometry

Detrusor overactivity (involuntary detrusor contractions during the filling phase: DO) was found in 45 patients (45%) of whom 15 (33.3 %) had a previous history of neurological disease.

In this population 16/45 (35%) had detrusor hyperactivity with impaired contractility (detrusor hyperactivity with incomplete bladder emptying leading to major post void residual (PVR) (detrusor hyperactivity with impaired contractility (DHIC).

Rhythmic rectal contractions (RRCs) were observed in 29 patients of whom 9 (31.0%) had a history of neurological disease. Among these 29 women, 18 (62%) had DO (7 with a history of neurological disease).

Intubated Flow

Among the 69 IF obtained, only 50 (72.5%) were interpretable. Voiding parameters were: maxi-

mum flow rate $Q_{max} = 11 \pm 5$ mL/s [2-30 mL/s], detrusor pressure at opening $p_{det.op} = 15 \pm 10$ cm H₂O [0-47 cm H₂O] and detrusor pressure at Q_{max} $p_{det.Qmax} = 19 \pm 11$ cm H₂O [5-48 cm H₂O] ($p < 0.0001$), and voiding time $t_{void} = 52 \pm 46$ s [7-300 s].

Urethral Pressure Profilometry

Maximum urethral closure pressure (MUCP) was 44 ± 22 cm H₂O bladder empty and 35 ± 17 cm H₂O bladder filled ($p = 0.01$). The “theoretical” value for the studied age range was 30-40 cm H₂O (14). It is important to note that between 47 patients who had at least one MUCP value (bladder empty or filled) ≤ 30 cm H₂O, only 25 had intrinsic sphincteric deficiency (ISD) (isolated low MUCP and urodynamic stress incontinence) as a final urodynamic diagnosis.

Final Urodynamic Diagnosis

DO was the main diagnosis, found in 45 patients of whom 16 had DHIC; ISD concerned only 25 patients, detrusor underactivity (defined as absence of detrusor contraction during voiding and large PVR) was found in 15, low bladder compliance ($\Delta V/\Delta p_{ves}$ less than 20 mL/cm H₂O) in 5 and normal urodynamic data in 10. In the population for which ISD was not predominant, 15 patients had DO, 5 detrusor underactivity and 2 low bladder compliance.

The Table-1 shows the distribution between main patient complaint and urodynamic diagnosis.

Complaint of urgency (symptom) was found to have a sensitivity of 54.3%, a specificity of 76.7% and a predictive positive value of 84.4% for the detection of DO; complaint of stress or mixed incontinence was found to have a sensitivity of 39.5%, a specificity of 85.9% and a predictive positive value of 68.0% for the detection of ISD.

COMMENTS

A major part (40%) of the studied population had failure of conservative treatment or recurrence of incontinence after surgical cure. These women

Table 3 – Feasibility of free and intubated flows during the urodynamic session.

Flow	Obtained		Interpretable ($V_u > 100$ mL)		Bell Shaped Curves	Not Obtained (n.o.) Not Performed (n.p.)
	nbr	V_u (mL)	nbr	V_u (mL)		
FF1	75	92 ± 105	33 (44.0%)	158 ± 113	20 (60%)	16 (n.o.) 9 (n.p.)
IF	69	209 ± 135	50 (72.5%)	263 ± 114	21 (42%)	31 (n.o.)
FF2	69	256 ± 116	63 (91.3%)	268 ± 109	27 (43%)	31 (n.p.)

FF = free flow; IF = intubated flow, nbr = number.

desired further attempts to correct or manage their incontinence. This condition implies urodynamics for a detailed and objective diagnosis. The other 60% agree to urodynamics as their LUT dysfunction has developed for many years (up to 20 years etc.) and has become a cause of decreased quality of life, or is an acute problem (e.g. incomplete retention after knee or hip surgery).

It is well known that the prevalence of urinary incontinence increases with ageing. In the age range higher than 80 years, the reported rate of incontinence is 35% for community-dwelling women in a questionnaire survey (15) and 82% for institutionalized women (2). We found an intermediate rate of 65% probably due to our recruitment, i.e. women with LUTS whose physicians requested urodynamics. It has been reported that urgency and urge incontinence increase with aging, while if stress incontinence is the main complaint among the women between 25 and 49 years of age it remains a constant complaint in women over 80 (15). In our population, urge and mixed incontinence were the main causes of leakage (54%) and pure stress urinary incontinence was moderately observed (11%). In contrast, urgency appears as the main symptom as it associates frequency and accounts for 70% (as opposed to 42.0% in the group of 748 female patients under age 80 explored during the same period in our laboratory). Urgency is a symptom related to bladder overactivity while DO is only a urodynamic diagnosis.

Acute complaint was only incomplete retention after hip or knee surgery and mainly secondary to hip arthroplasty.

Feasibility of urodynamics in the elderly has been previously demonstrated (2). An unexpected

result is the lower percentage of interpretable initial free uroflow (44%) compared with the 60.8% for the group of 748 women under the age of 80; the percentages were similar in the 2 groups for both IF and FF2. Therefore, to be reliable, FF has to be repeated, making certain that the bladder is full enough and taking into account the difficulty for some patients to void in an “unfriendly” environment.

Analysis of filling cystometry shows an increased frequency of DO in this elderly population which is consistent with previous studies (45% as opposed to 23.0% in the population less than 80 years old) but does not explain the complaint of urgency (70%). Hashim and Abrams (16) have found that 44% of women with urgency had DO; in our study 54% of the women who complained of urgency had DO, which is slightly higher. This finding could be related to the decline in central nervous system cholinergic activity occurring with normal aging (17). In addition, we observed a high prevalence of DHIC (low detrusor pressure and high residual volume - 35%). This specific association, first described by Resnick and Yalla (18), is characteristic of older patients and is a cause of urinary incontinence in the elderly. However, as this study was retrospective and as urodynamic studies are standardized in our laboratory, no provocative maneuver for DO was performed except for cough for quality control of pressure recordings.

Occurrence of RRCs confirmed the high prevalence of rhythmic rectal contractions in elderly patients (31.8% as compared to 16.5% in the population less than 80 years old). We observed a strong association between RRCs, DO and neurological disease. Despite the small group studied Ozawa et al. have reported a similar result and concluded that

RRCs may be regarded as one of the causes responsible for urinary difficulty in the elderly (19).

Maximum cystometric capacity was lower than the value reported by Pfisterer et al. (8); this difference could be the consequence of the high incidence of terminal DO in our population.

The mean MUCP value is the value expected for the age; bladder filled, the decrease of the MUCP value implies a lack of adaptation of the sphincter to bladder filling. However, approximately 50 % of the population had at least one measurement (bladder empty or filled) \leq 30 cm H₂O.

The main urodynamic diagnosis was DO found in 45 women of whom 38 had suggested LUTS (urge or mixed incontinence, frequency). The second diagnosis, in frequency, was suggested ISD found in 25 women of whom 17 had LUTS (stress or mixed incontinence). That finding is probably the consequence of the association of ISD with a major urodynamic finding such as detrusor overactivity.

Sensitivity, specificity and predictive positive value of urgency for the detection of DO, and stress or mixed incontinence for the detection of ISD are good but not sufficient enough to eliminate urodynamics, mainly to avoid inappropriate new treatment in patients with failure of previous treatment (chemical or surgical). In other patients, who have a number of complaints and who experience great discomfort in daily life, urodynamics should enable the physician to choose the less invasive and quickly effective treatment.

A limitation of our study was that the physician performing the urodynamic investigation was not the physician who originally requested urodynamics. Therefore, our findings can only be considered as advice. A prospective study would be required for a better evaluation of the role played by urodynamics in the management of LUT dysfunction in this specific elderly population.

CONCLUSION

In this population of community-dwelling of elderly females referred by their physician in our urodynamics outpatient clinic, urodynamics primarily allows to find the causes of treatment failure. How-

ever, the majority of the population complained of a decrease in their quality of life often due to LUTS which had developed over many years and asked for greater improvement.

