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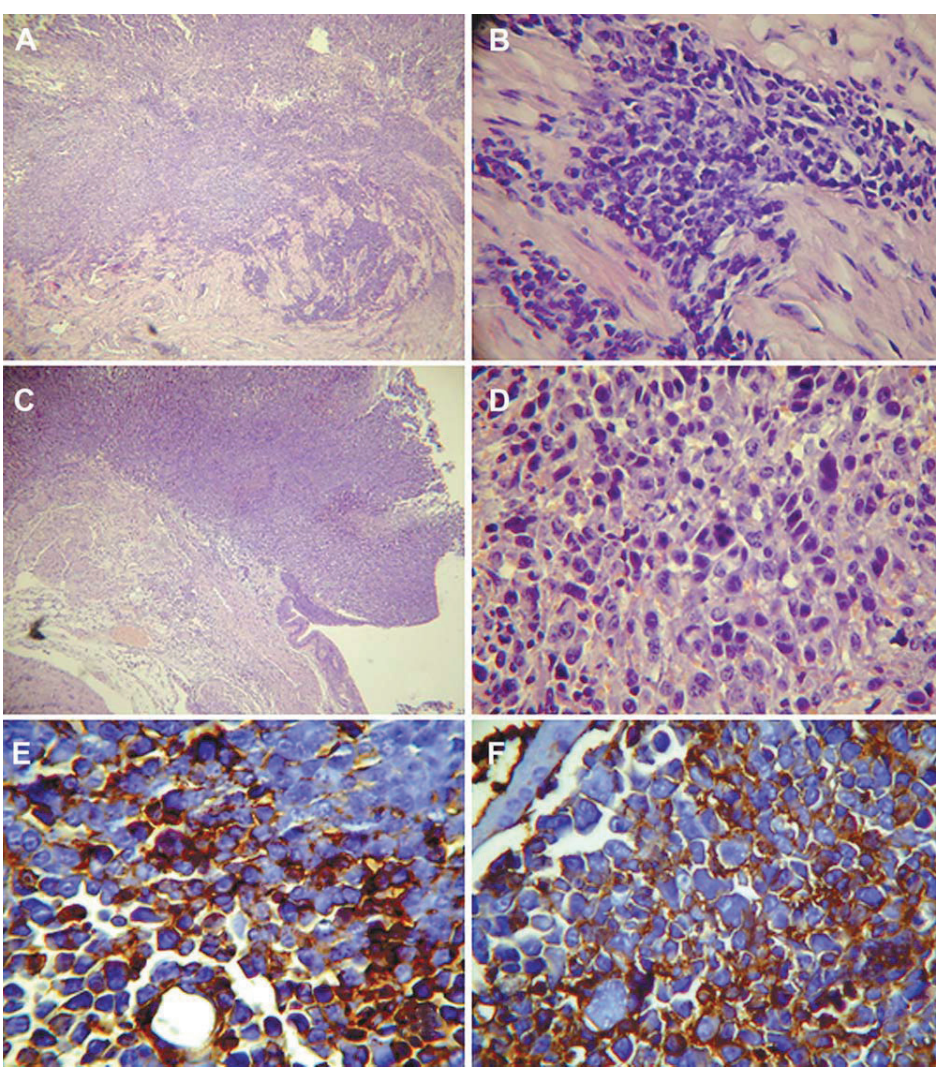


Histopathological Characterization of a Syngeneic Orthotopic Murine Bladder Cancer Model (Page 224)

International Braz J Urol

EDITOR'S COMMENT

Thai Urological Association

It is my pleasure to announce that starting with the March – April 2008 issue, the International Braz J Urol, in addition to being the official Journal of the Brazilian Society of Urology, and of the Confederácion Americana de Urologia, is now the official Journal of the Thai Urological Association under the Royal Patronage. The already known international characteristic of our Journal is now even more present. In additional to our four Associate Editors, Dr. Wachira Kochakarn, from Mahidol University, Bangkok, Thailand, was designated as Associate Editor for the Thai Urological Association side.

The March - April 2008 issue of the International Braz J Urol presents interesting contributions from different countries, and as usual, the editor's comment highlights some papers.

Doctor Canes and colleagues, from Lahey Clinic Medical Center, Burlington, Massachusetts, USA, assessed on page151 the outcomes of a selective drain placement strategy during laparoscopic radical prostatectomy (LRP) with a running urethrovesical anastomosis (RUVA) using cystographic imaging in all patients. The authors studied 208 patients submitted to surgery and cystogram was available for 206 patients. The authors found that routine placement of a pelvic drain after LRP with a RUVA is not necessary, unless the anastomotic integrity is suboptimal intraoperatively. Experienced clinical judgment is essential and accurate in identifying patients at risk for postoperative leakage. When suspicion is low, omitting a drain does not increase morbidity.

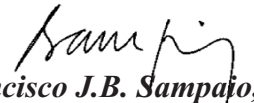
Doctor Demirkesen and co-workers, from University of Istanbul, Cerrahpasa School of Medicine, Istanbul, Turkey, evaluated on page 214 the sexual satisfaction rates of women who underwent tension-free vaginal tape (TVT) procedure for stress urinary incontinence and compare it with the results of Burch-colposuspension. By using a self-administered questionnaire given to 81 patients who had undergone TVT or Burch-colposuspension the authors determined the sexual satisfaction rates and reasons for dissatisfaction. When evaluating sexual satisfaction, 73% in the TVT group and 86% in the Burch-colposuspension group did not report any difference in sexual satisfaction following surgery, while in the TVT group, 23% expressed negative and 4% positive changes, and in the Burch-colposuspension group 9% expressed negative and 5% positive post surgical changes. The differences in sexual satisfaction rates between the two groups were not considered significant. The authors concluded that although sexual satisfaction seems to be more adversely affected by TVT compared to Burch-colposuspension, the difference was not statistically significant.

Doctor Shah and collaborators, from Northwestern University, Feinberg School of Medicine, Chicago, Illinois, USA, reported on page 159 the initial experience with 62 patients undergoing robotic-assisted laparoscopic prostatectomy (RALP), focusing on the primary parameter of positive surgical margins. The authors demonstrated that excellent oncologic outcomes can be attained with a less steep learning curve than previously hypothesized. The authors found that patients with pathologic T2 and T3 disease had a positive surgical margin rate of 1.8% and 16.7%, respectively. They concluded that RALP can have equal

if not better pathologic outcomes compared to open radical prostatectomy even during the initial series of cases. The authors argue that the learning curve for RALP is shorter than previously thought with respect to oncologic outcomes, and concerns asserting that lack of tactile feedback leads to poor oncologic outcomes are unfounded.

Doctor Freilich and co-workers, from Children's Hospital Boston, Harvard Medical School, Boston, Massachusetts, USA, evaluated on page 198 the safety and outcome of managing patients with bilateral UPJ obstruction with concurrent robotic-assisted laparoscopic pyeloplasty. They retrospectively review five patients with bilateral ureteropelvic junction obstruction who underwent concurrent bilateral robotic-assisted pyeloplasties. The operative time, complications, analgesic needs, length of hospitalization, and overall success of the procedure were evaluated. The patients did not present any kind of surgical complications. All kidneys demonstrated decreased hydronephrosis on postoperative ultrasound or improved drainage parameters on diuretic renography or intravenous pyelogram. The authors concluded that simultaneous bilateral robotic-assisted laparoscopic pyeloplasties utilizing 4-port access is feasible and safe. It provides an effective method of managing patients with bilateral UPJ obstruction, avoiding the burden and morbidity of performing staged surgeries.

Doctor Kulkarni and colleagues, from Bombay Hospital Institute of Medical Sciences, Mumbai, India reported on page 180 a series of female patients with transitional cell carcinoma of the bladder who underwent extraperitoneal retrograde radical cystectomy sparing the female reproductive organs with neobladder creation. They studied 14 female patients (45 to 72 years) who underwent gynecologic-tract sparing cystectomy (GTSC) with neobladder. The operating time ranged from 4.5 to six hours with a mean of 5.3 hours. Ten patients were able to void satisfactorily while four required self-catheterization for complete emptying of the bladder. Seven patients were continent day and night and another 7 reported varying degrees of daytime and nighttime incontinence. One patient died of metastases and another of pelvic recurrence. There were no urethral recurrences. Patient satisfaction with the procedure was high. The authors concluded that gynecologic-tract sparing cystectomy with orthotopic neobladder is a viable alternative in female patients with muscle invasive traditional cell carcinoma of the bladder, providing oncological safety with improved quality of life.



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

Review Article
International Braz J Urol Vol. 34 (2): 132-142, March - April, 2008

Lymph Node Dissection During the Surgical Treatment of Renal Cancer in the Modern Era

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ABSTRACT

The increasing use of routine CT scan, along with advances in imaging technology, have facilitated the early diagnosis of incidental renal masses. This has resulted in the reduction in the rate of metastatic disease diagnosis.
Although surgery remains the mainstay in the treatment of renal tumors, the decreasing incidence of lymph node involvement has created controversy regarding the importance and the ideal extent of lymph node dissection, formerly considered mandatory at the time of radical nephrectomy. In this review, we critically assessed the role of lymph node dissection at the time of radical nephrectomy. To date, randomized trials have failed to show a benefit of lymph node dissection when broadly employed. This is likely due to the low prevalence of lymph node metastasis at the time of presentation, the unpredictable pattern of lymph node metastasis from renal tumors, and the continued downward stage migration of the disease. As a result, lymph node dissection for renal cancer is currently not recommended in the absence of gross lymphadenopathy. In high risk patients, lymph node dissection may be considered, but it remains controversial and more clinical evidence is warranted. Extended lymph node dissection is still recommended in individuals with isolated gross nodal disease or those with lymphadenopathy at the time of cytoreductive surgery prior to systemic therapy. A practical approach is summarized in an algorithm form.

Key words: *kidney neoplasms; nephrectomy; lymph nodes; lymph node excision; disease management; review*
Int Braz J Urol. 2008; 34: 132-42

INTRODUCTION

The role of lymphadenectomy in the surgical management of renal cell carcinoma (RCC) still remains controversial among urologists. In an age of continuous decreasing incidence of lymph node metastasis, the broad application of lymph node dissection (LND) has recently been criticized by several authors due to the absence of demonstrated therapeutic benefit, as reported in the European Organization for Research and Treatment of Cancer trial number 30881 (EORTC 30881), the only prospective trial that compared the outcomes of radical nephrectomy alone versus associated with LND (1). In order to define the optimal contemporary approach to LND during the surgical management of RCC, we analyzed the most relevant data published regarding this issue. The review of retrospective studies can be challenging due to inherent bias such as variable inclusion criteria, disparate study designs, variable LND technique, use of inconsistent staging systems and selection bias. For this analysis, three important factors should be considered: 1) the prevalence of lymph node metastasis; 2) the morbidity associated with LND; and 3)

the benefit of performing LND in these cases. Once a balance between all these parameters is reached, the role of LND in clinical practice probably becomes more evident. In this review, we evaluate the prevalence of lymph node metastasis, the efficacy of LND, and present a rational algorithm for the selection of suitable candidates for LND at the time of radical nephrectomy.

PREVALENCE, RISK FACTORS AND RELEVANCE

The reported overall incidence of lymph node metastasis in renal cancer in surgical and autopsy series is approximately 20%, but there is a significant variability reported in the literature (2). As seen in Table-1, the incidence of identified lymph node

Table 1 *– Overall Prevalence of N+.*

Year	Author (Ref.)	Study Design	Number of Cases / Groups Included	LND Technique	Prevalence of N+
1982	Saitoh (15)	autopsy	1828/ all stages	autopsy	63.6%
1997	Johnsen & Hellsten (9)	autopsy	554/ all stages	autopsy	14.0%
1969	Robson (14)	retrospective	88/ all stages	extended	22.7%
1971	Skinner (18)	retrospective	309/ all stages	regional	19.4%
1978	De Kernion (4)	retrospective	86/ Tany N+ or M+	regional	22.0%
1979	Waters (23)	retrospective	130/ all stages	regional	24.0%
1980	Peters (13)	retrospective	356/ all stages	extended	10.3%
1981	Sigel (24)	retrospective		extended	38.0%
1982	Siminovitch (17)	retrospective	102/ T1-1N0M0	mixed	8.8%
1986	Golimbu (7)	retrospective	326/ all stages	extended	7.9%
1990	Giuliani (6)	retrospective	200/ all stages	extended	24.0%
1990	Tsukamoto (21)	retrospective	102/ all stages	extended	21.0%
1990	Studer (19)	retrospective	163/ all stages	extended	14.1%
1991	Herrlinger (8)	retrospective	511/ all stages	extended	17.5%
1992	Ditonno (5)	retrospective	97/ all stages	extended	6.2%
1997	Giberti (25)	retrospective	328/ all stages	regional/extended	20.4%
1999	Schafhauser (16)	retrospective	1035/ TanyN0M0	mixed	14.1%
1999	Moudoni (11)	retrospective	68/ TanyNanyM0	--	20.0%
2001	Minervini (10)	retrospective	167/ TanyN0M0	regional	5.0%
2001	Vasselli (22)	retrospective	154/ TanyNanyM+	mixed	46.0%
2003	Terrone (20)	retrospective	725/ all stages	extended	13.6% (> 12n = 20.4%)
2003	Pantuck (12)	retrospective	900/ all stages	mixed	14.3%
2004	Blute (3)	retrospective	2028/ all stages (pM0)	extended	4.4%
1999	Blom-EORTC (1)	prospective	731/ T1-3N0M0	extended	3.3%

LND = lymph node dissection; n = nodes; EORTC = European Organization for Research and Treatment of Cancer.

metastasis ranges from 3% in surgical series, up to 63.6% in autopsy series (1,3-25). The wide variation may be explained by the differences in patient selection, the extent of LND, and the presence or absence of distant metastases.

Clinical stage and pathological grade of the tumor is highly predictive of the prevalence of lymph node metastases (6,12,26). When excluding patients with metastatic disease undergoing cytoreductive nephrectomy, the incidence of lymph node metastasis in surgical series decreases to 3-10% (1,6,8). The relationship of stage and lymph node metastasis has been demonstrated by several authors. Giuliani and colleagues reported a prevalence of nodal involvement of 13.2% in stages pT1-2 and 36.1% in stage pT3-4 tumors (6). Pantuck and colleagues reported a nodal involvement of 5.2% versus 23.4% for T1-2 and T3-4, respectively (12). Similarly, higher tumor grade is also associated with higher rates of positive nodes (5,6,20). Pantuck et al. reported nodal metastasis in 33% of Fuhrman grade 1-2 tumors (27), as compared with a rate of 68% in those with grade 3-4 tumors (12).

The incidence of lymph node metastasis at the time of clinical presentation has been steadily decreasing over time as evidenced by longitudinal analysis. When comparing the incidence of positive lymph nodes in Robson et al's early series of radical nephrectomy and the more recent treatment arm of the EORTC 30881, a drop from 30% to 3.3%, was observed(1,14).

Another important factor contributing to the lower incidence of positive nodes is the downward stage migration in renal cancer seen with the increased incidental detection of the disease. Studying a series of 309 patients between 1935 and 1965, Skinner et al. found a 7% prevalence of incidental renal masses (18). More recently, the prevalence of incidental renal tumors reported in a series of 131 patients studied by Jayson and Sanders in 1998 was 61% (28). Konnak and Grossman also reported on the change in incidental detection of renal tumors over time, from 13% to 48%, comparing two series of patients treated between 1961 and 1973, and between 1980 and 1984, respectively (29). In addition a simultaneous decline in the stage at the time of diagnosis was also observed, once again confirming the stage migration phenomenon (29). Since one of the most important risk factors for the presence of lymph node metastasis is clinical stage, the increasing detection of incidental small renal tumors is presumably a major etiology for the observed decreasing prevalence of nodal metastasis at the time of presentation.

The importance of the discussion regarding nodal involvement in renal cell carcinoma is based on the fact that the cancer-specific survival is greatly impacted by the presence of lymph node metastasis. Early series reported the 5-year cancer-specific survival rate associated with lymph node metastasis for RCC ranging from 21% to 35% (14,30). More recently, Pantuck et al. and Blute et al. reported in a contemporary series an overall 5-year survival rate of 23% and 20.9%, respectively (3,12). They also noted on a multivariate analysis that the chance of dying from RCC was 7.87-fold higher with lymph node involvement than without (3), and that patients who did not undergo LND were three times more likely to die than those who did, regardless of the extent of the dissection (12). Despite all controversies about the necessity and extent of the dissection, the presence of lymph node involvement in RCC undoubtedly deserves attention, since the reported poor survival rates can definitely be improved with LND in selected cases. The great challenge is to properly identify those cases that would most benefit from this practice.

Renal Lymphatic Drainage

Another factor that adds controversy to the indication of performing LND during radical nephrectomy is the unpredictability of renal lymphatic drainage.