The major complaint was incontinence, often associated with urgency which was the main symptom. The low success of FF at arrival suggests that anxiety and an "uncomfortable" environment might play a role in addition to the changes in rate of urine production with ageing. Prevalence of DO and DHIC, and occurrence of RRCs during cystometry increased compared to younger patients. DO and RRCs are frequently a concomitant finding of cystometry. A surprising result was the small group of patients for whom the proposed diagnosis was ISD alone.

CONFLICT OF INTEREST

None declared.

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STONE DISEASE

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Percutaneous nephrolithotomy for proximal ureteral calculi with severe hydronephrosis: assessment of different lithotriptors

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Purpose: We compared the efficacy and safety of percutaneous nephrolithotomy (PCNL) with different intracorporeal lithotriptors for proximal ureteral stones in patients with severe hydronephrosis.

Patients and Methods: We retrospectively analyzed the records of 192 patients with proximal ureteral calculi and severe hydronephrosis who underwent PCNL between February 2003 and December 2007. Calculi were fragmented with a pneumatic lithotripter in 44 patients (group 1), Swiss Lithoclast Master in 54 (group 2), low-power holmium:yttrium-aluminum-garnet (YAG) laser in 56 (group 3) and high-power holmium:YAG laser in 38 (group 4). Patients were assessed about 12 months postoperatively with intravenous urography and ultrasonography for late complications. Stone size, operative time, stone-free rate, and follow-up were analyzed in each group.

Results: Mean stone size for different groups were 16.2 +/- 2.8 mm, 16.6 +/- 2.1 mm, 16.0 +/- 2.7 mm, and 16.4 +/- 1.1 mm, respectively. Average operative time for different groups were 118 +/- 17 minutes, 81 +/- 10 minutes, 85 +/- 14 minutes, 110 +/- 16 minutes, respectively. Group 2 and group 3 showed superior outcomes of shorter operative time ($P = 0.000$). The overall stone-free rate was 86.5%. As stratified by lithotriptors, the stone-free rate was 81.8% in group 1, 92.9% in group 2, 88.9% in group 3, and 78.9% in group 4 ($P = 0.190$). No significant difference was found among the groups in terms of blood loss and postoperative hospital stay. Repeated PCNL or shockwave lithotripsy was necessary as an auxiliary procedure in 26 patients. The overall complication rate was 18.2%; most complications were minor and insignificant. During the follow-up, ureteral stricture developed in 10 patients and new renal stones developed in 4 patients.

Conclusions: PCNL combined with Swiss Lithoclast Master or low-power holmium:YAG laser is the preferred endourologic modality for the management of proximal ureteral calculi in patients with severe hydronephrosis.

Editorial Comment

The authors do not comment on their use of basket devices for fragment removal. They comment that one deterrent to pneumatic lithotripsy is the large fragments that are formed, requiring "time-consuming" extraction. Indeed, the absence of a nephrostomy sheath in their surgical technique suggests that active fragment extraction is not performed. As such, this may impact their findings of higher efficacy for lithotriptors that either form smaller fragments (low-energy HO:YAG) or actively extract stone fragments (ultrasonic component of the Lithoclast). The finding of a higher ureteral stricture rate with High-energy HO:YAG is an important contribution to the literature.

The authors do not report their selection of calyx for percutaneous access; one would anticipate a high percentage of upper and middle calyces to facilitate access to the proximal ureter with a rigid nephroscope. For centers selecting a lower calyceal access and the use of a flexible endoscope, the low-energy HO:YAG would come out on top.

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Fever after shockwave lithotripsy--risk factors and indications for prophylactic antimicrobial treatment

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Purpose: To identify risk factors for fever after shockwave lithotripsy (SWL) and suggest guidelines for prophylactic antimicrobial treatment.

Patients and Methods: Between 1985 and 2007, a total of 15,324 SWL procedures were performed in our institution using the Dornier HM3 lithotripter. Because stone analyses were not available in the majority of patients, management of stones larger than 2 cm in diameter were excluded from this analysis to minimize the ratio of struvite stones as a possible cause for postprocedural fever. In this analysis, 11,500 SWL treatments were included. Clinical parameters before, during, and after treatments were prospectively registered using a computerized database. Potential risk factors for fever after SWL were evaluated.

Results: Fever >38.0 degrees C developed in 161 (1.4%) patients. The risk factors for fever after SWL were: A positive urine culture ($P < 0.05$), an indwelling nephrostomy tube or stent during the procedure ($P < 0.001$), lithotripsy of kidney or upper ureteral stones ($P < 0.05$) and preoperative symptomatic urinary tract infection (UTI) ($P < 0.05$) or sepsis ($P < 0.05$). Lithotripsy of mid and lower ureteral stones, stone size, and the use of ureteral catheters during the procedures were not associated with increased risk of fever after SWL.

Conclusions: Fever (>38.0 degrees C) develops in only 1.4% of the patients undergoing SWL. Therefore, prophylactic antibiotic treatment is not indicated in all patients. Selective prophylactic treatment is recommended in patients who present with UTI, kidney or upper ureteral stones, and those for whom a nephrostomy tube or stent is necessary.

Editorial Comment

At first glance, this paper suggests that the AUA statement regarding prophylactic antibiotics at the time of shockwave lithotripsy deserves further scrutiny. However, the great majority of stones treated with SWL in the United States are renal and proximal ureteral stones; which this study confirms may benefit from preoperative antibiotic prophylaxis. As ureteroscopic approaches to ureteral stones have been demonstrated to be more efficacious and more cost-effective, the use of SWL in this subset of patients would be less common.

The AUA statement for prophylaxis is based on Level 1a evidence - a meta-analysis of eight randomized prospective controlled trials. The current study suggests that routine antibiotics need not be used for mid-ureteral and distal ureteral stones that do not have an indwelling ureteral stent or nephrostomy tube. As this select group likely represents a very small portion of patients treated with SWL, for practical purposes, routine prophylaxis remains warranted!

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ENDOUROLOGY & LAPAROSCOPY

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Initial experience with 50 laparoendoscopic single site surgeries using a homemade, single port device at a single center

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Purpose: We report our technique of and initial experience with 50 patients who underwent laparoendoscopic single site surgery using a homemade single port device at a single institution.

Materials and Methods: Between December 2008 and August 2009 we performed 50 laparoendoscopic single site surgeries using the Alexis wound retractor, which was inserted at the umbilical incision. A homemade single port device was made by fixing a size 7 1/2 surgical glove to the retractor outer ring and securing the glove fingers to the end of 3 or 4 trocars with a tie and a rubber band. A prospective study was performed in 50 patients to evaluate outcomes.

Results: Of 50 patients 34 underwent conventional laparoendoscopic single site surgery, including radical and simple nephrectomy, and cyst decortication in 8 each, nephroureterectomy in 3, partial nephrectomy and adrenalectomy in 2 each, and partial cystectomy, ureterectomy and ureterolithotomy in 1 each, while 16 underwent robotic laparoendoscopic single site surgery, including partial nephrectomy in 11, nephroureterectomy in 3, and simple and radical nephrectomy in 1 each. Mean patient age was 52 years, mean body mass index was 23.4 kg/m², mean operative time was 201 minutes and mean estimated blood loss was 201 ml. Four intraoperative complications occurred, including 2 bowel serosal tears, diaphragm partial tearing and conversion to open radical nephrectomy. One case of postoperative bleeding was managed by transfusion. Surgical margins were negative in the 13 patients who underwent partial nephrectomy. Mean hospital stay was 4.5 days (range 1 to 16).

Conclusions: Our homemade single port device is cost-effective, provides adequate range of motion and is more flexible in port placement for laparoendoscopic single site surgery than the current multichannel port.

Editorial Comment

After the first laparoscopic nephrectomy performed many years ago, laparoscopic urological surgery has evolved. Recently, laparoendoscopic single site surgery has been developed allowing experienced surgeons to investigate new applications and feasibility of a new minimally invasive surgical approach. The clinical advantages are not clear yet and the platforms and instruments are not optimally developed. One of the major challenges is the entry portal that could allow the utilization of a small incision to permit all different laparoscopic maneuvers, as well as the insertion of robotic and/or laparoscopic instrumentation. The authors of this report should be congratulated for the creativity and high level of minimally surgery understanding for developing an easy access device with everyday use components (surgical gloves and laparoscopic ports). This idea may allow industry to mature this initial idea to an effective device.

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Experience with 750 consecutive laparoscopic donor nephrectomies--is it time to use a standardized classification of complications?

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Purpose: Laparoscopic living donor nephrectomy offers patients the benefits of decreased morbidity and improved cosmesis, while maintaining equivalent graft outcomes and complication rates similar to those of open donor surgery. With expressed concern for donor safety, using a standardized complication scale would allow combining data in a donor registry so potential donors could be adequately followed and counseled. We present the largest series to our knowledge of laparoscopic living donor nephrectomy by a single surgeon.

Materials and Methods: The institution's initial 750 laparoscopic living donor nephrectomies were included in the study, and a retrospective and prospective chart and database analysis was performed.

Results: Mean donor age was 40.5 years and average body mass index was 25.7 kg/m². There were 175 patients (23%) with 2 or more renal arteries while 161 (21.5%) had early arterial bifurcations. There were 3 open conversions (0.4%) and the overall complication rate was 5.46%. Median hospital stay was 1 day and the readmission rate was 1.2%. There were 5 reoperations (0.67%), none of which was for the control of bleeding. No patients required a blood transfusion and there were no mortalities. Using a modified Clavien classification of complications for living donor nephrectomy 65.8% were grade 1, 31.7% grade 2 (12.2% grade 2a, 14.6% grade 2b, 4.9% grade 2c) and 2.4% grade 3. There were no grade 4 complications.

Conclusions: With appropriate patient selection and operative experience, laparoscopic living donor nephrectomy is a safe procedure associated with low morbidity. The use of a standardized complication system specific for this procedure is encouraged and could aid in counseling potential donors in the future.

Editorial Comment

After the first Laparoscopic living donor nephrectomy by Kavoussi et al., many institutions have adopted this surgical technique worldwide due to the many advantages offered by it, such as, improved postoperative recovery and shorter convalescence with no effect on recipient renal function.

Live donor renal transplantation has many advantages including greater graft and patient survival, shorter waiting periods, improved HLA matching, and less cold ischemia. However, until recently disincentives from the operation such as prolonged hospitalization, postoperative pain, and significant convalescence have deterred live donor renal transplantation. The authors demonstrated a vast experience of 750 laparoscopic living donor nephrectomies with only 3 open conversions (0.4%) and the overall complication rate of 5.46%. A short hospital stay and low readmission rate. Using a modified Clavien classification of complications for living donor nephrectomy 65.8% were grade 1, 31.7% grade 2 (12.2% grade 2a, 14.6% grade 2b, 4.9% grade 2c) and 2.4% grade 3. There were no grade 4 complications. The data demonstrate the feasibility of an established technique with great outcome.

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IMAGING

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Utility of diffusion-weighted MRI in characterization of adrenal lesions

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Objective: The purpose of our study was to evaluate the utility of apparent diffusion coefficient (ADC) values for characterizing adrenal lesions and determine if diffusion-weighted imaging (DWI) can distinguish lipid-rich from lipid-poor adenomas.

Materials and Methods: We retrospectively evaluated 160 adrenal lesions in 156 patients (96 women and 60 men; mean age, 63 years). ADCs and signal intensity (SI) decrease on chemical shift imaging were measured in adrenal lesions with a wide variety of pathologies. Lipid-rich and lipid-poor adenomas were identified by unenhanced CT. The overall predictive power of ADC, SI decrease, and lesion size were determined by receiver operating characteristic (ROC) analysis. Areas under the ROC curve (AUC) were compared for equivalence using nonparametric methods. Sensitivity, specificity, and positive and negative predictive values were calculated. Correlation coefficients were used to assess ADCs versus percentage SI decrease and ADCs versus CT attenuation.

Results: ADCs of adrenal malignancies (median, 1.67×10^{-3} mm²/s; interquartile range, 1.41 - 1.84×10^{-3} mm²/s) were not different compared with those of benign lesions (1.61×10^{-3} mm²/s; 1.27 - 1.96×10^{-3} mm²/s; $p > 0.05$). Cysts (2.93×10^{-3} mm²/s; 2.70 - 3.09×10^{-3} mm²/s) showed higher ADCs than the remaining adrenal lesions ($p < 0.05$). The median ADCs of lipid-rich adenomas did not differ from those of lipid-poor ones ($p > 0.05$). The CT attenuation had no negative or positive correlation with the ADCs of adrenal adenomas ($r = -0.05$, $p = 0.97$).

Conclusion: Unlike lesion size and percentage decrease in SI, the ADCs were not useful in distinguishing benign from malignant adrenal lesions. Lipid-poor adenomas could not be distinguished from lipid-rich adenomas and all other nonfatty lesions of the adrenal gland with DWI.

Editorial Comment

Diffusion-Weighted MRI (DWI), is a technique used to detect the state of molecular translational motion of water in the tissue. In some tumors, densely packed malignant cells, causes restricted diffusion of water relative to that of normal tissue. DWI is quantified by the apparent diffusion coefficient map-ADC. Since apparent diffusion coefficient (ADC) reflects primarily diffusion coefficient of extra-cellular water, ADC values tend to be lower for tumors compared to normal tissue. Contrary to cancer, in benign lesions, extra-cellular space volume is higher, thus ADC values are higher as well. For this reason, DWI is an important complementary tool in the evaluation of pathologic conditions in the abdomen and is increasingly used in routine imaging. The authors of this study showed that lipid-poor adenomas could not be distinguished from lipid-rich adenomas and all other non-fatty lesions of the adrenal gland with DWI. They showed that ADCs were not useful in distinguishing benign from malignant adrenal lesions. Similarly recent report has been shown that this technique has also limitation in other abdominal organs since a lesion with restricted diffusion was found to be benign in about 22% of the lesions (1). Fortunately, radiological characterization of an adrenal incidentaloma can be done with high sensitivity and specificity using well established techniques such, CT attenuation without contrast enhancement, wash-out CT technique and chemical-shift MR imaging. Thus, further evaluation with diffusion-weighted MRI is not essential.

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Split-bolus MDCT urography: Upper tract opacification and performance for upper tract tumors in patients with hematuria

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Objective: Our purpose was to assess upper urinary tract opacification and the performance of split-bolus MDCT urography for upper tract tumors in patients with hematuria.

Materials and Methods: Between January 2004 and December 2006, we identified 200 patients (119 men, 81 women; median age, 58 years, age range, 18-89 years) who underwent MDCT urography for hematuria. MDCT urography included unenhanced and combined nephrographic and excretory phase imaging of the urinary tract. Images were independently reviewed by two radiologists blinded to the final diagnosis. The degree of upper urinary tract opacification and the diagnosis were recorded. Prospective interpretations were also reviewed. The standard of reference included all available clinical, imaging, and laboratory data for up to 12 months after MDCT urography. Sensitivity, specificity, accuracy, and positive and negative predictive values were calculated for upper tract tumors for prospective and retrospective interpretations.

Results: For reviewers 1 and 2, 85.1% and 84.5% of segments were at least 50% opacified, respectively. Final diagnoses for hematuria were no cause, 123 (61.5%); urothelial cancer, 27 (13.5%); nonmalignant, 46 (23%) and indeterminate, four patients (2%). There were nine upper tract cancers. Sensitivity, specificity, and accuracy for upper tract cancers for prospective interpretation, reviewer 1 and reviewer 2, were 100%, 99%, 99%; 100%, 99.5%, 99.5%; and 88.9%, 99.0%, 98.5%, respectively.

Conclusion: Split-bolus MDCT urography provided at least 50% opacification of the majority of upper urinary tract segments and had high sensitivity, specificity, and accuracy for the detection of upper urinary tract tumors.