The pathways of renal lymphatic drainage were initially described by Parker in 1935, during anatomical studies of the posterior lymphatic channels of the abdomen (31). He noted that the lymphatic drainage of the kidney was neither unique nor specific, and the patterns of drainage could be quite variable. Johnsen and Hellsten (9) in an autopsy study of 554 patients, observed the occurrence of unpredictable patterns of nodal metastasis and the presence of distant metastasis without regional lymph node involvement (9). Saitoh and colleagues in an autopsy study in Japan, analyzing 1828 cases of renal cancer, also observed cases with distant metastasis without regional lymph node invasion (15). They pointed out the im-

portance of the vascular nature of RCC and hence the predilection for early hematogenic dissemination (32). Clinical series mimic these results (6,22). Vasselli et al. reported an incidence of 53% of distant metastasis without lymph node invasion (22) and Giuliani and colleagues also observed the extremely poor negative predictive value of regional LND in predicting disease progression (6). It was postulated that the neovascularization of RCC distorts the normal anatomy and renders the lymphatic drainage unpredictable (33). Therefore, defining the role of lymphadenectomy during the surgical treatment of these tumors remains a difficult task and a balance between the morbidity of the procedure and the benefits of its practice must always be sought.

MORBIDITY VERSUS BENEFITS

Technique and Extent of LND

The recommended extent of LND has varied from an author to another. The extended dissection, first proposed by Robson et al. in 1969, included "all para-aortic and para-caval lymph nodes, from bifurcation of the aorta to the crus of the diaphragm" (14). Later, new limits were described dependent on laterality. Templates proposed for tumors on the right included the hilar, para-caval, pre-caval, retro-caval, interaortocaval and pre-aortic lymph nodes, whereas for left-sided tumors, inclusion of the hilar, para-aortic, pre-aortic, retro-aortic, interaortocaval and pre-caval nodes was recommended (34). It is important to note that the primary renal lymphatic drainage on the right is to the interaortocaval lymph nodes, and on the left to the para-aortic nodes.

In practice, many surgeons attempt to decrease morbidity by limiting the extent of dissection. Therefore, a limited regional dissection has been recommended, involving only the para-caval, pre-caval and hilar nodes on the right side, and para-aortic, pre-aortic and hilar nodes on the left side, particularly in the setting of laparoscopically treated patients where extended node dissection would be technically difficult. Also due to uncertainties about the benefit of LND, disagreement persists about the ideal limits of LND (3,6,20). Given the distribution of lymphatic drainage, the use of limited node dissection in patients with substantial risk of lymph node metastases is likely to result in understaging, particularly on the right side.

Some authors have tried to overcome the divergences in the templates and to improve the staging role of the procedure by analyzing the same issue from a different perspective. Terrone and colleagues reported on the impact of analyzing the number of dissected nodes, instead of anatomical extension of the LND and have found that a minimum number of 13 nodes should be retrieved, in order to properly stage and estimate the prognosis of these patients. This cutoff resulted in a significant increase in the rate of lymph node metastasis found (20). Thus, based on this data, the best approach to effectively yield an adequate lymphadenectomy and optimize staging, would suggest a dissection of a nodal package extending between the regional and the extended pattern, to assure that the proper number of nodes would be retrieved, irrespective of the specific template limits.

Morbidity

It seems intuitive that an increased extent of lymph node dissection would also increase the morbidity of the procedure. However, when compared to nephrectomy alone, nephrectomy associated with LND, did not show increased morbidity based on retrospective and prospective data (1,35). Additionally, a direct comparison of various dissection patterns was performed by Siminovitch et al. who reported a group of N0M0 patients, who underwent extended, regional or hilar LND templates. They also failed to demonstrate any difference in the morbidity or survival rates among these groups (17). Several other large retrospective series have likewise failed to demonstrate any difference in morbidity rates, as related to the extent of dissection (2,8,12,16,23,30,36).

The most common complications related to the surgical management of RCC are lymphocele, chylous ascites (36), bleeding from lumbar or great vessels, and injury to adjacent organs. However, it is difficult to establish the direct correlation of these events with the LND per se. The EORTC 30881 also addressed this issue and did not show any difference in complications rates, but an increased blood loss was observed among those undergoing LND (1).

Although a significant morbidity is not demonstrated in the literature, LND is still a highly

complex procedure and because it carries a great potential risk for serious intraoperative life-threatening complications, it should be performed only by skilled, well-trained surgeons, who are familiar with retroperitoneal dissections. In addition to providing surgical expertise, urologists should carefully identify only those candidates in whom there is a clear benefit in performing the LND.

Benefits

Throughout the years, three potential benefits of LND at the time of nephrectomy have been evaluated: 1) improved staging and prognostication; 2) improved survival following surgery; and most recently 3) improved response to systemic therapy. Given the limitations of the inconsistent lymphatic anatomy described above, the accuracy of staging and the therapeutic value of the procedure in the setting of radiologically normal lymph nodes are highly dependent upon the rigor of dissection utilized and the pathological features of the disease. Recently the practice of LND in localized renal tumors has not showed significant benefit. It is also questionable whether improved staging accuracy is important given the absence of efficacious adjuvant therapies for the disease (37,38). The recent approval in the United States of novel tyrosine kinase inhibitors for the treatment of advanced renal cancer will likely offer an opportunity for the adjuvant treatment of high risk pathology and for a rebirth of LND as staging and/or cytoreductive procedure (39-41).

Imaging Techniques and Staging role of LND

Although imaging advancements allow detection of nodules as small as 0.5 cm in the retroperitoneum, there is no imaging method that can confidently differentiate enlarged inflammatory nodes from metastatic ones in RCC (20,42). Studer et al. reported an incidence of only 42% of histologically positive nodes in his series of patients with preoperatively enlarged nodes seen on computed tomography (CT) scan (19). The sensitivity of CT for enlarged nodal masses greater than 1 cc is higher than 95% (1), but the low specificity of this finding and the poor predictive value of the method could argue both in favor and against routine LND in these patients. In fact, Studer et al. found that nodes detected by CT, that measured between 1 cm and 2.2 cm were more likely to be inflammatory (19). Because conventional imaging is unable to reliably discern lymph node metastasis from non-malignant lymph node enlargement, routine LND is recommended for any individual with radiologically identified lymphadenopathy.

Benefits for Patients with Localized Tumors

The practice of LND in localized renal tumors has not shown significant benefit. The low incidence of positive nodes, reported to range from 0.4% in the UCLA data, up to 3.3% in other series (1,10,12,43), and the lack of survival advantage demonstrated in randomized trial (1) have favored the omission of routine LND in localized tumors with no suspicious nodes in the preoperative imaging. Moreover, the increasing popularity and the successful oncological outcomes of minimally invasive methods and nephron-sparing techniques have also contributed to the decreased enthusiasm for LND in early stages of the disease.

The staging role of LND is also questionable given the absence of effective adjuvant therapies for RCC (37,38). As data regarding adjuvant strategies continues to improve, offering routine LND to high risk patients, defined as those with large tumors (particularly clinical stage = T3), high nuclear grade (Fuhrman's grade) (27), symptoms, and poor performance status (44,45), remains a topic of debate. These individuals have a reported incidence of positive nodes approaching 10% (46) and thus these patients warrant further attention in future clinical trials.

The application of a risk classification strategy, according to the presence of predictive risk factors, has been proposed as a means of identifying those patients at a higher risk of regional lymph node involvement, that are most likely to benefit from LND. The only study that brought insight into such risk factors was published by Blute et al.(3). Using a multivariate model to identify pathologic features of the primary tumor that were independent predictors of increased risk of having positive nodes in non-metastatic RCC, they identified 5 risk factors: clinical stage (T3-T4), size of the tumor (> 10 cm), tumor grade (Fuhrman III-IV) (27), presence of sarcomatoid differentiation and presence of necrosis (3). The presence of two or

more of these factors was associated with a 15-fold higher incidence of regional lymph node involvement. While provocative, the limitation of this approach is the lack of pre-treatment factors for segregating risk. In the absence of good pathologic support, its application could be difficult.

Benefits for Patients with Nodal Metastasis Only

Little controversy exists about recommending LND in those with isolated positive nodes without distant metastasis. Although this situation is usually found in between 0.9% and 10% of the cases, as shown in Table-2 (1,6,9,10,12,17,25), it may reach rates up to 20.4%, as demonstrated by Terrone et al., using extended templates of dissection and retrieving more than 12 nodes (20). Additionally, in spite of the vast majority of patients who have positive nodes also present with concurrent distant metastasis (58-95% of cases), and exclusive nodal disease is a situation difficult to detect, the survival of this group when treated with LND associated with radical nephrectomy is superior to that of nephrectomy alone (2). Moreover, the survival of this subset of patients who undergo LND associated with radical nephrectomy is far superior to those with distant metastasis, and more closely approximates that of those in the T3N0M0 stage disease (6,13). Data from Giuliani et al. shows that survival rates of this group of patients are 47.9% and 31.9%, at 5 and 10 years of follow-up, respectively, in comparison to the 7% 5-year survival rate of patients with distant metastases (6). Peters and Brown also demonstrated an improved survival associating LND with nephrectomy, which increased the survival rates from 56.5% to 87.5% at 1 year and from 25.79% to 43.75% at 5 years follow-up (13). In this situation, there is little controversy among the experts, and the LND must be performed with curative intent, therefore using an extended template (8). The challenge lies in identifying those cases preoperatively. Perhaps the lack of the proven morbidity associated with the LND, allows for a more liberal indication for the dissection of all suspicious nodes identified before or during surgery. Moreover, the incidental finding of suspicious nodes at radical nephrectomy should also be managed according to this same rationale, since the EORTC trial demonstrated that, despite only 16% of nodes removed due to suspicious palpation were positive, it was yet significantly more, than the 1% found to be positive, in those patients who underwent routine dissection (1).

Benefits for Patients with Systemic Metastasis

With the recent advances in systemic therapies using cytokines and tyrosine kinase inhibitors,

Table 2 *– Prevalence of N+M0 disease.*

Year	Author (Ref.)	Study Design	Number of Cases / Groups Included	LND Technique	Prevalence of N+
1982	Siminovitch (17)	retrospective	102/ T1-2N0M0	mixed	8.8%
1990	Giuliani (6)	retrospective	200/ all stages	extended	10.0%
1997	Johnsen & Hellsten (9)	autopsy	554/ all stages	autopsy	0.9%
1997	Giberti (25)	retrospective	328/ all stages	regional / extended	7.0%
1999	Blom (1)	prospective	731/ T1-3N0M0	extended	3.3%
2001	Minervini (10)	retrospective	167/ TanyN0M0	regional	5.0%
2003	Pantuck (12)	retrospective	900/ all stages	mixed	5.0%

LND = lymph node dissection; N+ = Node positive disease.

the value of the staging and therapeutic benefit of LND has been increasingly discussed. Although immunotherapy using cytokines such as interleukin-2 and interferon-α, alone or in combination, have been widely used as first-line treatment of metastatic RCC, response rates are usually low (5-20%) with median survival rates ranging 12-17.9 months (or lower in the presence of adverse prognostic factors) and with substantial toxicity (47-51). It has been previously shown that systemic therapy with cytokines improves survival after radical nephrectomy and that lymph node metastases typically have a poor response to chemotherapy and immunotherapy (12,22,52). Vasseli et al. observed that survival rates were longer in patients with systemic disease without retroperitoneal nodal metastasis (median survival of 14.7 months), and that the preoperative presence of retroperitoneal lymphadenopathy predicted a shortened survival. However, when the lymph nodes were completely resected during surgery, overall survival rates of these patients were similar to those without retroperitoneal lymphadenopathy (22). Although there was no benefit in survival rates between groups receiving immunotherapy, this data supports the cytoreductive role of the LND during the management of metastatic RCC with lymph node involvement. A more aggressive surgical approach could positively impact the outcomes of the systemic therapy, reducing the burden of the disease and eliminating the metastatic tissue that is less susceptible to the therapy agents (22). Therefore, the extent of the dissection should always be guided by the rationale of clearing the most as possible the grossly involved nodes and its regional packages. However, as this strategy is still considered palliative, extended (more morbid) templates should be avoided, since these patients benefit from a rapid and uneventful postoperative recovery allowing them to receive systemic therapy as soon as possible.

EVIDENCE-BASED RECOMMENDATIONS

Based upon the data reviewed above, we propose the following approach for each patient group (Figure-1).

Localized Disease/ Low Risk (T1-2, N0, M0)

In the contemporary age of decreasing incidence of nodal metastasis, lymph node dissection is of little value in this group. Despite the low morbidity rates, the majority of practitioners agree that there is no indication for LND in these patients, as no survival benefit has been demonstrated for LND with localized RCC.

Localized Disease/ High Risk (T3-4, N0, M0)

In this subset of tumors lies the greatest controversy. Most urologists generally do not perform LND in this situation because of the substantial risk of concomitant hematogenic metastasis regardless of the state of the lymph nodes, as well as due to the lack of validated criteria to predict nodal metastasis. However, with the poor negative predictive value of the imaging examinations and the promising emerging targeted therapies, the staging role of the LND again becomes a reasonable argument. We recommend regional LND in those patients that present with the risk factors aforementioned, including the hilar and para-aortic nodes for tumors on the left side, and the hilar, para-caval, retro-caval and interaortocaval nodes on the right side, from the crus of the diaphragm until the emergence of the inferior mesenteric artery. In the absence of any risk factors or incidental suspicious lymphadenopathy, probably any LND beyond the hilar nodes level is not justified.

Nodal Metastasis Only (Tany, N+, M0)

It is essential to first assure accurate preoperative staging and rule out any evidence of distant metastasis. The extended LND is indicated in these patients who, with LND, have survival outcomes similar to the T3N0M0 group. In addition to grossly enlarged nodes, the extended dissection must include all nodes anterior and posterior to the aorta and inferior vena cava, from the crus of the diaphragm until the bifurcation of the great vessels, including the interaortocaval nodes for tumors on the right side. The type of dissection should also be dependent on comorbidities and performance status, in order to select those patients who are more likely to tolerate the extended procedure. The timing of the surgical management in this setting is the key to successfully achieve a cure in these patients.

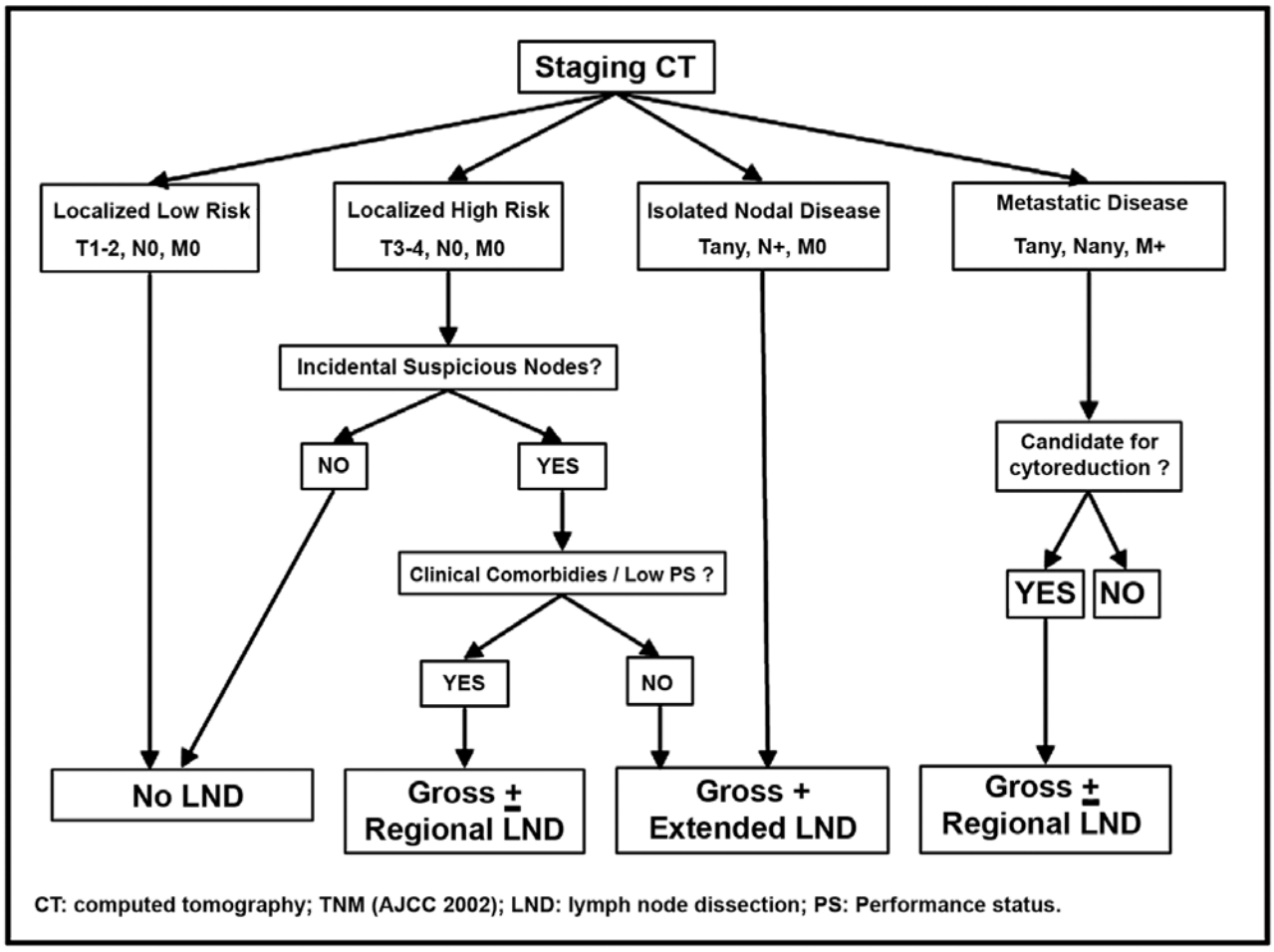

Figure 1 *– Lymph node dissection during radical nephrectomy algorithm.*

Metastatic Disease (Tany, Nany, M+)

In this group of patients, the cytoreductive approach is beneficial and will likely improve outcomes of systemic therapies. The surgical procedure should include a radical nephrectomy and regional lymphadenectomy including only the grossly positive nodes. As nodal disease shows poor response to immunotherapy, trying to extirpate all visible gross nodal metastasis is always a good practice in selected patients with good performance status, who are likely to tolerate the surgery and recover to receive systemic therapies. Since there is no curative intention, extended patterns of LND are not justified.