Editorial Comment

Multidetector CT-urography (MDCT-urography) has been shown to be an effective single comprehensive examination in the evaluation of patients with hematuria or with risk for the development of urothelial malignancies. Since protocols for MDCT urography varies from each institution, most MDCT-urography images are obtained in the unenhanced phase (detection of calculi), nephrographic-phase (detection of renal masses) and excretory-phase (detection of urothelial lesions). The authors present their results with a protocol called split-bolus MDCT- urography where the unenhanced phase is followed only by a combined nephrographic and excretory phase. During split-bolus, CT-urography the intravenous injection of contrast material is performed in two steps. First, 40 ml is injected at 2 ml/s and after 120 second from the beginning of the first injection, the

remaining 80 ml is injected. According the authors in patients with hematuria, split-bolus MDCT- urography and oral hydration provide complete opacification of the majority of upper urinary tract segments and are accurate for the diagnosis of upper tract urothelial tumors. Since the main objective of MDCT-urography is to detect all possible causes of hematuria, this study has some limitations. The authors did not include an analysis of the capability of split-bolus technique for the detection of urinary calculi, renal parenchymal tumor and bladder cancers. As we know small bladder cancer can be missed if only excretory phase of the full bladder is obtained.

Another issue that could be addressed is how the renal parenchymal masses can be adequately characterized by the combined nephrographic /excretory phase obtained with split-bolus technique. Classically, renal masses are best characterized by the combination of findings obtained without intravenous contrast enhancement, scans obtained in nephrographic phase (70-90") and scans obtained in the excretory phase. In our opinion split bolus MDCT- urography may be useful for follow up patients with higher risk of develop upper tract urothelial cancer, particularly those already evaluated with cystoscopy. These patients should benefit with the use of this examination, which has high accuracy for the detection of urothelial cancer and uses low dose of radiation.

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PATHOLOGY

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Should pathologists continue to use the current pT2 substaging system for reporting of radical prostatectomy specimens?

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Background: During the International Society of Urological Pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens, 65.5% of the attendants answered that the current pT2 substaging system should not be used. Answering to another question, 63.4% favored to be reduced to two categories based on studies showing that pT2b does not exist. There was no consensus in regard to a minimum size for a second tumor to be considered for the whole case to be classified as pT2c as well as in regard to the definition of index tumor. We compared clinicopathologic findings and biochemical progression following surgery classifying pT2 patients into two categories.

Design: The study was based on whole-mount consecutive surgical specimens from 142 patients with organ confined cancer. Using a semiquantitative method for evaluation of tumor extent, 10 positive points corresponds roughly to a 0.5ml tumor. We considered pT2a/pT2b substage (group 1) whenever a tumor presented > 10 positive points on only one side and pT2c whenever presented > 10 positive points on each of right and left side (group 2). The variables analyzed were: age, preoperative PSA, clinical stage, Gleason score on needle biopsy, and biochemical progression following surgery defined as PSA > 0.2ng/mL. The data were analyzed using

the Mann-Whitney test, and the Kaplan-Meier product-limit analysis using the log-rank test for comparison between the groups. Results: Substage pT2a/pT2b corresponded to 84/142 (59.2%) patients and substage pT2c to 58/142 (40.8%) patients. There was no statistically significant difference between the groups in relation to: age ($p = 0.30$), preoperative PSA ($p = 0.13$), clinical stage ($p = 0.34$), and Gleason score on needle biopsy ($p = 0.27$). In 5 years of follow-up, 61% of patients pT2a/pT2b and 71% of patients pT2c were free of biochemical progression (log-rank, $p = 0.68$).

Conclusions: There was no significant difference for several clinicopathological variables and time of biochemical progression following surgery between patients with stage pT2a/pT2b and patients with stage pT2c. The results of this study favor to discontinue using the current pT2 substaging system for reporting of radical prostatectomy specimens.

Editorial Comment

In 1997, the TNM staging of T2 prostate cancers was divided into T2a (unilateral tumor) and T2b (bilateral tumor). In 2002 and now in 2010, T2 stage was substaged as in 1992, i.e., into 3 groups: T2a (unilateral tumor, less than half lobe), T2b (unilateral tumor, more than half lobe), and T2c (bilateral tumor). The clinical staging of T2 prostate cancers gives a good prognostic information. Time of biochemical (PSA) recurrence shows significant difference among the 3 groups. The clinical staging is a reflection of the detection methods employed and the substaging of clinical stage T2 prostate cancers is largely based on the extent of the abnormality palpated during a digital rectal examination (DRE) or shown during transrectal ultrasonography (TRUS) in each half of the prostate.

In a Consensus Meeting held during the United States and Canadian Academy of Pathology meeting in Boston 2009, 65.5% of the uropathologists present answered that the current pathologic T2 substaging should not be continued. Why the pathologic T2 substaging should be discontinued?

In contrast to clinical substaging of T2 cancers, pathological substaging does not convey prognostic information. This happens because prostate cancer is essentially a multifocal tumor. In general, there is a larger tumor (index tumor) but almost always, other foci scattered along the gland. Therefore, a large unilateral tumor palpated by the urologist (cT2b) is always bilateral in the surgical specimen (pT2c) (1-3). It has been argued that the prognostic significance of clinical substaging by DRE and TRUS of T2 cancers is a direct effect of understaging (4). The paper surveyed was a platform presentation at the 99th Annual Meeting of the United States and Canadian Academy of Pathology held in Washington DC, 2010, and is supported by several other previous studies (5-8). The conclusions included no significant difference for several clinicopathological variables and time of biochemical progression following surgery between patients with pathologic stage T2a/pT2b and patients with pathologic stage T2c. The results of the study favor to discontinue using the current pathologic T2 substaging system for reporting of radical prostatectomy specimens.

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Radical prostatectomy (RP) findings in cases with only intraductal carcinoma of the prostate (IDC-P) on needle biopsy

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Background: When IDC-P is present on biopsy, it is usually seen with infiltrating acinar adenocarcinoma. In 2006, we reported 27 cases with IDC-P only on biopsy; however, only 6 cases had available RP findings.

Design: 82 men with IDC-P only on prostate biopsy were identified from the consult files of one of the authors. Follow-up information was available in 66 cases. 20 men were treated with RP, 17 radiation therapy (RT), 8 hormone therapy (HT), 13 RT and HT, 6 active surveillance, and 2 rebiopsy. An attempt was made to retrieve the slides of all 20 RP cases.

Results: Of the 20 RP cases, 5 showed extraprostatic extension, 3 seminal vesicle invasion, 10 were organ-confined, and 2 showed extensive IDC-P only without identifiable invasive cancer. Of the 18 cases with invasive cancer, the average Gleason score (GS) was 7.8. 1 patient developed bone metastases 3 years post-RP, and 3 others were post-RP PSA failures. 13 RPs were available for our review. 9 showed extensive IDC-P (including one case of IDC-P only), defined as > 10% of the tumor volume being intraductal; 3 focal IDC-P; and 1 no IDC-P. All cases with invasive carcinoma were acinar, although 3 cases were classified as ductal by referring pathologists. We concurred with the outside GS in 5/13 cases (5 undergraded, 3 overgraded). In the 3 cases that we gave lower GS, the outside institution graded cribriform IDC-P with and without necrosis as Gleason pattern 5 or 4, respectively.

Conclusions: Our study, the largest to date with RP findings following IDC-P only on needle biopsy, confirms that aggressive therapy is appropriate for patients whose biopsies show only IDC-P. It is likely that the pathological findings are even worse than we report herein, as most RPs were only partially sampled. Most cases likely represent intraductal spread of high grade cancer, but some cases represent in situ acinar adenocarcinoma.

Editorial Comment

Intraductal carcinoma of the prostate (IDC-P) is defined as presence of atypical cells that span the entire lumen of prostatic ducts or acini while the normal architecture of ducts or acini is still maintained including presence of basal cells (1,2). With presence of IDC-P on a biopsy, the pathologist considers 4 possibilities: 1)

ductal carcinoma; 2) high-grade intraepithelial neoplasia (HGPIN); 3) intraductal carcinoma; and, 4) intraductal spread of an invasive carcinoma.

Ductal carcinoma may be ruled out because of the presence of basal cells; in cases of irregularity and distortion of the ducts, HGPIN may also be ruled out; and, in presence of an invasive carcinoma, intraductal spread is most probable and the finding adds no additional information to the report. The problem is related to cases that IDC-P is the only finding on a biopsy.