CONCLUSIONS

Lymph node dissection has become an uncommon procedure during the surgical treatment of renal tumors, in the era of small, incidental and early stage renal masses. We have seen an increased rate of surveillance strategies, minimally invasive and nephron-sparing approaches substituting for the classic radical nephrectomy as described by Robson et al. (14). LND in high-risk cases has not shown any proven survival benefit, but in the future may be tailored, based on our better understanding of prognostic factors and the increasing knowledge about

genetic/molecular events in the carcinogenesis of RCC. To date, there are only two situations in which LND definitely benefits patients: in the presence of nodal involvement without distant metastasis, and as part of a cytoreductive approach. In the next few years, with advancements in novel targeted therapies, further prospective studies will be warranted to redefine the therapeutic/staging roles of LND in the management of renal tumors.

ACKNOWLEDGMENT

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CONFLICT OF INTEREST

None declared.

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Outcomes of Flexible Ureteroscopic Lithotripsy with Holmium Laser for Upper Urinary Tract Calculi

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ABSTRACT

Objective: To assess the perioperative and financial outcomes of flexible ureteroscopic lithotripsy with holmium laser for upper tract calculi in 44 patients.
Materials and Methods: Between February 2004 and September 2006, 44 patients treated for upper tract stone with flexible ureteroscopic lithotripsy were evaluated. Renal stones were associated with collecting system obstruction in 15 (34%) patients, failed extracorporeal shock-wave lithotripsy (SWL) occurred in 14 (32%) patients, unilateral multiple stones in 18 (41%) patients, and multiple bilateral stones in 3 (7%). In 29 (66%) patients, the stone was located in the inferior calyx. Perioperative and financial outcomes were also evaluated.
Results: 50 procedures were performed in 44 patients. The mean stone burden on preoperative CT scan was 11.5 ± 5.8 mm. The mean operative time was 61.3 ± 29.4 min. The stone free rate was 93.1% after one procedure and 97.7% after a second procedure, with overall complication rate of 8%. Therapeutic success occurred in 92% and 93% of patients with lower pole stones and SWL failure, respectively. Treatment failure of a single session was associated with presence of a stone size larger than 15 mm ($p = 0.007$), but not associated with inferior calyx location ($p = 0.09$). Surgical disposables were responsible for 78% of overall costs.
Conclusion: Flexible ureteroscopy using holmium laser is a safe and effective option for the treatment of upper urinary tract calculi. In addition, it can be considered an attractive option as salvage therapy after SWL failure or kidney calculi associated with ureteral stones. Stone size larger than 15 mm is associated with single session treatment failure.

Key words: *ureter; calculi; Lithotripsy; Holmium laser*
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INTRODUCTION

Ureteroscopy has evolved as the most minimally invasive approach to the ureter and kidney since it was first used in 1912 by Hampton, who accidentally entered a massive dilated ureter with a 12F cystoscope (1). The management of upper tract stone disease has shifted from the invasive nephrolithotomy to methods with more effective therapeutic options and lower morbidity. SWL has revolutionized the treatment of upper tract stones and has become the most employed option for these types of stones as well (2). However, its success rates are far from satisfactory and may vary from 80% for those smaller than 1 cm to 54% for stones greater than 2 cm (3). Percutaneous nephrostolithotomy (PCNL) has made

it possible to achieve a stone free rate of more than 90%, with inherent risks of the percutaneous access (4). Recognition of the limitations of SWL and PCNL has allowed the increased popularity of ureteroscopic treatment of renal stones.

Flexible ureteroscopy became clinically available after the development of the small diameter ureteroscope with passive and active deflection allowing access to the entire collecting system in up to 94% of the procedures (5). Its ability to access the upper tract collecting system, associated with the development of a safe, reliable, and flexible endoscopic lithotripsy source, combined with more efficient extraction instruments made the flexible ureteroscopic laser lithotripsy more attractive to effectively treat renal stones with high success rates and low morbidity.

This study evaluates the outcomes of holmium laser lithotripsy for upper tract calculi performed via flexible ureteroscopy.

MATERIAL AND METHODS

Between February 2004 and September 2006, 44 consecutive patients who underwent flexible ureteroscopy with holmium laser lithotripsy for upper tract stone disease were evaluated. Relevant demographic data and operative outcomes were retrieved from medical records with institutional review board approval.

Patients - The patient cohort presented a mean age of 42.2 ± 12 years, with the male gender in 28 (63%) patients. The indication for surgical treatment was renal stones associated with collecting system obstruction in 15 (34%), failure of SWL in 14 (32%) patients, unilateral multiple stones in 18 (41%), and multiple bilateral stones in 3 (7%), Table-1. All patients underwent a preoperative non-contrast CT scan with images acquired at 5.0- mm collimation thickness at 5.0- mm interval width. Collecting system obstruction was defined in patients presenting with flank pain and hydronephrosis associated with ureteral stones demonstrated by CT scan.

The mean stone size treated was 11.5 +/- 5.8 mm, located only in the right kidney in 23 (52%) cases, left kidney in 18 (41%), and bilaterally in 3 (7%). Nine patients presented with at least one stone > 15 mm in diameter. Twenty-nine only had intrarenal stones and 15 had combined ureteral and renal stones. Twenty-nine (66%) patients had at least one stone located in the lower pole, 8 (20%) had the stone in the renal pelvis and 18 (41%) in more than one location (Table-1).

Table 1 *– Demographics of patients treated with flexible ureteroscopy lithotripsy with holmium laser for upper tract calculi.*

N	**44**
Age (years)	42.2 ± 12.5
Male (%)	28 (63%)
Symptomatic (%)	40 (91%)
Associated ureteral stone (%)	15 (34%)
SWL Failure (%)	14 (32%)
Mean stone size (mm)	11.5 ± 5.8
Bilateral stones (%)	3 (7%)
Multiple stones (%)	18 (41%)
Lower calyx (%)	29 (66%)

Surgical procedure - All patients received prophylactic parenteral third generation cephalosporin antibiotics prior to the procedure. In each case, intervention was performed under general anesthesia and endotracheal intubation or laryngeal mask associated with neuromuscular blockage, allowing respiratory motion to be interrupted for short periods.

Briefly, after the retrograde pyelography, a safety guide wire was smoothly positioned in the kidney to avoid bleeding into the pelvis due to urothelial lesion that could alter visibility during the procedure. Ureter dilatation was performed with the inner part of the access sheath for 2 minutes, with complete insertion of the sheath over the wire under fluoroscopic guidance (Figure-1). The presence of a preexisting stent or ureteral dilatation due to ureteral stone obstruction obviated the need for dilatation. When ureteral stones were not associated, the authors employed a 12/14F, 35 cm, (Applied Medical) access sheath for female patients and a 12/14F, 55 cm (Applied Medical) access sheath for males yielding direct access to the renal pelvis. As upper ureteral stones were associated, 12/14F, 20 cm (Applied Medical)

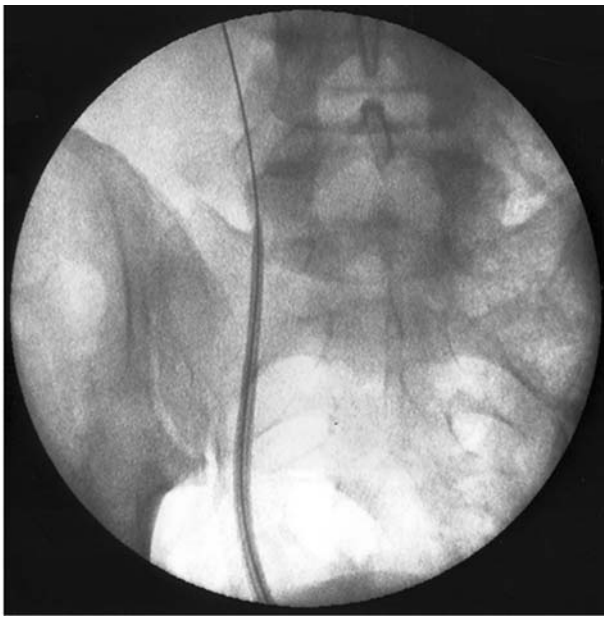

Figure 1 – *Access sheath placed over a guide wire in the right ureter.*

and 36 cm (Navigator, Boston Scientific) sheaths were employed for females and males, respectively, allowing larger fragment removal and better irrigation flow. We attempted to use the access sheath in all cases. When resistance at the iliac vessel level was encountered, the flexible ureteroscope was introduced without an access sheath via its placement over a guide wire under fluoroscopic guidance to avoid further dilation of the mid-ureter. If an access sheath was not used, a small-caliber Foley catheter was inserted into the bladder to assist in upper tract drainage.

The flexible ureteroscope (7.5F Karl Storz Flex-X or 6.8F ACMI DUR-8) was introduced over the guide wire to the renal pelvis. The wire was then withdrawn to optimize irrigant flow and a complete inspection of the collecting system was performed. Holmium:YAG laser lithotripsy was performed through a 200 μm core sized fiber (Dornier Lightguide Super 200) for fragmentation until only very small stone fragments (< 2 mm) were observed, avoiding the need for basket stone retrieval. Our current settings for the laser (Medilas H, Wave Light Laser Technology, Germany) were 1 Joule at 8 Hertz with a total power of 8 Watts. If the lower pole calyx stones could not be fragmented in spite of a fully deflected ureteroscope, it was moved to a less dependent calyx position by using a 2.4 zero-tip nitinol basket or water flush, thus facilitating stone fragmentation. All collecting systems were inspected at the end of fragmentation. A double J stent was placed in all patients at the conclusion of surgery and was removed after approximately 2 weeks. Stents attached with pull-strings were used in a few cases where small stones were completely fragmented and the access sheath was not used. In these cases, stent removal was performed 1 week later on an outpatient basis.

Operative outcomes - Stone-free status was determined after stent removal by CT scan at approximately 2 months postoperatively in all patients. Results were classified by the largest single fragment as stone-free (no residual fragments observed or residual fragments smaller than 3 mm), residual stones greater than 3 mm requiring a second procedure, and failure when it was not possible reach stone free due to intraoperative complications or technical problems. Complications were categorized into intraoperative complications limited to ureteral perforation or postoperative complications characterized by consistent hospitalization for pain that required a patient hospital stay for more than 1 night.

Financial analysis - Detailed surgical cost data from one private institution (SLH) was available for 25 selected patients with no perioperative complication. The data was collected from patients' billing statements and categorized in material and operating room costs. The first one included the regularly used disposables (ureteral sheath, basket, guide wire, and ureteral stent), and the second included operating room, laser and video units, and fluoroscopy/x-ray using time for each procedure. The costs of anesthesia supplies, laboratory, medication, and nursing were not analyzed, and no adjustment for inflation was made. When a patient stayed overnight due to a late surgical schedule and they were discharged early in the next morning, and the overnight stay was not charged. Costs for SWL were not available in our Institutions.

Statistical analysis - Univariable analysis to identify all potential predictors of treatment failure was performed. It was conducted using the Pearson χ^2 statistic or Fisher's exact test for categorical data, the Student's-t-test for continuous normally distributed

data, and the Wilcoxon rank sum test for continuous, non-normally distributed data. All statistical tests were two-tailed and $p < 0.05$ was considered statistically significant.

RESULTS

Fifty procedures were performed in 44 patients, with a mean operative time of 61.3 ± 29.4 min. The ureteral sheath was used in 88% of the procedures. The stone free rate was 93.1% after one procedure, and 97.7% after a second procedure. Three patients required two procedures in order to become stone free. Treatment success occurred in 92% of patients with lower pole stones. In the patients with salvage therapy after SWL failure and multiple stones the stone free rate were achieved in 93% and 90%, respectively. However, therapeutic success occurred in 70% and 66% of patients with stone size > 15 mm and > 20 mm, respectively. Operative data are shown in Table-2.

Ninety-two percent of the patients were discharged 1 day after the procedure. The overall complication rate was 8%. Intraoperative complications consisted of two proximal ureteral perforations caused by the guide wire and confirmed by the recognition of contrast leakage under fluoroscopic evaluation. In one case, the inner part of the ureteral sheath was passed over the wire and mistakenly dilated through the perforation, hence the procedure was suspended. Both cases were treated with ureteral stenting for 30 days and no further complications occurred thereafter until one year of mean follow up. Postoperative complications consisted of two patients, who required postoperative hospitalization for pain control during 2 days. No patient presented symptoms of urinary tract infection nor was readmitted to the hospital until follow-up with CT scan at approximately 2 months after the procedure.

Treatment failure of one single session was associated with the presence of stone greater than 15 mm ($p = 0.007$) but not associated with the inferior calyx stone location ($p = 0.09$), nor the presence of multiple stones ($p = 0.45$). When considering stone location, no significant differences were found between intraoperative parameters and multiple versus solitary stones.

The mean overall cost (± SD) for procedure was US$ 5042 ± 352. Surgical disposables were responsible for 78% of the total (US$ 3942 ± 476) and the remaining 22% (US$ 1100 ± 179) were due to operating room expenses.

Table 2 – *Operative data of flexible ureteroscopy lithotripsy with holmium laser for upper tract calculi.*

Procedures	**50**
Operative time (min.)	61.3 ± 29.4
Ureteral sheath (%)	39 (88%)
Stone free/1 procedure (%)	93.1 %
Stone free/2 procedures (%)	97.7%
Stone free/ Stone size > 15 mm (%)	70%
Stone free/ Stone size > 20 mm (%)	66%
Stone free/ Lower calyx (%)	92%
Stone free/ Multiple stones (%)	90%
Stone free/ SWL Failure (%)	93%
Intraoperative complications (%)	2 (4%)
Postoperative complications (%)	2 (4%)

COMMENTS

Technological advances over the past 2 decades were responsible for the flexible ureteroscopy evolution from a simple diagnostic procedure to a basic therapeutic tool. These changes included downsizing the ureteroscope, upsizing working channels, modern stone extraction tools and holmium laser as an energy source. With the actively deflectable ureteroscopes, all calyces can be accessed in up to 95% of kidneys, including lower pole (6).

Flexible ureteroscopy for upper urinary tract stones is a delicate procedure comprised of intricate details. These details must be respected since they may be the difference between success or failure. The procedure is best performed under general anesthesia, since it allows temporary respiratory motion interruption enhancing the precision of the laser probe as well as reducing the rate of urothelial lesions and operation time.

The proposed advantages of the ureteral sheath allow fast, safe, and multiple accesses to the upper urinary tract. The sheath also increases ureteroscope life span, decreases intrarenal pressure, and provides improved visibility as a result of more effective irrigant flow (7).

The other major factor that made it possible to expand the flexible ureteroscopy use for upper tract stones was the introduction of holmium:YAG laser energy. This energy is rapidly absorbed by water and has minimal tissue effect through a 200 μm core sized fiber while allowing for greater ureteroscope deflection without compromising irrigant flow and consequently visibility (4). In few cases where the 200 μm core sized fiber caused a deflection angle loss, the fragmentation of lower pole stones could be facilitated after repositioning the stone to a more cephalic calyx. Auge et al. reported reduced strain on endoscopes and improved stone-free rates when using the repositioning technique (8).

Minimally invasive techniques should be considered an attractive option for asymptomatic renal stones when associated ureteral stone obstruction is present, requiring intervention. Treatment for asymptomatic calyceal calculi is recommended based on the premise that 70% of these stones increase and will cause symptoms requiring treatment during a 5-year period (9).

Stone-free status after a single procedure appears directly related to stone burden. SWL should be considered the first line of therapy for stones ≤ 10 mm, with stone-free rate reports as high as 85% after one procedure (10). Although success rates of flexible ureteroscopy may be similar, the more invasive nature of endoscopic surgery counteracts this advantage. The presence of residual fragments following SWL, necessitating multiple procedures, is often associated with stones greater than 20 mm and lower calyceal location (11). Flexible retrograde ureteroscopy can be considered for salvage therapy after SWL failure, based on the universal effect of the holmium laser in fragmenting unresponsive stones (4).

Stones greater than 20 mm may be considerer a limitation for SWL and flexible ureteroscopy, with approximately 30% and 60% stone free rates, respectively, with PCNL being considered the first line therapy in this situation (12). However, Grasso et al. showed successful treatment for stones greater than 20 mm with retrograde flexible ureteroscopy, with an average of 1.6 procedures per patient (13).

Although technical efforts were made to increase ureteroscope durability, Afane et al. reported an average of 6 to 15 procedures in the first generation of small-caliber ureteroscopes before requiring some sort of repair. The loss of deflection during treatment of lower pole stone was the most frequent defect (14). These repairs are expensive, and the durability of these instruments represents a major financial concern (14,15). During 50 procedures, a disruption in the laser fiber during a lower pole stone fragmentation with full deflection damaged the working channel of one ureteroscope. Lower-pole ureteronephroscopy requires transmission of holmium:YAG energy along a deflected fiber. There is also a risk of fiber fracture from thermal breakdown and laser-energy transmission to the endoscope. The performance and safety of laser fibers differs both between manufacturers and as regards manufacturer's line of fibers (16).

The new generation of ureteroscopes as the DUR-8 Elite ACMI (Southborough, MA.) has secondary active deflection improving access to lower pole calyx and also exhibiting improved durability (17). Carey et al. reported that newer model flexible ureteroscopes less than 9F provided more than 40 uses before an initial repair was needed (15).

Two ureteral perforations occurred during the use of a standard wire (non-hydrophilic) prior to the insertion of an access sheath. Both of them occurred in a dilated ureter setting due to distal stones. We currently recommend the use of hydrophilic guide wires before inserting the access sheath. The overall complication rate of 8% observed in this study is comparable to that reported in the literature (4). Ureteral stricture rate of 1% has been reported, however the postoperative follow-up is not long enough to determine its incidence in this series. Although, the standard care for ureteroscopy is to discharge patients the same day, our patients remained in hospital overnight as the procedure was performed under general anesthesia late in evening.

The current study presented stone-free rates slightly better than the major series presented in the

literature (4,18). This result may be due to the smaller mean stone size and longer operative time in our series, which could indicates longer laser firing time to achieve small residual fragments. The use of ureteral sheath in the majority of cases could possibly have a role in the overall results, and should be investigate further in a randomized study context. Also, stone free rates were strongly influenced by definition of success (residual fragments smaller than 3 mm) and only 36 out of 44 patients (81.8%) were found to be completely stone free. Portis et al. reported 94.6% stone free rate when success was defined as achieving fragments smaller than 4 mm (19). In addition, our protocol used 5.0-mm sections for non-contrast CT scan, however small calculi (< 3 mm) may be missed on 5.0-mm thick sections (20).

Holmium laser flexible ureteroscopy is an economically viable treatment modality and demonstrates an acceptable financial analysis profile. Material costs, excluding operating room expenditure, has accounted for the majority of treatment related expenses in this study. There is some reluctance to accept this procedure due to high equipment costs and by the inherent learning curve related to a new surgical technique. Some series have demonstrated that flexible ureteroscopy is as effective as SWL in the treatment of renal stones with low complications rates, but in an era of cost containment, it is also necessary to evaluate the financial differences of the treatments (4,12). Although in the United States ureteroscopic laser stone treatment is considered more cost-effective than SWL, in Brazil the costs related to SWL are much lower, hence, a prospective study is still needed to determine the cost effectiveness of each technique in our country (21).

The limited number of patients is a drawback in this series. However, the data were collected prospectively, and all patients received a close and pre-established follow-up, which could be considered strengths of this study.

The authors believe the data presented herein support the minimally invasive treatment with flexible ureteroscopy and holmium laser of upper tract stones. Precise indication, knowledge of capability and limitations of flexible endoscopes are crucial for a high success rate while preserving the equipment for a long life span.

CONCLUSION

Flexible ureteroscopy with Holmium:YAG laser is a safe and effective option for the treatment of upper urinary tract calculi. The procedure should be considered an attractive treatment option for associated kidney calculi with obstructing ureteral stones as well as salvaging therapy after SWL failure as well. Stone size larger than 15 mm is associated with single session treatment failure.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

While shockwave lithotripsy has been the first-line treatment for upper ureteral calculi < 2.0 cm over the last twenty years, there appears to be an increasing number of urologists performing flexible ureteroscopy with holmium:YAG laser lithotripsy for these stones. The miniaturization of the flexible

ureteroscope, the development of the holmium:YAG laser, ureteral access sheaths, and small caliber tipless nitinol stone baskets have led to safer, more efficacious procedures (1,2). Furthermore, a recent report suggesting a link between shockwave lithotripsy and diabetes mellitus has raised concerns (3). However, further refinement of flexible ureteroscopy is required to both improve patient outcome and reduce costs. The development of durable < 7.0 Fr sized digital ureteroscopes, improvements in holmium:YAG laser fiber technology to reduce fiber failure during lower pole procedures, and updated stent designs that minimize symptoms are all needed to further advance this field.

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Laparoscopic Radical Prostatectomy: Omitting a Pelvic Drain

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ABSTRACT

Purpose: Our goal was to assess outcomes of a selective drain placement strategy during laparoscopic radical prostatectomy (LRP) with a running urethrovesical anastomosis (RUVA) using cystographic imaging in all patients.
Materials and Methods: A retrospective chart review was performed for all patients undergoing LRP between January 2003 and December 2004. The anastomosis was performed using a modified van Velthoven technique. A drain was placed at the discretion of the senior surgeon when a urinary leak was demonstrated with bladder irrigation, clinical suspicion for a urinary leak was high, or a complex bladder neck reconstruction was performed. Routine postoperative cystograms were obtained.
Results: 208 patients underwent LRP with a RUVA. Data including cystogram was available for 206 patients. The overall rate of cystographic urine leak was 5.8%. A drain was placed in 51 patients. Of these, 8 (15.6%) had a postoperative leak on cystogram. Of the 157 undrained patients, urine leak was radiographically visible in 4 (2.5%). The higher leak rate in the drained vs. undrained cohort was statistically significant ($p = 0.002$). Twenty-four patients underwent pelvic lymph node dissection (8 drained, 16 undrained). Three undrained patients developed lymphoceles, which presented clinically on average 3 weeks postoperatively. There were no urinomas or hematomas in either group.
Conclusions: Routine placement of a pelvic drain after LRP with a RUVA is not necessary, unless the anastomotic integrity is suboptimal intraoperatively. Experienced clinical judgment is essential and accurate in identifying patients at risk for postoperative leakage. When suspicion is low, omitting a drain does not increase morbidity.

Key words: *prostatectomy; urinoma; laparoscopy; complications; drainage; surgical anastomosis*
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INTRODUCTION

Acceptance of the laparoscopic radical prostatectomy (LRP) since its inception, and later its robotic counterpart, has been motivated by a drive to minimize perioperative morbidity. Room for improvement still exists, with the hope that minor technical adjustments will further decrease morbidity. The following editorial remark accompanies a 1996 article addressing the morbidity of drains following radical retropubic prostatectomy (RRP): "anything that reduces patient discomfort deserves consideration" (1).

Savoie et al. first suggested a pelvic drain might be omitted following an open RRP in an analysis of 116 consecutive cases (2). These same authors updated this concept with 552 patients, arriving at the same conclusion (3). In a recent comprehensive review of published LRP literature, drain placement was not addressed (4), since published series seldom report this detail. In many centers, pelvic drainage remains a routine part of open and minimally invasive

prostatectomy. We hypothesized that improved optical magnification and a running urethrovesical anastomosis (RUVA) may obviate routine pelvic drainage. We assessed the relationship between pelvic drainage and postoperative complications in a consecutive series of 268 LRP in which routine postoperative cystography was performed in all patients, regardless of drain status.

MATERIALS AND METHODS

Laparoscopic radical retropubic prostatectomy (LRP) was performed on 268 patients at the Lahey Clinic Medical Center between January 2003 and December 2004. Two hundred and eight patients were identified in whom an RUVA was performed. Complete preoperative, operative, and post-operative patient information was obtained from a combination of a prospective database maintained by the Department of Urology Clinical Research Assistants and from a retrospective chart review. The age, comorbidities, prostate specific antigen (PSA), Gleason score, clinical stage, estimated blood loss, blood transfusions, pelvic lymph node dissection (PLND), pathological stage, pathological Gleason score, prostate size, intravenous narcotic use, length of stay, and complications were recorded. The body mass index (BMI) was calculated from the preoperative height and weight documented in the anesthesia report. The operative time was calculated from incision start time to procedure end time as recorded in the operative nursing report. Narcotic use was calculated to be the sum of intravenous narcotics recorded by the nursing staff and administered via patient controlled analgesic or on an as needed basis. Different narcotics medications were converted to morphine equivalents for comparison.

All patients underwent either a transperitoneal or extraperitoneal LRP as described previously (5,6) by a single surgeon (IT). When nerve sparing was indicated and technically feasible, this was performed using a harmonic scalpel (Ethicon Endo-Surgery). Lymphadenectomy included the external iliac and obturator lymph nodes. The anastomosis was performed with two 2-0 monocryl sutures each with a polydioxanone absorbable suture clip Lapra-Ty™ on one end. The first suture was placed at the 5:30 position, and 2 - 3 running stitches were made in the counterclockwise direction. The second suture was placed at the 6:30 position, and 2 - 3 running stitches made in the clockwise direction. Therefore, prior to cinching the sutures, at least 4 to 6 running stitches were placed. Therefore, the initial tension is distributed over 4 - 6 stitches instead of 1. Then the sutures were continued in a running manner in their appropriate direction until they meet at the anterior aspect of the anastomosis and tied together with an intracorporeal knot.

Anastomotic integrity was tested by distending the bladder with approximately 200 mL of saline, prior to inflating the Foley balloon. A Jackson-Pratt closed suction or Penrose drain was placed at the discretion of the senior surgeon (IT) when a leak was visualized at the anastomosis or a complex bladder neck reconstruction was performed. Indications for drain placement were obtained from the operative report. When omitted from the operative report, the indication was recorded as unspecified. The drain was placed in close proximity to the anastomosis. If drainage was less than 50 cc per 8-hour shift, the drain was removed. A routine cystogram was performed within the first 7 postoperative days in 90% of patients. The remaining patients had a cystogram prior to postoperative day (POD) 14 due to scheduling difficulties.

Patients were seen postoperatively at 1 week, 5 weeks, 3 months, 6 months, 9 months, and 1 year in follow-up. The Foley catheter was removed on POD 7 if the cystogram showed no evidence of leak, defined as any amount of contrast extravasation. Patients were asked a series of questions to screen for symptomatic intra-abdominal collections, and complete abdominal examination was performed. Directed radiographic imaging was performed when warranted by clinical symptoms. The primary endpoint was the incidence of early postoperative complications: urine leak, urinoma, lymphocele, and hematoma.

Fisher's exact test was used to analyze the association between categorical data: (1) urine leak and drain placement, (1) urine leak and surgical approach, and (3) drain placement and performance of PLND. Two-tailed p values were reported. Unpaired t-test was used to compare mean values between the drained and undrained groups for the following parameters:

age, PSA, biopsy Gleason, pathologic Gleason, BMI, prostate size, operative time, estimated blood loss, morphine equivalents used, and length of stay. The chi-square test was used to compare the distribution of clinical and pathologic stage between both groups.

RESULTS

A total of 208 patients underwent LRP with a RUVA between January 2003 and December 2004. The drained and undrained groups did not differ with respect to age, preoperative PSA, biopsy Gleason sum, pathologic Gleason sum, BMI, clinical stage, pathologic stage, or prostate size (Table-1).

The operative and post-operative data demonstrated a statistically significant difference between the drain and undrained groups in regards to operative time, post-operative narcotic use, and length of stay (Table-2). However, there was no statistical difference in estimated blood loss between groups. When a drain was placed, operative time was longer by an

Table 1 – *Patient, tumor characteristics.*

	Drained	Undrained	p Value
Age (years)			
Mean age ± SD	57 ± 7	59 ± 6	0.07
Median	57	59	
Range	28 - 71	41 - 74	
PSA (ng/mL)			
Mean PSA ± SD	5.9 ± 2.7	6.0 ± 4.1	0.81
Range	1.1-14.1	0.5 - 27.5	
Mean biopsy Gleason sum	6.3	6.3	0.23
Mean pathologic Gleason sum	6.6	6.5	0.83
BMI (kg/m^2)			
Mean BMI ± SD	28.3 ± 4.4	28.2 ± 4.1	0.85
BMI range	22.5 - 41.5	18.1 - 41.6	
Clinical stage (%)			0.38
cT1	42 (82)	124 (79)	
cT2	9 (18)	33 (21)	
Pathologic stage (%)			0.69
pT2	44 (86)	137 (88)	
pT3	7 (14)	18 (12)	
Prostate size (grams) ± SD	45 ± 18	48 ± 17	0.24

BMI = body mass index; SD = standard deviation.

Table 2 – *Operative and postoperative data.*

	Drained	Undrained	p Value
Operative time (min) ± SD	186 ± 32	169 ± 23	< 0.0001
Estimated blood loss (mL) ± SD	158 ± 92	174 ± 119	0.38
Morphine equivalents ± SD	32.0 ± 21.0	17.2 ± 17.8	< 0.0001
Length of stay (days) ± SD	2.6 ± 1.4	1.6 ± 0.6	< 0.0001

Table 3 – *Indications for drain placement.*

	N (%)
Leak visible at anastomosis	4 (7.8)
Intraoperative cystotomy	3 (5.9)
Bladder neck reconstruction	2 (3.9)
Hemostasis concerns	2 (3.9)
Unspecified	40 (78.4)

average of 17 minutes (95% CI 9-25, $p < 0.0001$). Postoperative narcotic use and average length of stay were significantly greater when comparing the drained and undrained groups, respectively. In the majority of cases, the indication for drain placement was not specified in the operative record (Table-3). Reasons stated for drain placement included the following: visible leak during testing of the anastomosis, inadvertent cystotomy during bladder neck dissection, extensive bladder neck reconstruction, and concerns for hemostasis (Table-3).

The incidence of urinary extravasation on post-operative cystogram is outlined in Table-4. Drains were placed in 51 patients (25%), and omitted in 157 (75%). Cystograms were available for 206 patients (99%). Mean duration of drainage was 48 hours. Overall, 12 patients had radiographic evidence of a urinary leak (5.8%). The patients with a drain had a statistically higher incidence of a urinary leak. Presence of radiographic urine leak was not significantly associated with surgical approach ($p = 0.23$), either transperitoneal (n = 32, 4 leaks) or extraperitoneal (n = 172, 8 leaks). As shown in Figure-1, 90% of patients had postoperative cystograms within the first 7 postoperative days; the remainder were performed the following week. As expected, earlier cystograms demonstrate the majority of leaks, with 50% seen on POD 1 or 2. All leaks resolved on follow-up imaging after prolonged drainage. No patient developed a urinoma in this series.

Of the 208 patients, non-nerve sparing, unilateral nerve sparing, and bilateral nerve sparing procedures were performed in 21 (10.1%), 55 (26.4%), and 126 (60.6%) patients. Nerve sparing data was missing in 6 (2.9%) patients. There were no postoperative bleeding complications, including hemorrhage or hematoma. No patient required intraoperative or postoperative blood transfusion, or reoperation for bleeding. One patient required a secondary procedure for anastomotic urine leak. This patient had mild unilateral hydronephrosis and a clinical leak with increasing drain output. He returned to the OR on POD 7 for ureteral stent and suprapubic catheter placement. Of note, had cystograms not been performed in any patient, this is the only patient whose leak was apparent from increased pelvic drain output. The remaining 11 patients with a radiographic leak had no increased drainage.

Three patients underwent laparoscopic lymphocele fenestration. Their lymphoceles (12.5% of

Table 4 – *Complication rates, PLND status.*

	Drained	Undrained	Total	p Value
Total number of patients	51	157	208	
Cystogram performed	51	155	206	
Cystographic leak (%)	8 (15.6)	4 (2.5)	12 (5.8)	0.002
Resolved with prolonged catheterization	7	4	11	
Second procedure for drainage	1	0	1	
Urinoma	0	0	0	
PLND performed	8	16	24	0.32
Lymphocele	0	3 (18.8)	3 (12.5)	
Lap lymphocele fenestration	0	3 (18.8)	3 (12.5)	

PLND = pelvic lymph node dissection.