The Johns Hopkins group studied 20 radical prostatectomy specimens of patients who presented on biopsy only the diagnosis of IDC-P. Two out of twenty patients showed extensive IDC-P only, without identifiable invasive cancer. IDC-P in these 2 patients may represent: 1. an early phase of ductal or acinar carcinoma; or 2. intraductal spread of an invasive not detected tumor.

According to the authors, IDC-P as the only finding on needle biopsy corresponds to almost always to aggressive tumors and the patients may have definitive treatment. A more conservative approach would be an extended rebiopsy in order to detect a possible invasive cancer.

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BASIC AND TRANSLATIONAL UROLOGY

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Potential mechanism of action of human growth hormone on isolated human penile erectile tissue

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Urology. 2010; 75: 968-73

Objectives: To evaluate the mechanisms of growth hormone (GH) action on isolated human penile erectile tissue. Human GH (hGH) has been suggested to play a role in male reproductive function, including penile erection. Nevertheless, it still remains unclear which intracellular pathways mediate the physiological effects of GH on the human corpus cavernosum (HCC).

Methods: Using the organ bath technique, the effects of GH were investigated on electrical field stimulation (EFS)-induced relaxation of isolated HCC in the absence and presence of the guanylyl cyclase inhibitor 1H-

[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ) and nitric oxide synthase (NOS) inhibitor N(G)-nitro-L-arginine (L-NOARG, 10 microm). Effects of GH on the production of tissue cyclic guanosine monophosphate (cGMP) in the absence and presence of ODQ and L-NOARG were also elucidated using radioimmunoassay.

Results: ODQ and L-NOARG abolished the relaxation of the tissue induced by EFS, whereas amplitudes were increased by physiological concentrations of GH (1-100 nm). The attenuation of EFS-induced amplitudes by L-NOARG but not ODQ was, in part, reversed by GH. The production of cGMP (pmol cGMP/mg protein) induced by 10 nm GH was abolished in the presence of 10 microm ODQ. In contrast, the combination of GH (10 nm) and L-NOARG (10 microm) maintained cGMP production significantly greater than baseline (0.68 +/- 0.36 vs 1.07 +/- 0.48 pmol cGMP/mg protein).

Conclusions: Our data provide evidence that GH may act on human HCC by an NO-independent effect on guanylyl cyclase activity and may thus explain how growth factors, such as hGH, regulate male erectile function. Copyright 2010 Elsevier Inc. All rights reserved.

Editorial Comment

This group of investigators has been studying the effects of growth hormone for more than 10 years. They have demonstrated previously that growth hormone likely mediates penile erection through its stimulating effect on the cGMP pathway in human cavernous smooth muscle. Later, they compared the in vivo serum profiles of growth hormone in the systemic and cavernous blood samples obtained from healthy volunteers were compared to the serum profiles of patients with erectile dysfunction. In the healthy subjects, systemic growth hormone serum levels significantly increased during penile tumescence, followed by a transient decline from tumescence to rigidity and detumescence. During penile tumescence, the mean increase in the growth hormone levels in the systemic and cavernous blood of patients with organogenic dysfunction, this increase was found to be negligible.

In the present study they found evidence that growth hormone may act on human corpus cavernosum by an effect independent of nitric oxide on guanylyl cyclase activity. The group has to be commended for the important contribution they have been providing during the last years to elucidation of growth hormone activity in human erection

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Atorvastatin protects renal function in the rat with acute unilateral ureteral obstruction

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Objectives: To examine the effects of atorvastatin on renal hemodynamics and urinary microalbumin levels in rats with acute unilateral ureteral obstruction (UUO). Previous studies have demonstrated that treatment with statins attenuated renal structural damages in rodents with chronic UUO. However, it is not known whether statins afford protection of renal function.

Methods: UUO was created by ligation of the left ureter in rats maintained on a regular diet or the same diet but supplemented with atorvastatin (50 mg/kg/d) for 2 weeks. Renal clearance experiments were performed after release of UUO at 1 hour, 6 hours, or 12 hours.

Results: Atorvastatin treatment lowered plasma triglyceride but not cholesterol levels. Both glomerular filtration rate and effective renal plasma flow were significantly greater in atorvastatin-treated rats after release of UUO at 1 hour, 6 hours, and 12 hours. Significant reduction of urinary microalbumin to creatinine ratios occurred in the atorvastatin-treated group at 12 hours but not earlier.

Conclusions: Atorvastatin treatment affords protection of renal function in acute UUO and reduces urinary microalbumin levels without lowering cholesterol levels. This pleiotropic action of atorvastatin on preservation of renal hemodynamics may be important in attenuating subsequent renal structural injury in chronic UUO.

Editorial Comment

Previous studies examined molecular markers of fibrosis and histologic changes in chronically obstructed kidney. This is the first research that analyzed the effects of statins (atorvastatin) on renal hemodynamics of kidneys with ureter acutely obstructed unilaterally. The present investigation showed by the first time that treatment with atorvastatin in rats with acute unilateral ureteral obstruction resulted in improvement in renal perfusion and filtration function.

The authors emphasized that these findings raise the possibility that some of the benefits of statins in the clinical trials may originate from the pleiotropic effects of statins and not specifically from the lipid-lowering effect alone. Also, it is worth to note that the dose of statin used in the present study is proportionally much higher than the doses current used in clinical practice. The authors also remembered that other studies also used supra-pharmacological doses of statins to demonstrate attenuation of tubulo-interstitial inflammation and fibrosis in rats with unilateral ureteral obstruction. Therefore, the dosage of statins required to exert their pleiotropic actions is still unknown and remains to be determined. Anyway, the present study shown that treatment with a statin in rats with acute unilateral ureteral obstruction, resulted in improvement in renal perfusion and filtration function. This open new avenue for renal protective agents.

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RECONSTRUCTIVE UROLOGY

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Management of radiotherapy induced rectourethral fistula

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Purpose: An increasing number of men are being treated with BT or a combination of external beam radiation therapy and BT for localized prostate cancer. Although uncommon, the most severe complication following

these procedures is RUF. We reviewed our recent experience with RUF following radiotherapy for prostate cancer to clarify treatment in these patients.

Materials and Methods: We recently treated 22 men with RUF following primary radiotherapy for adenocarcinoma of the prostate in 21 and adjuvant external beam radiation therapy following radical prostatectomy in 1. Time from the last radiation treatment to fistula presentation was 6 months to 20 years.

Results: Four patients underwent proctectomy with permanent fecal and urinary diversion. RUF repair in 5 patients was performed with preservation of fecal or urinary function. Six patients were candidates for reconstruction with preservation of urinary and rectal function, including 5 who underwent proctectomy, staged colo-anal pull-through and BMG repair of the urethral defect. The additional patient underwent primary closure of the rectum, BMG repair of the urethra and gracilis muscle interposition. Successful fistula closure was achieved in the 9 patients who underwent urethral reconstruction. All 8 candidates for rectal reconstruction showed radiological and clinical bowel integrity postoperatively with 2 awaiting final diverting stoma closure.

Conclusions: With the increasing use of prostate BT the number of patients with severe rectal injury will likely continue to increase. Radiotherapy induced RUF carries significant morbidity and most patients are treated initially with fecal and urinary diversion. In properly selected patients good outcomes can be expected following repair using BMG for the urethral defect along with colo-anal pull-through or primary rectal repair and gracilis muscle interposition.

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Incidence, clinical symptoms and management of rectourethral fistulas after radical prostatectomy

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Purpose: Rectourethral fistula is a rare but severe complication after radical prostatectomy and there is no standardized treatment. We retrospectively evaluated the incidence, symptoms and management of rectourethral fistulas based on our experience. **Materials and Methods:** From 1999 to 2008 we performed 2,447 radical prostatectomies. Patients in whom postoperative rectourethral fistulas developed were identified. Based on the therapeutic approach patients were categorized into group 1-conservative treatment, group 2-colostomy with or without surgical closure and group 3-immediate surgical closure without colostomy.

Results: Rectourethral fistulas developed in 13 of 2,447 patients (0.53%) after radical prostatectomy. The risk of rectourethral fistulas was 3.06-fold higher ($p = 0.074$) for perineal (7 of 675, 1.04%) than for retropubic prostatectomy (6 of 1,772, 0.34%). In 7 of 13 patients (54%) a rectal lesion was primarily closed at radical prostatectomy. Median followup was 59 months. In all patients in group 1 (3) the fistula closed spontaneously with conservative treatment. None of these patients had fecaluria. In group 2 of the 9 patients 3 (33%) experienced spontaneous fistula closure after temporary colostomy and transurethral catheterization. In this group 6 patients (67%) required additional surgical fistula closure, which was successful in all. Surgical fistula closure (1) without colostomy in presence of fecaluria failed (group 3).

Conclusions: The therapeutic concept for rectourethral fistulas should be guided by clinical symptoms. Rectal injury during radical prostatectomy is a major risk factor. In cases with fecaluria colostomy is required for control of infection and may allow spontaneous fistula closure in approximately a third of cases. In the remainder of cases surgical fistula closure was successful in all after protective colostomy.

Editorial Comment

These two single institution case series review management and outcome of rectourethral fistula repair in two vastly different patient groups: surgery vs. radiation. It is well accepted that rectourethral fistula repair

is made more difficult by prior radiotherapy. Another difference between the two groups is that the post-radical prostatectomy patients were primarily managed by the authors whereas in post-radiation patients were referred for management after a failed period of conservative management.

In the radical prostatectomy series by Thomas et al., nearly half of the fistulas closed spontaneously, a few even without a colostomy. Importantly, the authors note that the absence of fecaluria was a good indicator of a fistula that would close spontaneously: 4 of 8 closed spontaneously in the absence of fecaluria (3 without a colostomy) but only 1 of 5 with fecaluria. Spontaneous closure occurred after 1-3 months of urethral catheterization. All fistula repairs were accomplished transperineally.

The radiation series is quite different. No fistulas closed spontaneously. Fistulas were much larger, ranging in size up to 7 cm. Patients presented with severe problems secondary to the fistula such as sepsis and Fournier's gangrene. Only 6/22 could be repaired with preserved orthotopic fecal and urinary function; the remainder had one or both streams diverted with an ostomy. Perioperative morbidity was likewise much higher in those undergoing fistula repair after radiation.

Rectourethral or rectovesical fistula is a rare but morbid complication of surgery or radiation for prostate cancer. These series highlight the fact that with appropriate expertise good outcomes can be achieved in those who have not been previously radiated however

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UROLOGICAL ONCOLOGY

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Characteristics and outcomes of patients with clinical T1 grade 3 urothelial carcinoma treated with radical cystectomy: results from an international cohort

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Eur Urol. 2010; 57: 300-9

Background: Management of T1 grade 3 (T1G3) urothelial carcinoma of the bladder (UCB), with its variable behaviour, represents one of the most difficult challenges for urologists and patients alike.

Objective: To evaluate the characteristics and long-term outcome of patients with clinical T1G3 UCB treated with radical cystectomy (RC).

Design, Setting, and Participants: Data from 1136 patients treated with RC for clinical T1G3 UCB without neoadjuvant chemotherapy were collected at 12 centres located in Europe, the United States, and Canada. Median age was 67 yr (range: 29-94), with a male-to-female ratio of 4:1.

Measurements: Patients' characteristics and outcome are evaluated.

Results and Limitations: Of the 1136 patients, 33.4% had non-organ-confined stage at cystectomy, and 16.2% had lymph node (LN) metastasis; 49.7% were upstaged after RC to muscle-invasive disease, while 21.4% were

downstaged to lower than T1G3. Within a median follow-up of 48 mo, 35.5% of patients died of metastatic UCB.

Conclusions: Approximately half of the patients treated with RC without neoadjuvant chemotherapy for clinical T1G3 UCB are upstaged to muscle-invasive UCB. These rates support the inadequacy of clinical decision making based on current treatment paradigms and staging tools. Therefore, identification of patients with clinical T1G3 disease at high risk of disease progression is of the utmost importance, as these patients are likely to benefit from early RC.

Editorial Comment

The optimal primary treatment of stage and grade T1G3 bladder cancer, radical or conservative, is a matter of debate since years. Here, 12 international centers with a large experience in radical cystectomies present their data on this aggressive “borderline” tumor. They found a high rate of nearly 50% of tumor upstaging to muscle invasive disease.

Alas, this study suffers from several drawbacks. No indication on previous intravesical therapy, or on the time between first diagnosis of bladder cancer and cystectomy are given. These data would have made it much easier to judge on the delay as reason for the high rate of upstaging and to get information on the proportion of “true aggressive” T1G3 tumors which would indeed need immediate cystectomy without an initial trial of TUR, re-TUR and BCG.

All in all, these data reflect the aggressive nature of T1G3 bladder cancer and the need for stringent management, be it conservative or radical.

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Should all patients with non-muscle-invasive bladder cancer receive early intravesical chemotherapy after transurethral resection? The results of a prospective randomised multicentre study

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Eur Urol. 2009; 55: 773-80

Background: To decrease recurrences in non-muscle-invasive bladder cancer (NMIBC), the European Association of Urology (EAU) guidelines recommend immediate, intravesical chemotherapy after transurethral resection (TUR) for all patients with Ta/T1 tumours.

Objective: To study the benefits of a single, early, intravesical instillation of epirubicin after TUR in patients with low- to intermediate-risk NMIBC.

Design, Setting, and Participants: In this prospective randomised multicentre trial, 305 patients with primary as well as recurrent low- to intermediate-risk (Ta/T1, G1/G2) tumours were enrolled between 1997 and 2004. Patients were randomly allocated to receive 80 mg of epirubicin in 50 ml of saline intravesically within 24 h of TUR or no further treatment after TUR.

Measurements: The primary end point was time to first recurrence.

Results and Limitations: A total of 219 patients remained for analysis after exclusions. The median follow-up time was 3.9 yr. During the study period, 62% (63 of 102) of the patients in the epirubicin group and 77% (90 of 117) in the control group experienced recurrence ($p=0.016$). In a multivariate model, the hazard ratio (HR) for recurrence was 0.56 ($p=0.002$) for early instillation of epirubicin versus no treatment. In a subgroup analysis, the treatment had a profound recurrence-reducing effect on patients with primary, solitary tumours, whereas it provided no benefits in patients with recurrent or multiple tumours. Furthermore, patients with a modified European Organisation for Research and Treatment of Cancer (EORTC) risk score of 0-2 with and without single instillation had recurrence rates of 41% and 69%, respectively ($p=0.003$), whereas the corresponding rates for those with a risk score of ≥ 3 were 81% and 85%, respectively ($p=0.35$).

Conclusions: A single, early instillation of epirubicin after TUR for NMIBC reduces the likelihood of tumour recurrence; however, the benefit seems to be minimal in patients at intermediate or high risk of recurrence. Future trials will determine the value of early instillation in addition to serial instillations in NMIBC.

Editorial Comment

Bladder cancer has a high rate of recurrence. Two pathways are considered responsible for this behavior, namely genetically instable urothelium resulting in truly new tumor formation, and re-implantation (seeding) of tumor cells resulting in new occurrences from the previous tumor. The best way to date to interfere with the second pathway, seeding of tumor cells, is immediate post-TUR single shot instillation of cytotoxic drugs. However, is this sufficient therapy for all tumors? The authors answer this important question in their randomized study. First, they show that single-shot instillation (in this study given within 24 hours, but best within 6 hours after TUR) indeed is highly effective, resulting in a significant overall reduction of recurrences. This effect was pronounced in the low risk group with single primary tumors, whereas barely evident in the intermediate risk group or that with multiple tumors. The numbers needed to treat (NNT) was 3.5, which supports similar figures from previous calculations.

The authors state correctly that single-shot treatment has little or no impact on genetically instable urothelium. Therefore, next to single – shot instillation therapy, all intermediate to high-risk group patients with bladder cancer deserve more instillation therapy, be it regular courses of cytostatics or BCG.