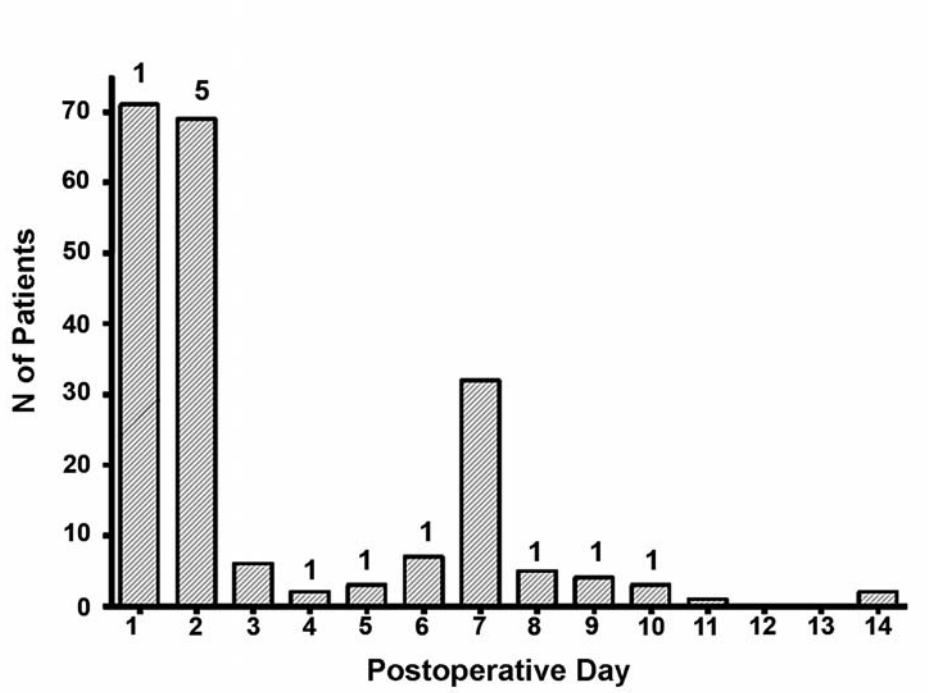

Figure 1 *– Distribution of cystogram based on postoperative day performed. Leaks are indicated as numbers above bar graphs.*

patients undergoing PLND) presented on average 3 weeks postoperatively with symptoms of low-grade fever, urinary retention with bladder spasms, or lower extremity edema. Of the patients undergoing PLND in whom drains were omitted, the approach was extraperitoneal in 14/16 (87.5%). Drain placement was not significantly associated with the performance of PLND ($p = 0.32$).

COMMENTS

The Miami group, who were the first to suggest that routine pelvic drainage after open RRP was unnecessary (2,3) placed drains with a similar selective strategy. Since their report, the Roswell Park group has also supported the safety of drain omission (7). These reports relied on global comparisons of complication rates, without imaging studies. The present study is the first, to our knowledge, in which routine postoperative cystograms were used to assess the true radiographic leak rate underlying this clinically driven algorithm, adding to a growing body of literature to support selective drain omission. Using this selective algorithm, drains were placed in 25% of patients, approximately the same frequency as prior reports (2,7). The overall cystographic leak rate defined as any radiographic extravasation in this series is 5.8% and objective imaging was available for 99% of patients. Interestingly, only one of the ten patients with radiographic evidence of a leak had a clinical leak.

What is the correlation between clinical and radiographic impressions of water tightness? Ischia and Lidsay, in a study of 68 patients undergoing open prostatectomy, found a strong correlation between intraoperative assessment with saline instillation, and subsequent low leak rate on cystogram. Out of 68 consecutive patients, 53 had no intraoperative leakage, and of these only two (3.7%) had leaks on day 7 cystograms (8). Our data are similar, in that unsuspected leaks in the undrained group occurred in only 4 patients (2.5%).

Our overall cystographic leak rate compares favorably with published series. Cystography data has generally been analyzed to assess the feasibility of early catheter removal, and to correlate leak rates with the occurrence of anastomotic strictures. Studies often

have inconsistent reporting (clinical vs. radiographic leak rate) and discrepant testing intervals. Leibovitch et al. found 5.7% of patients with significant contrast extravasation in a consecutive series of 245 patients undergoing open RRP. However, minimal or contained extravasation was observed in an additional 11.4%, for a total leak rate of 17.1% (9). Cystography was performed late (19.2 days postoperatively) compared to the current study.

Contrast extravasation in the first 5-8 days postoperatively has historically been reported to range from 67-78% (9). Similar statistics have fueled conventional wisdom that early extravasation was common following open RRP. Dalton et al. (10) reported a leak rate of 34.5% in a series of 55 patients studied with cystograms starting on day 7. Ramsden et al. reported a 31% leak rate in 275 consecutive open RRP cases where cystography was performed between postoperative days 8 and 10 (11). Contemporary numbers are much lower. Guazzoni et al. reported a 12% leak rate on postoperative day 5 cystograms in patients undergoing LRP with an interrupted anastomosis (12). In another review of 619 open RRP with cystograms at day 10 a leak rate of 4.6% was reported (13), which is similar to our findings.

Even when timing of cystography and anastomotic technique are similar, leak rates may differ. Nadu et al. reported the only other series of LRP with a RUVA in which cystography was routinely performed (14). A cystographically apparent leak was present in 17/113 patients (15.1%), even though most parameters mirror our series. The RUVA was performed with a single 3-0 polyglactin suture. Cystograms were performed between postoperative days 2-4. No urinomas developed, and drain status was not reported. What accounts for the higher leak rate? Patients were asked to Valsalva during cystography, which may transmit greater pressures to the anastomosis, whereas patients are imaged while voiding without Valsalva at our institution.

Hoznek et al. were the first to describe a RUVA, which has significantly decreased operative time and efficiency during this portion of the procedure (15). The difference in early integrity between running and interrupted techniques is not known. Theoretically, suture tension may be distributed more evenly over the circumference of the anastomosis. Authors have assumed, based on lack of symptomatic urine leak, that the anastomosis is watertight (16). Our cohort includes the learning curve for the RUVA, as well as objective imaging. Therefore, a low leak rate of 5.8% lends further evidence to this clinical observation. Although a selective drain placement strategy may be appropriate when a laparoscopic interrupted anastomotic technique is employed, our study did not include patients with this technique, nor was it designed to compare different anastomotic techniques. We also noted that although the senior surgeon had performed several hundred LRP prior to this time period, this cohort contains his learning curve for the RUVA. We have previously reported that a low leak rate may be a good surrogate endpoint for advanced acquisition of technical skill (17).

Intuitively, a senior surgeon's judgment of anastomotic integrity should be accurate, and objective imaging substantiates this impression. When a drain was placed, the leak rate was significantly higher. When the anastomosis was watertight intraoperatively and a drain omitted, the leak rate was indeed significantly lower, but not zero. Four patients in the undrained group did have leaks, none of which developed into urinomas. The longer operative time in the drained group was statistically significant. However, we did not conclude that placing a drain led to a statistically longer operative time. In the majority of cases the reason for drain placement was not specified. A narrow pelvis or otherwise small working space, fibrotic bladder neck tissue, presence of a median lobe, or a difficult posterior dissection from previous prostatitis may all contribute a sense of complexity to performing a LRP. These factors are less quantifiable, and translate into prolonged operative time. Since indications for placement were neither prospective nor randomized, selection bias of the senior surgeon is inherent in this study. That this bias has statistically significant clinical utility, however, is an important finding.

Traditionally, drains are placed to allow the egress of urine, blood, and lymphatic fluid. Clinical suspicion was sufficient to omit a drain without increasing the chance of urinoma. Symptomatic lymphoceles were also acceptably uncommon (3/24 PLND). Since PLND was performed in only 24 patients, we are unable to draw firm conclusions

regarding drainage following PLND. However, our data suggests that lymphoceles should generally not be used as a justification for drain placement. Lymphoceles in this series became symptomatic 3 weeks postoperatively. Lymphoceles therefore accumulate long after the pelvic drain has been removed. Fried et al. observed a similar time course, where two symptomatic lymphoceles occurred at 4 and 9 weeks postoperatively (18). Pepper et al. reported a series of 260 open RRP with PLND in which 9 patients developed lymphoceles (3.5%) 12-120 days postoperatively (19). The mean time at diagnosis was not provided.

In general, the lymphocele rate after open PLND is between 4.7-14.8% (19). The wide range depends on the surgical technique used, and whether clinical or radiographic diagnostic triggers are employed. Freid et al. reported clinically detected lymphoceles in 1% of 111 patients, although 7/23 (30.4%) who subsequently underwent CT imaging for adjuvant radiation had lymphoceles (18). The approach, whether transperitoneal or extraperitoneal, also contributes. With the former, lymphatic fluid is absorbed, compared to an extraperitoneal approach where the retropubic space is an enclosed area where any lymphatic drainage can readily form a lymphocele. However, our data suggests that drainage is not mandatory even after PLND and an extraperitoneal approach. Of the 16 patients undergoing PLND without postoperative drainage, 87.5% were approached extraperitoneally and only 3 developed symptomatic lymphocele. A larger study with power to address this question is needed before definitive recommendations can be made.

The morbidity of the drain itself is not a primary endpoint of this study. The drained group utilized more narcotic medication than the undrained group. We cannot conclude that the increased pain was attributable to the drain. Without directed questionnaires and pain score assessment, the contribution of drains to increased narcotic use is speculative. Evidence for drain related pain was reported by Niesel et al., who found that roughly one out of every four patients experience pain after RRP attributable only to the drain site and not the incision (1). The longer length of stay in the drained group is also likely multifactorial. The single patient with a clinical urine leak had an 11 day hospital stay, which may have contributed to the increased mean length of stay in the drained group.

In addition to the retrospective, nonrandomized nature of this study, a potential criticism is the role of the cystogram itself in subsequent decision making. Here, 90% of leaks were only apparent radiographically, and prolonged catheterization and repeat imaging were performed. Can the cystogram itself be omitted? At the present time, after the results of the present study and with increased experience, we have ceased performing routine cystography. Using this selective drain algorithm we have found no increased incidence of complications.

CONCLUSIONS

Routine pelvic drainage has traditionally accompanied radical prostatectomy. Our results suggest a pelvic drain can be omitted in patients undergoing an LRP with a RUVA if the anastomosis is watertight intraoperatively. Incidence of clinically detected urine leak, urinoma, hematoma, and lymphocele is not increased with this selective strategy.

CONFLICT OF INTEREST

None declared.

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Pathologic Outcomes during the Learning Curve for Robotic-Assisted Laparoscopic Radical Prostatectomy

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ABSTRACT

Objective: We report our initial experience with 62 patients undergoing robotic-assisted laparoscopic prostatectomy (RALP), focusing on the primary parameter of positive surgical margins. The authors demonstrate that excellent oncologic outcomes can be attained with a less steep learning curve than previously hypothesized.
Materials and Methods: The first 62 patients undergoing RALP by a single physician (DPD) at our institution between November 2005 and August 2007 were retrospectively assessed. Surgical pathology records were reviewed for Gleason score, pathologic tumor stage, nodal status, location of prostate cancer within the specimen, extracapsular extension, surgical margin status, presence of perineural invasion, tumor volume, and weight of the surgical specimen. Margin status was determined using surgical specimens only, and not intraoperative frozen sections. All cases in this series were completed using the four-arm da Vinci Robotic System (Intuitive Surgical, Sunnyvale, California).
Results: Sixty-one patients had prostate cancer on their final surgical pathology specimens. Pathologic stage T2 and stage T3 patients were 88.7% and 9.7% of all cases, respectively. The pathologic Gleason score was 7 or greater in 62.3%. Our overall positive surgical margin rate was 3.3%. Patients with pathologic T2 and T3 disease had a positive surgical margin rate of 1.8% and 16.7%, respectively.
Conclusions: Our study suggests that RALP can have equal if not better pathologic outcomes compared to open radical prostatectomy even during the initial series of cases. We argue that the learning curve for RALP is shorter than previously thought with respect to oncologic outcomes, and concerns asserting that lack of tactile feedback leads to poor oncologic outcomes are unfounded.

Key words: *prostate cancer; prostatectomy; laparoscopy; robotic-assisted; outcomes*
Int Braz J Urol. 2008; 34: 159-63

INTRODUCTION

Robotic-assisted laparoscopic prostatectomy (RALP) is becoming increasingly prevalent as the desire for less-invasive procedures continues to grow and the surgery itself becomes more refined. Robotic surgery first appeared in urology in 2000 (1). Since its debut, refinements and the relative increase in ease of the surgery have allowed an increasing number of surgeons to adopt RALP (1,2). Critics have complained of a steep learning curve and lack of tactile feedback during the procedure. Estimates for the number of cases required to complete the learning curve vary widely, ranging from 20 by some authors to 250 by others (3-5). Our study assesses the first 62 RALP surgeries performed by a single physician at our institution, focusing on the primary parameter of positive surgical margins to evaluate oncologic outcomes during the learning curve.

MATERIAL AND METHODS

We retrospectively reviewed surgical pathology data for the first 62 consecutive RALPs performed at our institution by a single surgeon (DPD) between November 2005 and August 2007. Although not fellowship-trained in laparoscopy, the surgeon had extensive experience with open radical prostatectomy and laparoscopic renal surgery. Surgical pathology records were reviewed for Gleason score, pathologic tumor stage, nodal status, locations of prostate cancer within the specimen, extracapsular extension, surgical margin status, presence of perineural invasion, tumor volume, and weight of the surgical specimen. One patient had Stage pT0 disease and was excluded from our analysis.

All cases in this series were completed using the four-arm da Vinci Robotic System (Intuitive Surgical, Sunnyvale, California). A transperitoneal approach was used for all cases with 4 robotic arm ports and 2 assistant ports. Pelvic lymphadenectomy was performed if clinically indicated (Gleason score ≥ 7, PSA > 10). We routinely attempt to spare the bladder neck, as it is our subjective impression this improves early return of continence. Nerve sparing is performed by identifying the plane between the prostatic capsule and neurovascular bundle at the base of the prostate and carrying it distally to the prostatic apex while staying as close to the prostatic capsule as possible. No attempt at a primary lateral release of the neurovascular bundle is made. Posterior dissection consists of dividing Denonvilliers' fascia and dissection along the capsule distally to the prostatic apex. Apical dissection is always performed with apical capsule in view. If a previously placed dorsal vein ligature is obstructing visualization of the apex during dissection, it is removed so the natural planes of dissection are not altered. A second ligature is then placed after apical dissection is complete. A urinary catheter and abdominal drain was placed in all patients. One patient in our series required a blood transfusion.

RESULTS

Patient and pathologic variables are summarized in Table-1. There was one open conversion for moderate bleeding in a Jehovah's Witness (patient 23). This patient had the sole T2 positive margin. Three additional patients whose procedures were converted (one failure to maintain pneumoperitoneum, two failures to progress) had negative margins. Pathologic stage T2 and stage T3 patients were 88.7% and 9.7% of all cases, respectively. The pathologic Gleason score was 7 or greater in 62.3%. Mean prostate weight was 54.4g and median tumor volume was 10%. Perineural invasion was present in 68.9% of patients.

Our overall positive surgical margin rate was 3.3%. Patients with pathologic T2 and T3 disease had a positive surgical margin rate of 1.8% and 16.7%, respectively. Of the 11 patients in our series who had apical disease, none had a positive surgical margin. Pelvic lymph node dissection (PLND) was completed in 68.9% of patients. No patient had lymphatic metastasis identified.

COMMENTS

RALP has the obvious benefit of being minimally invasive; however, in order to become universally adopted, surgeons must be confident that oncologic and functional outcomes are at least equivalent to open surgery. Ahlering et al. concluded that RALP offers the benefits of minimally invasive surgery without compromising clinical or pathologic outcomes (6). Our study confirms that superior pathologic outcomes can be attained even during the initial set of RALP cases performed.

To put into perspective what is an acceptable positive surgical margin rate for RALP, one can refer to the literature for radical retropubic prostatectomy. In a consecutive series of 1,000 cases between 1994 and 2000, Lepor et al. demonstrated a positive surgical margin rate of 19.9% (7). In a large series of 9,035 cases, Han et al. showed an overall positive margin rate of 14.7% (8).

Of the 61 RALPs performed and analyzed in our study, only 2 patients (3.3%) had positive surgical margins. Current RALP literature has typically demonstrated positive surgical margins between 10-20%. For example, Rozet et al. reported a positive surgical margin rate of 19.5% (9). Mikhail et al. and Patel et

Table 1 – *Patient and pathology characteristics (N = 62).*

Mean age ± SD (yrs.)	62.8 ± 6.8
Pathologic stage (% of all cases)	
T0	1 (1.6)
T2a	9 (14.5)
T2b	0
T2c	46 (74.2)
T3a	5 (8.1)
T3b	1 (1.6)
T4	0
Postoperative Gleason score	
6	23 (37.7)
7	33 (54.1)
8	5 (8.2)
9-10	0
Mean weight (g)	54.4 ± 17.8
Median % tumor volume (range)	10 (1-50)
% Perineural invasion	68.9
% Undergoing PLND	68.9
% Positive lymph nodes	0
Positive margin by location of disease	
Apical	0/11
Other	2/50
Number of positive margins by stage	
T2	1 (1.8)*
T3	1 (16.7)
T4	0
All Stages	2 (3.3)

** = patient 23 - Jehovah's Witness who underwent open conversion for moderate bleeding. PLND = pelvic lymph node dissection.*

al. reported rates of 16% and 13%, respectively (3,10). Finally, a large series of 2,652 patients demonstrated a positive surgical margin rate of 13% (11). When broken down by pathological stage, our data showed positive margin rates of 1.8% and 16.7% for stage T2 and T3 disease, respectively.

Multiple studies show that positive margins following radical prostatectomy are more likely to result from cancers in the apical region than from other regions (12,13). Among our 61 patients, 11 had apical disease, but none had positive margins. In contrast, Mikhail et al. reported positive apical margins in 4 of their 100 patients (10).

A literature review article by Hegarty & Kaouk showed that positive surgical margin rates were comparable between radical retropubic prostatectomy, laparoscopic radical prostatectomy, and RALP (14). Others have suggested the positive margin rate is related to experience with RALP (15). These studies suggest the margin rate is less a function of the procedure than the experience of the surgeon. It is our belief, however, that the enhanced visualization of important anatomic landmarks provided by RALP results in lower positive margin rates. Anecdotally, it has been the experience of one of the authors (MRP) that prostatectomies by a surgeon who has performed a large number of RALPs generally have intact, non-fragmented capsular tissue making the microscopic assessment of the surgical margins easier.

Our series allows us to draw conclusions that may possibly affect the view regarding usage of RALP in the field of urology. We were able to demonstrate not only that a superior positive surgical margin rate is attainable via RALP, but it is possible without as steep a learning curve as previously hypothesized. To our knowledge, our positive margin rate was lower than any previous RALP series, and we have the added study characteristic that all of the surgeries were done by a single physician. Of course, we recognize that our low positive margin rate would not be possible were it not for the surgeons who pioneered RALP; their work in fine-tuning the surgical technique was essential in attaining our results. Our results indicate that the lack of tactile feedback with RALP has absolutely no impact on oncologic outcomes.

CONCLUSION

The pathologic outcomes of our study cohort indicate that excellent, perhaps superior, oncologic outcomes can be obtained during the learning curve for RALP. Fear of exposing one's patients to an inferior result should not dissuade the urologist from learning this excellent technique. Furthermore, the lack of tactile feedback with RALP appears to have absolutely no negative effect on surgical margin rates.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

This initial experience of authors with robotic-assisted laparoscopic radical prostatectomy was very enthusiastic, specially considering that the surgeon had never done pure laparoscopic prostatectomy but had renal laparoscopic skills.

I am very impressive with the very low rate of positive margins in his initial robotic experience, maybe one of the lowest of the literature, even considering surgeons with much more surgeries done. I am intrigued with this and I might consider the possibility that the surgeon had been not so closed to prostatic capsule as he stated. I am curious about the functional results even considering the short follow-up. The space between prostatic capsule and the nerves is very restricted. In order to obtain the best oncologic result one could compromise the functional results and vice-versa. It is well established that successful treatment of prostatic cancer considers three aspects: PSA free, full return of continence and full return of sexual function.

Anyway, this paper encourages those no laparoscopist surgeons to start in robotic assisted laparoscopic prostatectomy.

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Changing Profile of Prostatic Abscess

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ABSTRACT

Purpose: To compare the clinical presentation of prostatic abscess and treatment outcome in two different time frames with regards to etiologies, co-morbid factors and the impact of multidrug resistant organism.
Materials and Methods: We retrospectively assessed the charts of 48 patients with the diagnosis of prostatic abscess from 1991 to 2005. The period was divided arbitrarily into two different time frames; phase I (1991-1997) and phase II (1998-2005). Factors analyzed included presenting features, predisposing factors, imaging, bacteriological and antibiotic susceptibility profile, treatment and its outcome.
Results: The mean patient age in phase I (n = 18) and phase II (n = 30) were 59.22 ± 11.02 yrs and 49.14 ± 15.67 respectively (p = 0.013). Diabetes mellitus was most common predisposing factor in both phases. Eleven patients in phase II had no co-morbid factor, of which nine were in the younger age group (22 - 44 years). Of these eleven patients, five presented with pyrexia of unknown origin and had no lower urinary tract symptoms LUTS Two patients with HIV had tuberculous prostatic abscess along with cryptococcal abscess in one in phase II. Two patients had melioidotic prostatic abscess in phase II. The organisms cultured were predominantly susceptible to first line antibiotics in phase I whereas second or third line in phase II.
Conclusion: The incidence of prostatic abscess is increasing in younger patients without co-morbid factors. The bacteriological profile remained generally unchanged, but recently multi drug resistant organisms have emerged. A worrying trend of HIV infection with tuberculous prostatic abscess and other rare organism is also emerging.

Key words: *prostate; infection; abscess; antibiotics; predisposing factors*
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INTRODUCTION

The incidence of prostatic abscess (PA) has declined markedly with the widespread use of antibiotics and the decreasing incidence of urethral gonococcal infections. Predisposing factors for PA include indwelling catheter, instrumentation of lower urinary tract, bladder outlet obstruction, acute and chronic bacterial prostatitis, chronic renal failure, hemodialysis, diabetes mellitus, cirrhosis and more recently, the acquired immunodeficiency syndrome (1,2). The clinical diagnosis of PA has historically been regarded as difficult because of the lack of pathognomonic symptoms or specific clinical signs. With the advent of transrectal ultrasound (TRUS) (3) and computed tomography (CT), the diagnosis of prostatic abscess has been greatly facilitated (4,5).

The pathologic spectrum of PA ranges from microabscesses that resolve with antimicrobial treat-

ment alone to large multilocular abscesses requiring drainage. Although rare prostatic abscess can result in severe complications, including rupture into the periprostatic space, urethra, rectum (rectourethral fistula), perivesical space, perineum, as well as into the peritoneum and bladder due to either delayed diagnosis or inadequate drainage (6-8).

The spectrum of organisms responsible for the causation of prostatic abscess has changed. In the past, Neisseria gonorrhoeae and Staphylococcus aureus were common (6), nowadays the most common organisms responsible for PA have been gram-negative bacteria, especially Escherichia coli (1,8,9). Recently, we encountered several cases of PA caused by Klebsiella pneumoniae, Entererococci spp, Mycobacteria spp and Burkholderia pseudomallei suggesting the possibility of a shift in the pattern of causation of the disease that prompted us to review the clinical and laboratory data therapeutic details on prostatic abscess over a fourteen-year period.

MATERIALS AND METHODS

A retrospective study was carried-out on 48 patients with prostatic abscess diagnosed between June 1991 and June 2005. In order to determine changes in disease pattern over time, the 14-year study period was arbitrarily divided into two 7-year periods, phase I (1991 - 1997) and phase II (1998 - 2005). Institutional review board approval is not required for a retrospective study in our country. The factors analyzed were age, presenting features, digital rectal examinations, diagnostic imaging, associated co-morbidity, bacteriological profile, antibiotic susceptibility pattern, treatment modalities and its outcome during each phase. Urine samples were collected as clean catch midstream voided sample and catheter specimen by sterile technique. Pus from prostatic abscess was collected in a sterile culture bottle during transurethral resection of the prostate or ultrasound guided aspiration by aseptic technique. Identification of causative organisms was performed by standard microbiologic methods (10). Antimicrobial susceptibility testing was carried out using disk diffusion method (11). The interpretation was based on the recommendations of Clinical Laboratory Standards Institute (CLSI) (12). E. coli American Type Culture Collection (ATCC) 25922, P. aeruginosa ATCC 25922 and S. aureus ATCC 27853 were used as quality controls.

Statistical analysis was performed using SPSS (Version 11.0) software. Age was compared using Mann-Whitney U Test between the two phases. Other variables like lower urinary tract symptoms (LUTS), acute urinary retention, pain localization, fever, chills, sepsis, diabetes and digital rectal examination (DRE) findings, were compared between the two phases using Chi-Square Test. All p values less than 0.05 were considered significant. The data are expressed as mean and ± SD or median and range.

RESULTS

The baseline data and clinical presentations in both the phases are shown in Table-1. There was a recent statistically significant shift to younger age at presentation ($p = 0.013$). The clinical presentations in both phases were similar except LUTS and chills (Table-1). DRE measured size, tenderness and induration and revealed similar findings in both phases.

Although the diabetes mellitus was the most common factor in both phases, it was seen less frequently in phase II (53.33%) than in phase I (77.77%) (Table-2). There were four patients with no co-morbidity in phase I. There were 11 patients in phase II with no co-morbid factor, of which nine were in the younger age group (22 - 44 years). Of these 11 patients five presented with pyrexia of unknown origin (PUO) and the cause was prostatic abscess with no LUTS. There were two patients with HIV infection, two with perinephric abscess and one each with chronic liver disease and end stage renal disease in Phase II.

Urine culture was available in 13 of 18 patients in phase I and 28 of 30 patients in phase II (Table-3), it was positive in 9 and 23 respectively. The pus culture was performed in eight patients in phase I and 16 patients in phase II that was positive in two and 14, respectively (Table-3). The urine culture and pus culture were similar in only six cases. The organisms cultured were predominantly susceptible to first line antibiotics (ampicillin, gentamicin, cotrimoxazole

Table 1 *– Clinical presentation.*

Variables	Phase I (1991 - 1997) (N = 18)	Phase II (1998 – 2005) (N = 30)	p Value
Mean age in yrs. + SD	59.22 + 11.0	49.14 + 15.7	0.013
N of Patients with			
LUTS (%)	17 (94.44)	22 (73.33)	0.021
AUR (%)	13 (72.22)	20 (66.67)	0.375
Fever (%)	10 (55.55)	23 (76.66)	0.175
Chills (%)	4 (22.22)	19 (63.33)	0.016
Sepsis (%)	4 (36.67)	11 (36.67)	0.332

AUR = acute urinary tension; LUTS = lower urinary tract symptoms.

Table 2 *– Predisposing factors.*

Variables	Phase I (1991-1997) (N = 18)	Phase II (1998-2005) (N = 30)
Diabetes mellitus	14	16
HIV	0	2
Chronic liver disease	0	1
End-stage renal disease	0	1
Perinephric abscess	0	2
Absent co-morbidity	4	11

and quinolones) in phase I whereas organisms were predominantly susceptible to second line (amikacin, ceftazidime) or third line antibiotics (imipenem or meropenem), in phase II. In phase I, of nine isolates four were E. coli and three of them were sensitive to commonly used first line drugs (ampicillin, ciprofloxacin, co-trimoxazole and gentamicin) and one was resistant. In phase II , of nine E. coli isolates only two were sensitive to first line antibiotics (ampicillin, cefuroxime, co-trimoxazole, gentamicin) and rest 7 were resistant and were susceptible to second line (amikacin, ceftazidime) or third line antibiotics (imipenem and meropenem).

Of four Pseudomonas spp two were susceptible to gentamicin and amikacin, and rests were susceptible only to ceftazidime, imipenem and meropenem. Klebsiella spp was susceptible only to ceftazidime, imipenem and meropenem. Burkholderia pseudomallei was susceptible only to ceftazidime, imipenem and meropenem However, the susceptibility of the gram positive organisms remained the same in both the phases.

In phase I diagnosis was confirmed by abdominal ultrasound in nine patients and transrectal ultrasound (TRUS) in three whereas in phase II the common mode of diagnosis was TRUS in 17, trans-

Table 3 *– Bacteriological profile of urine and pus cultures.*

Culture	**Phase I (1991 - 1997)** (N = 18)	**Phase II (1998 - 2005)** (N = 30)
Urine	13	28
Escherichia coli	4	9
Staphylococcus aureus	3	2
Pseudomonas aeruginosa	0	4
Klebsiella spp	0	3
Serratia spp	1	0
Citrobacter spp	0	1
Burkholderia pseudomallei	0	2
Fungus	1	2
No Growth	4	5
Culture not available	5	2
Pus	8	16
Escherichia coli	1	6
Staphylococcus aureus	1	3
Pseudomonas aeruginosa	0	1
Ps. aeruginosa + Enterococci	0	1
Klebsiella spp	0	2
Cryptococcus spp	0	1
No growth	6	2
Culture not done	10	12

abdominal ultrasound in six (Figure-1) and CT scan in one patient with perinephric abscess and other two with ruptured prostatic abscess making it possible to exactly define the extra-prostatic extent of pus in the ischiorectal fossa and perirectal tissue (Figure-2).

The value of DRE in diagnosing prostatic abscess remained the same in both phases demonstrated by the fact that six patients in phase I and four in phase II were diagnosed based solely on DRE.

As treatment, in addition to appropriate antibiotics, in phase I, 10 patients underwent transurethral resection of the prostate (TURP) along with transurethral drainage of pus, as they were older and with symptoms of prostatic enlargement. Three patients had TUR drainage, four had spontaneous rupture and one patient underwent transperineal aspiration. In phase II, TUR drainage was the most common mode of treatment, which was performed in 14 patients as

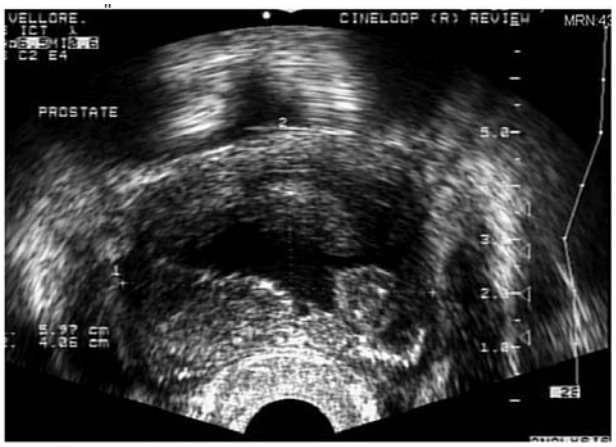

Figure 1 *– Transrectal ultrasound showing prostatic abscess.*

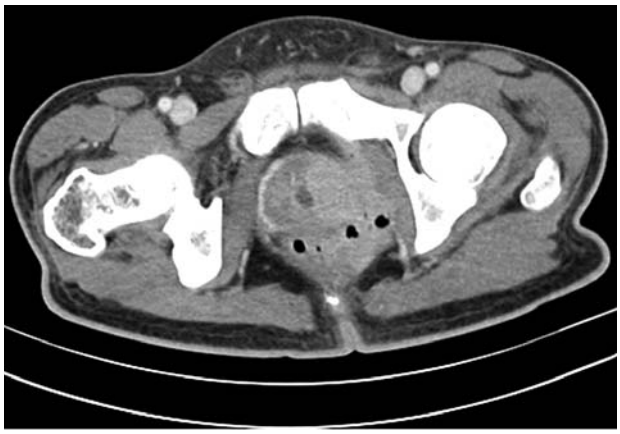

Figure 2 *– CT scan showing prostatic abscess ruptured into left ischiorectal fossa.*

patients were of a younger age group, only four elderly patients with concomitant prostatic enlargement had TURP. Three had TRUS guided aspiration, one with distal penile urethral stricture had transperineal aspiration with statistical process control and four had spontaneous rupture. Two patients with microabscesses and one with melioidosis were treated exclusively with antibiotics. One patient who underwent transperineal aspiration in phase II developed septic shock requiring ventilatory and vasopressure support in intensive care unit. None of the patients in phase I or phase II had septicemia due to formal TURP and TUR drainage.

In phase I, four patients had spontaneous rupture due to delayed diagnosis. One developed perineal abscess and one pararectal abscess requiring open drainage, and in two patients abscesses had ruptured into the prostatic urethra. In phase II, there were four patients with spontaneous rupture due to delayed diagnosis. One developed horse shoe perineal abscess that required open drainage and temporary sigmoid colostomy. One had pararectal abscess that was managed by incision and drainage. One had rectourethral fistula that was treated with antibiotic and suprapubic drainage for three months. In one abscess ruptured into the prostatic urethra. In phase II, there were two patients of HIV infection with tuberculous prostatic abscess, along with tuberculous pyocele and Cryptococcus neoformans isolated on pus culture in one.

All patients recovered well in both the phases except one death in phase II who had melioidosis. Three young patients in phase II following TUR drainage of prostatic abscess developed retrograde ejaculation. Mean duration of hospital stay were similar in both the phases, 11.37 days (range 6 - 23 days) and 9.33 days (range 2 - 28 days) as was the duration of antibiotic therapy 28 days (14 - 42 days) and 30 days (9 - 90 days) in phase I and phase II respectively.

COMMENTS

Prostatic abscess is an infrequent condition in the modern antibiotic era with an incidence of 0.5% to 2.5% of all prostatic disease (8). Prostatic abscess can occur in patients of any age but is mainly found in men in their 5th and 6th decade of life (13). As seen in our series, prostatic abscess is occurring in a younger age group.

Predisposing factors for development of prostatic abscess are diabetes mellitus, bladder outlet obstruction, indwelling catheter, chronic renal failure, patients on hemodialysis, chronic liver disease and more recently HIV infection (14). In our series, diabetes was the most common predisposing factor, with HIV causing tuberculous abscesses, in two patients. In phase II 53% of patients were diabetic. They were younger and keeping with the WHO report (15) of diabetes occurring in younger individuals in the Indian subcontinent. Three patients (21.42%) in phase I and 7 patients(43.75%) in phase II were diagnosed to be diabetic for the first time when they presented with

prostatic abscess. This could be a major new form of presentation in keeping with the increased incidence of diabetes.

Prostatic abscess should be considered as a possible etiology when evaluating for PUO in younger men as five of 11 patients without predisposing factor presented with PUO.

The clinical diagnosis of prostatic abscess is sometimes difficult because of nonspecific symptoms (8). This condition usually presents as an irritative voiding symptoms, perineal pain, and fever and occasionally as acute urinary retention (1). In our series, 17 patients (94.44%) in phase I and 22 patients (73.33%) in phase II presented with irritative LUTS. This may be due to the fact that patients were of the older age group in phase I than in phase II. The patients with prostatic abscess presented more commonly with fever and chills in phase II than in phase I. The number of patients with sepsis was higher in phase II (36.67%) than in phase I (22.2%). This is most probably due to infection caused by multi drug resistant bacteria related to the misuse of antibiotics in the community. In our series in phase I, 75% of E. coli were sensitive to commonly used first line drugs (ampicillin, ciprofloxacin, co-trimoxazole and gentamicin) and in phase II, more than 75% of E. coli were resistant to first line antibiotics and were susceptible to second line (amikacin, ceftazidime) or third line antibiotics (imipenem and meropenem).