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NEUROLOGY & FEMALE UROLOGY

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Regular moderate intake of red wine is linked to a better women's sexual health

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Introduction: While some evidence does exist for a positive correlation between moderate wine intake and men's sexual health, there is no study addressing the potential correlation between red wine intake and women's sexual function.

Aim: The aim of our study was to assess whether there is a tie between daily red wine intake and sexual function in a sample of healthy Italian women, living in the Chianti area (Tuscany) not complaining of any sexual disorders.

Methods: We recruited 798 women (age 18-50), living in the Chianti area (Tuscany), not complaining of any sexual disorders. We divided the participants into three groups: daily moderate (one to two glasses) red wine intake (group 1); teetotallers (group 2); and daily intake of more than two glasses of red wine and/or other types of alcoholic drinks (including white wine), as well as of those reporting occasional drinking (group 3).

Main outcome measures: All participants completed anonymously the Female Sexual Function Index (FSFI) questionnaire and were asked to report on their amount and type of alcohol consumption.

Results: Group 1 had significantly higher total ($P = 0.001$), as well as desire and lubrication domain ($P = 0.001$ and $P = 0.001$, respectively) FSFI scores than participants in groups 2 and 3. No significant differences between the groups were observed concerning sexual arousal, satisfaction, pain, and orgasm. Univariate analysis showed a significant correlation between age, alcohol consumption ($P = 0.009$), and a better score at questionnaire examination. During multivariate analysis, alcohol consumption was identified as an independent prognostic parameter ($P = 0.002$) in predicting the better score at questionnaire examination.

Conclusions: The finding that regular moderate intake of red wine is associated with higher FSFI scores for both sexual desire, lubrication, and overall sexual function as compared to the teetotaller status is intriguing. While this finding needs to be interpreted with some caution, because of the small sample size, self-reported data, and the lack of support from laboratory exams, it nevertheless suggests a potential relationship between red wine consumption and better sexuality.

Editorial Comment

A fascinating paper that examines the effect of wine on women's sexual health. The authors reviewed a population of females that was subdivided into three groups with the first group being women who drank 1-2 glasses of wine daily; the second group that did not intake alcohol; and the third group being occasional drinkers, reporting less than 1 glass per day. Women who drank more than 2 glasses of red wine or 2 glasses or more of other types of alcoholic drinks including white wine were excluded from the study. The authors limited their population to women who were very sexually normal based on responding affirmative to "are you happy with your sexuality?" and responding no to the question "have you ever had a sexual problem?". Any woman who was pregnant, lactating, used supplemental hormones as well as had any kind of previous genitourinary surgery or substance abuse were excluded from the study. The primary metric of the assessment was the Female Sexual Function Index (FSFI). The authors found that the moderate alcohol drinkers of red wine (2 glasses a day) had an overall higher score on the FSFI as well as increased responses in the desire and lubrication domain. There was no difference between the groups with regards to arousal, satisfaction, pain or orgasm.

Though the authors freely admit that their data is mildly handicapped secondary to the low study numbers and the use of self-reported data they present a wonderful discussion on the potential pathways of efficacy that moderate wine intake may have on female sexual health. The discussion alone makes reading this paper worthwhile in view of the ideas presented. As with many excellent reports, this study engenders much scientific thought after the content has been appropriately digested.

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A multicenter, prospective, randomized clinical trial comparing tension-free vaginal tape surgery and no treatment for the management of stress urinary incontinence in elderly women

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Aims: The aim of our study was to test the hypothesis that elderly women undergoing tension-free vaginal tape surgery (TVT) will have a better quality of life (QOL) and satisfaction compared to non-treated women despite age- and technique-related potential morbidity.

Methods: This multicenter, prospective, randomized, controlled trial enrolled a total of 69 women aged over 70 years who initially consented to be randomized to either undergo immediate TVT surgery or to wait for 6 months before submitting to the same surgery (control group). The main outcomes measured at every visit (pre-randomization, 8-12 weeks and 6 months) consisted of the Incontinence-Quality of Life (I-QOL) Questionnaire, the Patient Satisfaction Questionnaire and the Urinary Problems Self-assessment Questionnaire, among others.

Results: The analysis included 31 patients in the immediate surgery group and 27 subjects in the control group. Peri-operative complications in the immediate surgery group were bladder perforation (22.6%), urinary retention (12.9%), urinary tract infection (3.2%) and de novo urgency (3.2%). At 6 months, the mean I-QOL scores for the TVT and control groups were respectively 96.5 +/- 15.5 and 61.6 +/- 19.8 ($P < 0.0001$); mean Patient Satisfaction scores were respectively 8.0 +/- 2.7 and 2.0 +/- 2.4 ($P < 0.0001$); and mean Urinary Problems scores were respectively 4.5 +/- 4.3 and 11.6 +/- 3.5 ($P < 0.0001$).

Conclusion: At 6 months post-randomization, the group of elderly women who underwent immediate TVT surgery showed a significant improvement in QOL, patient satisfaction and less urinary problems compared to the group of women waiting for the same surgery

Editorial Comment

The authors provide a study with the primary goal of deciding whether elderly women who underwent surgery with its attendant risks would have an improved quality of life and satisfaction than those patients who deferred surgery and merely continued on in their state of incontinence or in simpler terms: should an elderly woman have surgery or just live with her symptoms. The population studied included patients that either refused or failed conservative therapy and were on no medication for bladder dysfunction (including overactive bladder or urinary tract infection). The patients had no evidence of detrusor overactivity and had normal compliance on cystometrogram. The patient population was randomized to either having surgery immediately or waiting six months and being reevaluated and then having their surgery at that time. The metrics for both groups were quantified at baseline and again at 6 months and then compared. The tools that were utilized to assess the patient's quality of life included the IQOL Questionnaire; Patient Satisfaction scores; in addition to a Urinary Problems quantification. The authors found that patients who had the surgery had improvement in the measured parameters over those practicing watchful waiting thus supporting their hypothesis that surgery was worthwhile over watchful waiting in the elderly population.

This is an excellent paper to review when pondering whether to offer surgery to an elderly woman versus telling her to live with her problem. Many times, the surgeon must make the simple but really complex assessment of whether the treatment will outweigh the cure; this report emboldens one to choose intervention.

The study begs the authors to take the next step of determining if the same promise of therapy can be applied to the super elderly population such as those of 80, 85 or 90 years of age.

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PEDIATRIC UROLOGY

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Improvement in vesicoureteral reflux grade on serial imaging predicts resolution

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Purpose: When children are initially diagnosed with vesicoureteral reflux most undergo a period of antibiotic prophylaxis followed by serial imaging. Although improvement in reflux grade through time presumably predicts eventual resolution, the significance of changing grade through time is unknown. We examined whether improvement in reflux on serial imaging predicts resolution.

Materials and Methods: We retrospectively reviewed 1,761 children diagnosed with vesicoureteral reflux, of which 965 had a minimum of 2 years of follow-up. We examined initial reflux grade and grade on serial imaging up to 5 years after the original diagnosis. For each child it was determined whether reflux was resolved, eventually resolved or never resolved. Groups were further stratified by clinical characteristics.

Results: Multivariate analysis revealed that male gender (HR 1.33, $p = 0.05$), age younger than 1 year at diagnosis (HR 1.35, $p = 0.004$), lower grade at presentation (grade I HR 2.2, grade II HR 1.96, grade III HR 1.33; $p < 0.001$) and unilateral reflux (HR 1.39, $p = 0.001$) were all independent predictors of reflux resolution. Multivariate analysis also showed that reflux improvement on imaging 1 year after diagnosis (HR 3.14, $p < 0.0001$) and improvement from the previous year at any point during follow-up (HR 1.8, $p = 0.009$) were independent predictors of reflux resolution.

Conclusions: Consistent with previous findings, male gender, lower reflux grade at presentation, age less than 1 year at presentation and unilateral reflux were all predictive of reflux resolution. Our analysis also demonstrated that improvement in reflux grade on imaging study 1 year after diagnosis was predictive of resolution, and that reflux improvement from the previous year at any point during follow-up was an independent predictor of resolution. This information will prove valuable in clinical counseling and therapeutic decision making.