The microbiology of prostatic abscess has undergone a complete metamorphosis in the antibiotic era. More recently, various reports have shown that the common organisms causing prostatic abscess are E. coli and other enteric gram negative bacilli (1,8,9). More recently we have reported two cases of prostatic abscess due to Burkholderia pseudomallei (16).

However, the prevalence of immunocompromised individuals has increased in the modern era (phase II), and the potential for uncommon fastidious pathogens, particularly mycobacterial, fungal and anaerobic pathogens, melioidosis, in addition to typical gram-negative bacilli, will make the diagnosis of prostatic abscess more complicated (14,16,17).

Surprisingly urine culture and pus culture isolates were similar in only six cases (all in phase II). Of these, 4 were gram negative bacilli, this includes E. coli (n = 2), Klebsiella spp (n = 1) and Pseudomonas spp (n = 1) and 2 were gram positive cocci (S. aureus). Of six patients, five were diabetic and four had sepsis at presentation. It is important to send material for culture (pus, urine, and/or prostatic chips) in order to identify the etiologic agent, especially in immunocompromised patients because they usually present with uncommon microorganisms (18). Urine culture may be negative unless the abscess ruptures into urethra or bladder. Thus it is important to emphasize that pus culture and sensitivity should be performed routinely for management of prostatic abscess.

Although the bacteriological profile was similar in both phases, it is important to note that the antibiotic susceptibility profile had changed, with organisms resistant to first line drugs and sensitive only to higher antibiotics.

In our series, trans-abdominal USG was the most common modality of diagnosis in phase I, but in phase II, TRUS became the major diagnostic tool and was performed in 56.67% of patients and has now become a standard protocol as the transrectal probe was acquired later part of 1st phase.

Prostatic abscess currently occurring in a relatively younger population has treatment implications. Transurethral drainage could result in retrograde ejaculation as seen in three patients in this series and hence one would like to resort to transperineal / transrectal aspiration. TURP is indicated in elderly patients with associated bladder outlet obstruction due to prostatic enlargement. In our series, in phase I most of the patients being older with associated obstructive LUTS had a formal TURP, in addition to drainage and the abscess. In phase II, 50% of patients were treated by transurethral drainage of abscess, 3 patients had TRUS guided aspiration where one required TUR drainage due to recurrent prostatic abscess. In very few cases, open surgical drainage may be indicated mainly in those patients with extraprostatic involvement (17). In this series two patients with spontaneous rupture in each phase required open surgical drainage.

Potential complications due to a late diagnosis include spontaneous rupture into the urethra, perineum, bladder or rectum and the development of septic shock with a mortality rate of 1% to 16% (8). There was one mortality due to infection with melioidosis in this series.

CONCLUSIONS

Prostatic abscess should be considered in the differential diagnosis of young men who present with pyrexia of unknown origin. It could be the primary presentation in a recently diagnosed diabetic. The incidence of prostatic abscess is increasing in younger males. This is probably related to the higher incidence of diabetes in younger males in this region. Clinical findings could be subtle especially in younger men who may not present with LUTS. While the bacteriology remains largely unchanged, the emergence of multi drug resistant organisms points to the rampant misuse of antibiotics. The emergence of HIV brings the added concern that some of the abscesses could be the result of tuberculous infection.

CONFLICT OF INTEREST

None declared.

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Endorectal Magnetic Resonance Imaging in Persistent Hemospermia

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ABSTRACT

Objective: To present the spectrum of abnormalities found at endorectal magnetic resonance imaging (E-MRI), in patients with persistent hemospermia.
Materials and Methods: A review of E-MRI findings observed in 86 patients with persistent hemospermia was performed and results compared with those reported in the literature. Follow-up was possible in 37 of 86 (43%) patients with hemospermia.
Results: E-MRI showed abnormal findings in 52 of 86 (60%) patients with hemospermia. These findings were: a) hemorrhagic seminal vesicle and ejaculatory duct, isolated (n = 11 or 21%) or associated with complicated midline prostatic cyst (n = 10 or 19.0%); b) hemorrhagic chronic seminal vesiculitis, isolated (n = 14 or 27%) or associated with calculi within dilated ejaculatory ducts (n = 2 or 4 %); c) hemorrhagic seminal vesicle associated with calculi within dilated ejaculatory duct (n = 4 or 7.7%) or within seminal vesicle (n = 4 or 7.7%); d) non-complicated midline prostatic cyst (n = 6 or 11.5%); and e) prostate cancer (n = 1 or 2%). Successful treatment was more frequent in patients with chronic inflammatory and/or obstructive abnormalities.
Conclusion: E-MRI should be considered the modality of choice, for the evaluation of patients with persistent hemospermia.

Key words: *hemospermia; diagnostic imaging; magnetic resonance imaging*
Int Braz J Urol. 2008; 34: 171-9

INTRODUCTION

Hemospermia or hematospermia is not an uncommon clinical urological problem among adult men, but its exact prevalence remains unknown. Hemospermia is prevalent in young males with a mean age of 37 years (1-5). Urogenital inflammation and infection are usually considered the most common cause of hemospermia in this group of patients. In young males often only simple, tailored investigations and appropriate treatment are required. In older patients, above 40 years of age, or those with recurrent hemospermia or associated symptoms, other benign causes and rarely malignancy can be found (5,6).

Imaging evaluation of patients with recurrent hemospermia is usually performed by transrectal ultrasound (TRUS) (7-10). In contrast to TRUS, endorectal magnetic resonance imaging (E-MRI) has the ability to identify hemorrhage within the reproductive structures, but despite its superior diagnostic capability there are only few reports describing its utility in the assessment of persistent hemospermia (10-12).

Our aim was to illustrate the spectrum of abnormalities found at E-MRI in patients with persistent hemospermia.

MATERIALS AND METHODS

Between March 2000 and May 2007, 86 consecutive patients with persistent hemospermia of an average duration of 16.7 months (range, 6-48 months), underwent E- MRI at our institution. Mean patient age was 37 years (range, 25-72 years). Sixty patients (70%) were asymptomatic except for hemospermia. One or more associated symptoms, laboratorial or clinical findings were obtained in the remaining 26 patients (30%): frequency or urgency (n = 10), perineal discomfort or pain (n = 8), ejaculatory pain (n = 4), arterial hypertension (n = 2) and hematuria (n = 2). After treatment follow-up was obtained in 37 patients. Conventional MR imaging was performed with a 1.5-T MR imager (Signa; GE Medical Systems, Milwaukee, WI.). Patients were examined by using the body coil for signal acquisition and a combination of a pelvic phased-array coil (GE Medical Systems, Torso PA) with a commercially available balloon-covered endorectal coil (Endo ATD; Medrad, Pittsburgh, PA.), for signal reception. The balloon-covered endorectal coil was inflated with 90 mL of liquid perfluorocarbon (12). On MR images, the prostate was evaluated with transverse spin-echo T1-weighted MR images by using the following parameters: repetition time msec/echo time msec, 575/minimum; section thickness, 3 mm; matrix, 256 x 224; two signals acquired; field of view, 13 cm; intersection gap, 0 mm; bandwidth, 20.83 kHz. Transverse and transverse-oblique T2-weighted images were obtained with the following parameters: 3500/130, section thickness, 3 mm; matrix, 256 x 224, three signals acquired; field of view, 13 cm; intersection gap, 0 mm; bandwidth, 20.83 kHz. For the transverse images, phase encoding was in the right-to-left direction. T2-weighted sagittal MR images were obtained with the following parameters: 4000/150; section thickness, 5 mm; matrix, 256 x 192; two signals acquired; field of view, 15 cm; intersection gap, 2 mm; bandwidth, 41.67 kHz. For the T2-weighted sagittal MR images, phase encoding was in the superior-to-inferior direction. After treatment follow-up was possible in 37 of 86 (43%) patients.

RESULTS

In patients with hemospermia, E-MRI showed abnormal findings in 52 out of the 86 patients (60%). Hemorrhage within the seminal vesicle or the ejaculatory duct was recognized in 45 of 86 patients (52 %). Blood within seminal vesicle or ejaculatory duct appears as areas of high signal intensity on T1-weighted spin-echo images representing the presence of metahemoglobin due to subacute hemorrhage (12).

The imaging criteria used to characterize seminal vesiculitis were: diffuse wall thickening of the seminal vesicle with low T2-weighted signal intensity, loss of convolutions and proteinaceous or hemorrhagic fluid content with variable signal intensity on T1-weighted and T2-weighted images(10). Thus, significant abnormal E-MRI findings observed in this group of patients were: a) hemorrhagic seminal vesicle and ejaculatory duct, isolated (n = 11 or 21%) or associated with complicated midline prostatic cyst (n = 10 or 19.0%) (Figure-1); b) hemorrhagic chronic seminal vesiculitis, isolated (n = 14 or 27%) (Figure-2) or associated with calculi within dilated ejaculatory ducts (n = 2 or 4 %); c) hemorrhagic seminal vesicle associated with calculi within dilated ejaculatory duct (n = 4 or 7.7%) or within seminal vesicle (n = 4 or 7.7%) (Figure-3); d) non-complicated midline prostatic cyst (n = 6 or 11.5%); and e) prostate cancer (n = 1 or 2%), Figure-4.

Thirteen patients with hemospermia underwent transurethral endoscopic treatment (unroofing of the midline cysts or ductal obstruction and resection, fulguration, and dilatation of ejaculatory duct obstruction). This approach was successful in 5 patients with dilated hemorrhagic seminal vesicle(s) and ejaculatory duct associated with complicated midline prostatic cyst; in 4 patients with hemorrhagic seminal vesiculitis and calculus within dilated ejaculatory duct and in 1 patient with non-complicated midline prostatic cyst. The same procedure was unsuccessful in 3 patients with non-complicated

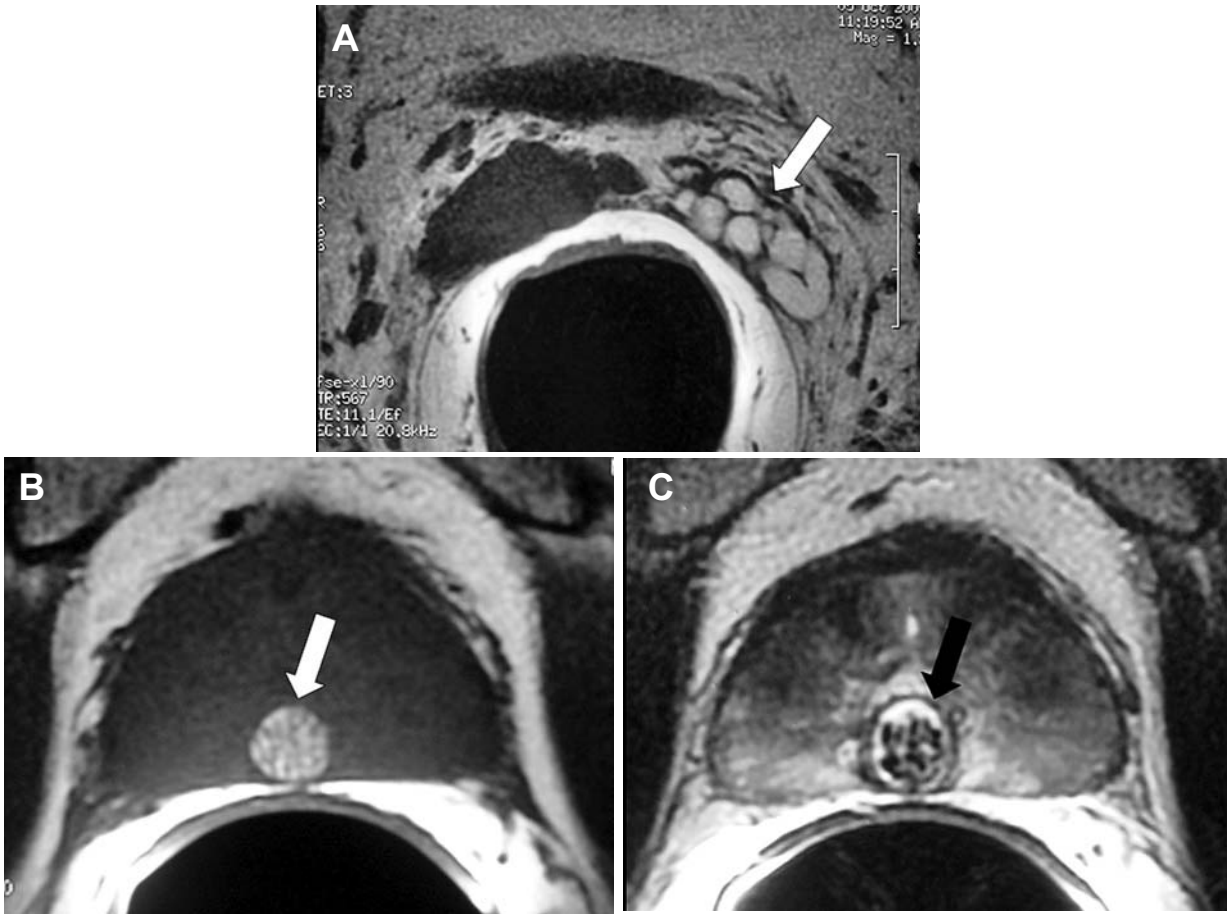

Figure 1 – *Hemorrhagic seminal vesicle associated with a complicated midline prostatic cyst (utricular cyst). A 54-year-old man, with history of persistent hemospermia. A) E-MRI, axial plane, T1-weighted image, showing a hemorrhagic normal-walled left seminal vesicle (arrow). Hemorrhage is recognized due the presence of high signal intensity on T1-weighted images. B) and C) E-MRI, axial T1 and T2-weighted images respectively, showing a complicated midline prostatic cyst (arrow) containing blood and several small calculi.*

midline prostatic cyst. Hemospermia disappeared completely in 9 out of 12 patients following an E-MRI diagnosis of hemorrhagic chronic seminal vesiculitis and subsequent antimicrobial and or anti-inflammatory drugs. Spontaneous elimination of a seminal vesicle calculus was reported by one patient with complete remittance of the hemospermia. Two patients suspected to have prostate cancer due to the presence of focal hypointense area on T2-weighted images, in the peripheral zone of the prostate, were further evaluated with TRUS-guided biopsy guided by magnetic resonance imaging findings (13). This technique allowed the diagnosis of cancer in only one of these patients.