Editorial Comment

The authors utilized their database of over 1,700 children with vesicoureteral reflux to determine whether improvement in reflux grade on serial imaging would predict resolution of reflux. They were able to identify 965 patients who had 2-5 years of follow-up for the study and then performed a multivariate analysis to identify predictors of resolution. Nuclear cystograms were performed routinely for follow-up studies in these children, therefore they considered Grade I reflux on a nuclear cystogram to be equivalent to a grade 1 on VCUG study. A nuclear cystogram with Grade II reflux was equivalent to a VCUG with Grade II and III on VCUG and Grade III reflux on nuclear cystogram was equivalent to Grade IV and V reflux on VCUG. Their

results demonstrated that male gender, age less than one year at diagnosis, lower grade of reflux at presentation and unilateral reflux were all predictors of spontaneous resolution, which is consistent with previous studies. In addition, they were able to demonstrate that reflux improvement on imaging one year after diagnosis, as well as improvement in reflux grade from the previous year at any point during follow-up, were both independent predictors of resolution.

This study has important clinical implications when counseling with parents over the decision to continue waiting for spontaneous resolution versus pursuing surgical correction of reflux. Though many of us have assumed that improvement in the grade of reflux is a positive indicator of a greater likelihood for spontaneous resolution, we now have data to back up our assumptions.

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Incidence of new onset metabolic acidosis following enteroplasty for myelomeningocele

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Purpose: Extant literature is mixed regarding risk of metabolic acidosis after enteroplasty for myelomeningocele. This study is the first known attempt to describe the pattern of developing metabolic acidosis in a group of children who underwent enteroplasty and served as their own controls. Multiple preoperative and postoperative laboratory measures for each child were obtained for comparison.

Materials and Methods: This retrospective cohort study allowed participants to serve as their own controls for pre-intervention and post-intervention analysis. The setting was a tertiary, university affiliated, interdisciplinary spina bifida program. All patients followed in the spina bifida program who had undergone ileal or colonic enteroplasty were included for review (total 113). Strict exclusion criteria were preoperatively diagnosed renal insufficiency, preexisting metabolic acidosis consistent with renal tubular acidosis (pH less than 7.35, bicarbonate 20 mmol/l or less) and history of augmentation using gastric or ureteral tissue. Final analysis included 71 children who met inclusion criteria. Children in our spina bifida program periodically undergo routine laboratory evaluation of electrolytes, blood urea nitrogen, creatinine, blood count, and venous blood gases including pH, bicarbonate and partial pressure of carbon dioxide. Primary outcome measures were comparative shifts in blood gases and electrolytes that would confirm the new onset of metabolic acidosis after enteroplasty. Changes in electrolytes and serum creatinine were secondary outcome measures to identify potential markers for postoperative effects. With each child as his/her own control, analysis included paired t tests.

Results: No statistically significant differences ($p < 0.05$) were found when comparing laboratory values before and after bladder augmentation, including pH, bicarbonate, partial pressure of carbon dioxide and electrolytes. No child had metabolic acidosis based on the aforementioned criteria. Followup ranged from 1 to 138 months after enteroplasty (mean 46.8). Respiratory compensation was considered in the analysis, and no difference in partial pressure of carbon dioxide following surgery was noted ($p = 0.65$).

Conclusions: To our knowledge no previous study has examined the matched paired results of before and after development of metabolic acidosis among children (serving as their own controls) with myelomeningocele

undergoing ileal or colonic enteroplasty. The negative statistical results in this controlled cohort are clinically significant. If a child with myelomeningocele has metabolic acidosis after enteroplasty, other clinical reasons beyond the effects of surgery warrant careful consideration.

Editorial Comment

The development of metabolic acidosis following enterocystoplasty is a common concern particularly in the pediatric population where such a procedure is intended to last a lifetime. The authors reviewed data from their spina bifida program that had undergone bladder augmentation using either ileum or colon. They excluded patients with preoperative renal insufficiency or metabolic acidosis. Patients in their spina bifida program routinely undergo serum evaluation of electrolytes, BUN, creatinine blood count, and venous blood gases giving them a unique opportunity to look at changes in serum values both before and after enterocystoplasty. They identified 71 children who met the inclusion criteria and had both preoperative and postoperative laboratory values. Their primary outcome was a shift in blood gases and electrolytes consistent with new onset of metabolic acidosis following bladder augmentations. Secondary outcomes included changes in electrolytes and serum creatinine. They found no evidence of new onset of metabolic acidosis following surgery for a mean follow-up period of almost four years.

Although concern for metabolic changes following enterocystoplasty in the pediatric population must be considered over extremely long time periods, it is interesting to note that these authors found no significant changes even after following their patients for a mean of four years. They also wisely point out that the spina bifida patient population is at risk for metabolic acidosis for other reasons including nutritional issues, chronic infection, pulmonary insufficiency, and/or renal insufficiency. As the authors point out in their conclusion, it may be just as important to consider other sources of metabolic acidosis (some of which may be correctable) rather than assuming the enterocystoplasty is to blame.

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Laparoscopic Nephrectomy through a Pfannenstiel Incision

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ABSTRACT

Purpose: Laparoscopic urologic surgery is generally performed using three to six ports by transperitoneal or retroperitoneal access. Recent developments regarding laparoscopic surgery have been directed toward reducing the size or number of ports to achieve the goal of minimal invasive surgery, by mini-laparoscopy, natural orifices access and transumbilical approach. This video reports three cases of laparoscopic nephrectomies performed through a Pfannenstiel incision using conventional laparoscopic trocars and instruments

Materials and Methods: Since March 2009, laparoscopic nephrectomy through a Pfannenstiel incision has been proposed for selected patients in our service. Patient selection was determined by any situation, pathologic or not, for which laparoscopy was deemed appropriate as the standard of care in our practice. The Veress needle was placed through the umbilicus which allowed the carbon dioxide inflow. One 5mm (or 10mm) trocar was placed at the umbilicus for the laparoscope, to guide the placement of three trocars over the Pfannenstiel incision. Additional trocars were placed as follows: a 10mm in the midline, a 10mm ipsilateral to the kidney to be removed (two centimeters far from the middle one), and a 5mm contralateral to the kidney to be removed (two centimeters far from the middle one). The entire procedure was performed using conventional laparoscopic instruments. In the end of the surgery, trocars were removed and all three incisions were united into a single Pfannenstiel incision for the specimen retrieval.

Results: Three nephrectomies were performed following this technique: one atrophic kidney, one kidney donation and one renal cancer. Median operative time was 96 minutes (ranging from 80 to 120 minutes) and median intraoperative blood loss was 116 cc (ranging from 50 to 150cc). No intraoperative complications occurred and no patients needed blood transfusion. Median length of hospital stay was 32 hours (ranging from 24 to 48 hours).

Conclusion: The use of the Pfannenstiel incision for laparoscopic nephrectomy seems to be feasible even using conventional laparoscopic instruments, and can be considered a potential alternative for traditional laparoscopic nephrectomy.

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EDITORIAL COMMENT

In this surgical video by Branco et al., the authors demonstrate how placement of laparoscopic surgical trocars along incision sites which can be connected thereafter to a Pfannenstiel incision for specimen extirpation is a feasible alternative to conventional laparoscopic trocar placements at time of nephrectomy. This video provides a nice illustration of how this port placement strategy can be used by most practicing urologists. The video provides a nice overview of 3 separate surgical cases (i.e. simple, radical, and donor nephrectomy) in which this approach was utilized. The specialty of urology is in evolution as it has been one of the first to embrace the significant improvements in surgical instrumentation, ergonomics, and optics. With the integration of robotics and now single port access surgery to our

surgical armamentarium, we are now faced with an equally challenging clinical question which is how far can we push the envelope without compromising safety or patient outcome? Another pertinent question is how can urologists keep abreast and competent with these evolving surgical technologies? I don't think there is a simple answer to that question other than stating that clinicians must perform procedures that they are comfortable with and that fall within our surgical specialties realm of the standard of care at this point in time. Evolving technologies have and will continue to shape our surgical specialty for years to come however they must be compared in a rigorous evidence based approach to the surgical techniques which have up until now weathered the test of time.

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