COMMENTS

Although hemospermia is usually a benign and self-limiting condition, it provokes great concern and anxiety in sexually active patients. Hemospermia may be secondary to inflammation, infection, ductal obstruction or cysts, benign neoplasm, vascular abnormalities, systemic or iatrogenic factors and rarely malignant tumors. History and physical examination are often unrevealing (1). In patients younger than 40 years an infective cause in the urogenital tract is the most common etiological factor (5). Factors that dictate the extent of investigation are patient age, the

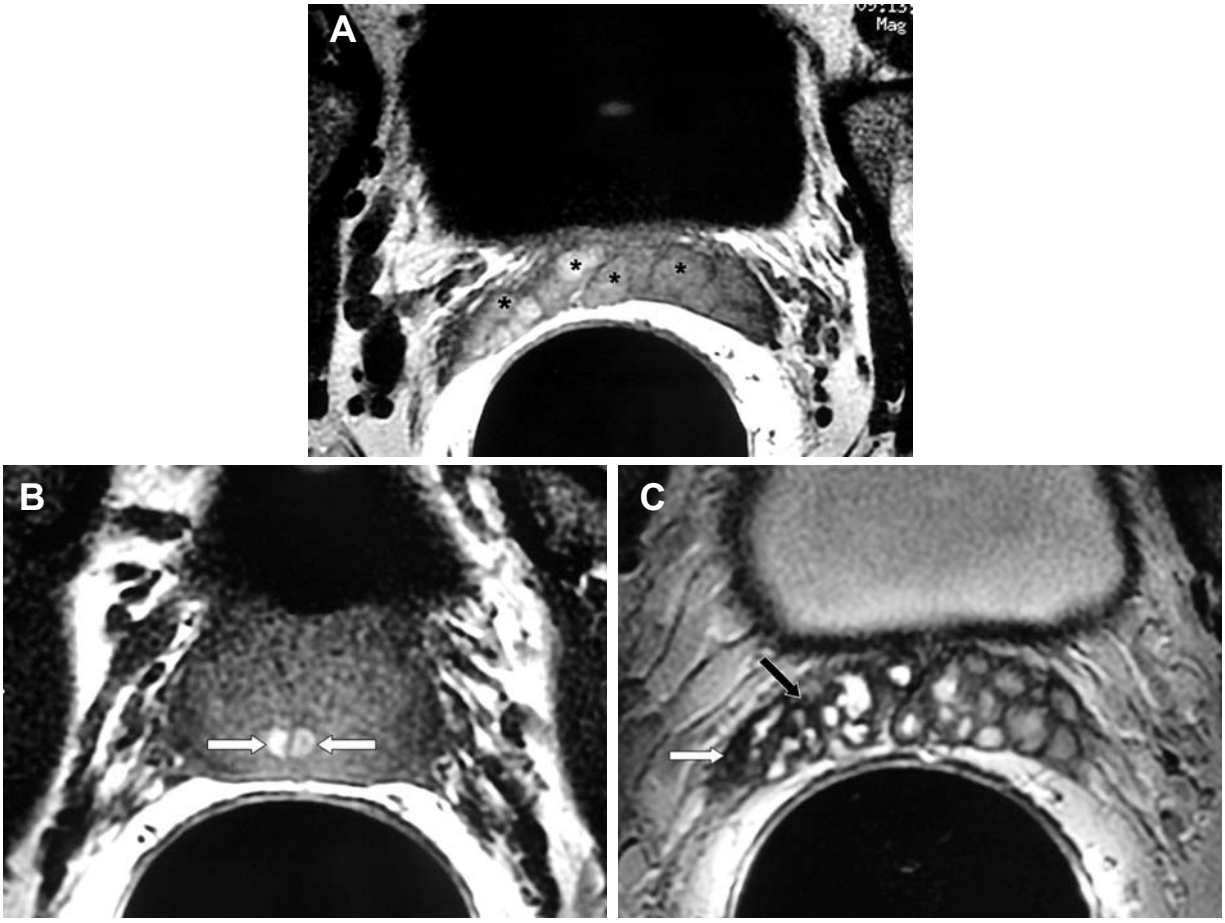

Figure 2 – *Hemorrhagic chronic seminal vesiculitis. A 62-year-old man, with history of persistent hemospermia and perineal discomfort. A) and B) E-MRI ,axial plane, T1-weighted images. Note high-signal intensity hemorrhage in both seminal vesicles (asterisk) and in both ejaculatory ducts (white arrows). C) and D) E-MRI, axial plane, T2-weighted images ,showing imaging features consistent with chronic seminal vesiculitis: diffuse thickening of the of the seminal vesicles with low T2-weighted signal intensity (dark arrow) and loss of convolutions(white arrow).These abnormalities are more evident in the right seminal vesicle which appeared contracted in comparison with the left seminal vesicle.*

duration of hemospermia, whether it is persistent and the presence of associated symptoms or signs such as weight loss, local or bony pain, fever, lower urinary tract symptom and hematuria. It is widely accepted that persistent hemospermia or hemospermia with an associated symptom and hemospermia in older patients requires more extensive investigation (1-9).

In our small series of patients, laboratorial or clinical findings were present in 26 out 86 patients(30%): frequency or urgency (n = 10), perineal discomfort or pain(n = 8), ejaculatory pain (n = 4), arterial hypertension (n = 2) and hematuria (n = 2). Both patients with hematuria with normal E-MRI findings were submitted to direct rigid and flexible cystoscopy. Papillary urethritis was found in one patient.

TRUS can be considered a safe, noninvasive and relatively inexpensive method, which allows clear images of the reproductive system structures. TRUS has an accurate diagnostic rate of between 74% and 95% for the evaluation of hemospermia (5). E-MRI has superior imaging capability since offers higher spatial resolution for the visualization of the whole seminal tract. E-MRI allows the demonstration of normal variations; presence of hemorrhage and evident signs of chronic infection, obstruction

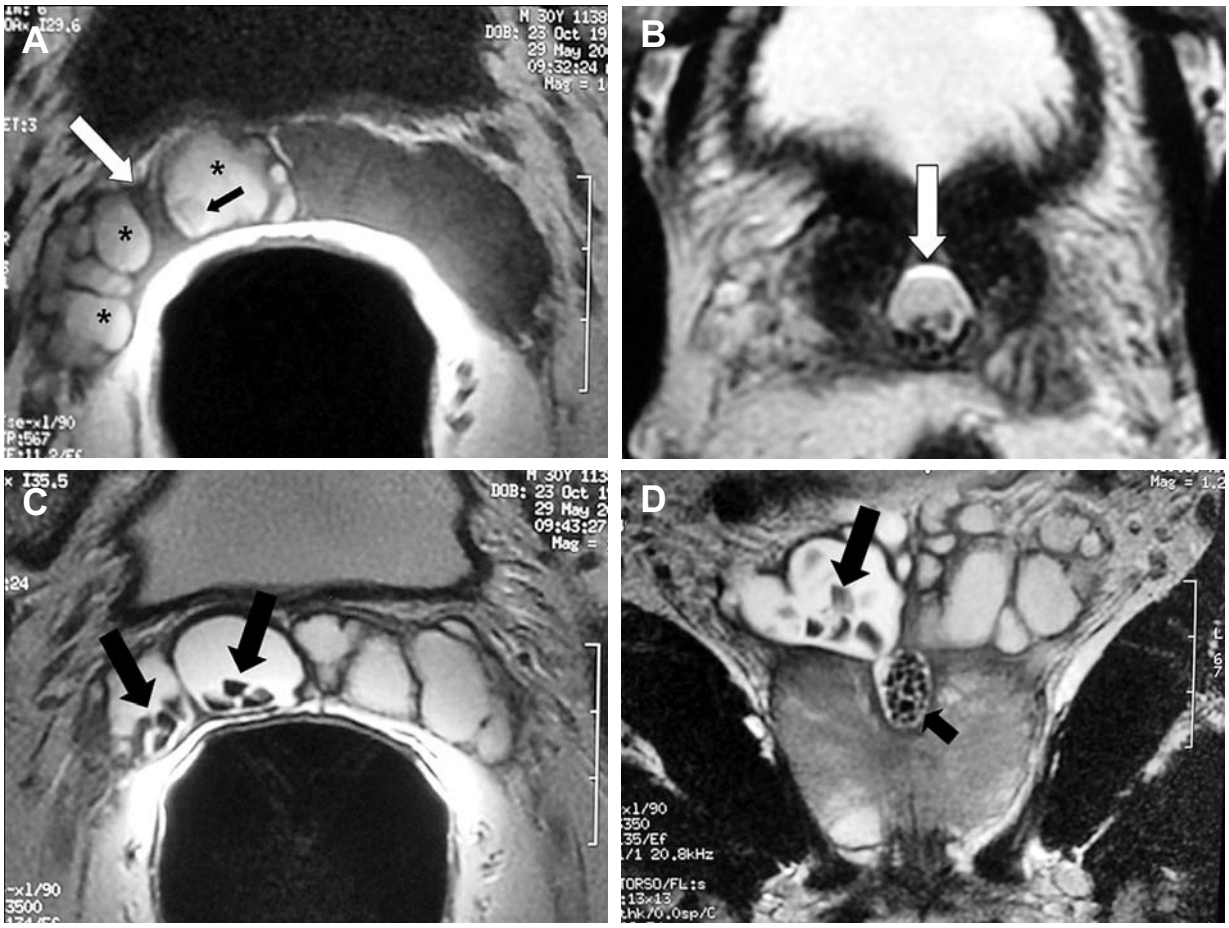

Figure 3 – *Hemorrhagic seminal vesicle associated with calculi within the right seminal vesicle and dilated ejaculatory duct. A 30-year-old man, with history of persistent hemospermia and ejaculatory pain. A) E-MRI, axial plane, T1-weighted image, showing a hemorrhagic dilated ejaculatory duct (white arrow), containing blood (asterisk) and calculi (black arrow). B) E-MRI, axial,T2-weighted image ,better shows the calculi within the dilated ejaculatory duct (arrow). C) and D) E-MRI, axial and coronal T2-weighted images respectively, nicely demonstrates the presence of several stones within the right seminal vesicle (arrows) and within the dilated right ejaculatory duct (small arrow). Note the contiguity of the dilated seminal vesicle with the dilated right ejaculatory duct. This is an essential finding for the differentiation between dilated ejaculatory cyst from midline prostatic cyst.*

and malignancies. Contrary to TRUS, MRI has the ability to accurately identify hemorrhage within the seminal tract due to its characteristic signal behavior (high signal intensity on T1-weighted images).

Imaging studies have considered a wide range of etiological factors for hemospermia: prostatic calcification, prostatic hypertrophy, prostatitis, midline prostatic cyst (utricular), midline extra-prostatic cyst, seminal vesicle cyst or calculi, dilatation of the seminal vesicles or the ejaculatory ducts, ejaculatory duct cyst, blood within normal or thick-walled seminal vesicle (seminal vesiculitis) or the ejaculatory duct, seminal vesicle amyloidosis, periprostatic varicosities and prostatic carcinoma (5-11,13-17).

Some of these abnormalities such as prostatic hypertrophy, dilatation of the seminal vesicle(s), prostatic calcification and non-complicated midline prostatic cyst, can be found in asymptomatic patients. Seminal vesicle(s) dilatation for example, has been described as a very common cause of hemospermia (9,12,14) but it is known that various filling states of the seminal vesicles are quite normal. For this reason, we are speculating that perhaps there is a tendency to consider many incidental and common

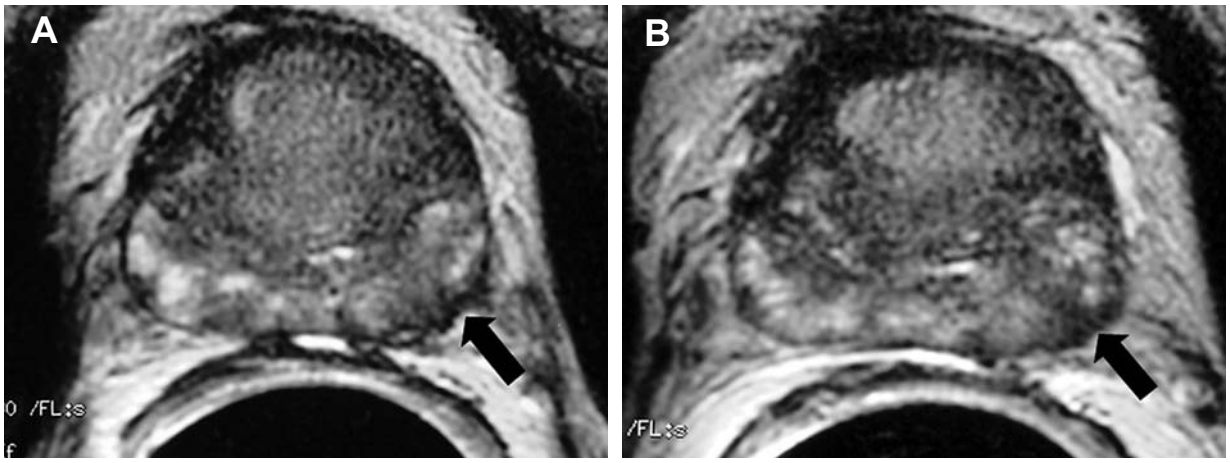

Figure 4 – *Prostate cancer. A) and B) E-MRI, axial plane, T2-weighted images showing focal area of low signal intensity in the lateral aspect of the left peripheral zone (arrow) associated with irregular thickening of the capsule of the prostate. TRUS-guided biopsy directed by these findings, allowed the diagnosis of prostate cancer, Gleason score (3+4).*

urological abnormalities as the etiological factor of hemospermia (14,18,19). This could possibly explain why the success rate of the treatment was variable in our small series of patients. Transurethral endoscopic treatment was more effective in patients with clear obstructive findings and failed in 3 patients with non-complicated, non obstructive, midline prostatic cyst. This mechanism could also explain why therapy with antimicrobial and or anti-inflammatory drugs was more effective in patients with evident manifestation of seminal vesiculitis and failed in the majority of patients with hemorrhagic seminal vesicle. Although the lack of histological confirmation of chronic seminal vesiculitis (no seminal vesicle biopsy) is a limitation of our study, we may assume that our imaging criteria for chronic seminal vesiculitis is correct since in most of the patients with this MRI findings, hemospermia disappeared after adequate antimicrobial/anti-inflammatory treatment.

In conclusion, E-MRI should be considered the modality of choice for the evaluation of patients with persistent hemospermia. In our series, the most significant E-MRI findings were: hemorrhagic seminal vesicle and ejaculatory duct, isolated or associated with complicated midline prostatic cyst; hemorrhagic chronic seminal vesiculitis, isolated or associated with calculi within dilated ejaculatory ducts, hemorrhagic seminal vesicle associated with calculi within dilated ejaculatory duct or within seminal vesicle, non-complicated midline prostatic cyst and prostate cancer. Successful treatment was, in fact, more frequent in patients with chronic inflammatory and/or obstructive abnormalities.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

Hemospermia can be considered a challenging situation for both urologists and radiologists, given its relatively high prevalence and poor understanding. Transrectal ultrasound, despite being a good modality for prostate evaluation and guided-intervention, has limited applications for dedicated seminal vesicles imaging, especially regarding identification of blood within the ducts (1). The article from Dr. Prando confirms the evolving role of Magnetic Resonance Imaging (MRI) in the evaluation of hemospermia and other seminal vesicles diseases, since it combines high spatial resolution with outstanding

contrast resolution (the ability to characterize different structures and components, like blood). Endorectal MRI is now considered the modality of choice for local staging of prostate cancer, including seminal vesicles invasion (2). The development and increasing availability of 3 Tesla MR scanners can further improve the application of this imaging modality in the evaluation of the seminal vesicles, since its intrinsic high signal intensity might exempt the need for an endorectal coil (3). Nowadays, regardless these specific technological aspects, we can confidently state that MRI is the imaging modality of choice for evaluation of hemospermia and other seminal vesicles diseases.

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EDITORIAL COMMENT

In his paper published in this issue of the International Brazilian Journal of Urology, Prando presents an overview of abnormalities found at endorectal coil magnetic resonance imaging (MRI) in patients with persistent hemospermia.

The use of MRI instead of imaging modalities such as transrectal ultrasonography or computed tomography seems quite evident. Magnetic resonance imaging allows direct multiplanar image acquisition and offers superb soft tissue contrast, enabling accurate depiction and characterization of soft tissues within the pelvis and facilitating the demonstration of blood products within the male reproductive system. When combined with an endorectal coil, the image resolution can be further increased, providing unsurpassed image detail of the prostate gland, ejaculatory ducts and seminal vesicles. Hence, Prando found abnormalities that were directly related to hemospermia in about 60% of cases.

On the other hand, uncomplicated hemospermia usually has only minor clinical significance and needs no immediate imaging evaluation, especially in younger patients (less than 40 years of age). However, in cases of persistent or complicated hemospermia, it can be very disquieting for patients and frustrating for urologists to have no information about the location or the etiology of the bleeding. So far, transrectal ultrasonography has been the examination of first choice in these patients. It is a relatively inexpensive and readily available technique that allows the identification of benign prostatic hyperplasia, dilated ejaculatory ducts or seminal vesicles, and obvious lithiasis, cystic lesions, or tumors. On the other hand, transrectal ultrasound cannot directly prove the presence of blood products within the ejaculatory ducts or seminal vesicles and will fail to disclose more subtle abnormalities. Although computed tomography (CT) can readily demonstrate the presence of calcifications and high-density blood within the seminal ductal system, its diagnostic application is hampered because of its low tissue discriminating ability (all structures in and around the prostate and seminal vesicles have about the same density, and also contrast-enhancement is not usually helpful), and because of its radiation exposure, which is not trivial

in the younger patient group. MRI does not suffer from the abovementioned inconveniences.

We strongly believe, however, that in the majority of patients with hemospermia no immediate imaging evaluation is required. Furthermore, transrectal sonography remains a valid and readily accessible primary technique to disclose more obvious abnormalities of the prostatovesicular complex. However, in complicated or persistent hemospermia, certainly in patients above 40 years of age, MRI may have the potential to disclose more subtle abnormalities that remain obscure on transrectal ultrasonographic examination. Although we are currently not aware of any study having directly compared the diagnostic value of transrectal ultrasound with that of MRI, it is not unreasonable to expect that MRI might become the imaging modality of first choice to evaluate patients with persistent or complicated hemospermia.

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EDITORIAL COMMENT

I read with great interest the article by Dr. Prando in which he evaluates findings of endorectal magnetic resonance (E-MRI) in patients with persistent hemospermia. Although in the majority hemospermia is a benign and self-limiting condition, the question lies in how to investigate these patients. To date, a small number of studies using an endorectal coil for evaluation of patients with hematospermia have been published. Magnetic resonance is the current gold standard for imaging the accessory sex glands and their ducts and, E-MRI promotes an excellent multiplanar anatomic evaluation of the prostate gland, seminal vesicles and ejaculatory ducts. However, we know that transrectal ultrasonography (TRUS) is an effective and widely used technique as a primary modality for patients with hemospermia. TRUS can also detect dilatation, cysts and stones in the seminal vesicles, prostate and ejaculatory ducts. The greatest advantage of E-MRI over TRUS is its ability to reveal hemorrhage in the seminal vesicles or prostate. I also agree that Dr. Prando imaging criteria for chronic seminal vesiculitis is by far superior to those that we can infer by using TRUS. Probably, the addition of contrast gadolinium further improves resolution of magnetic resonance for inflammatory signs.

Infective cause in the urogenital tract is the most common etiological factor. Dr. Prando confirms findings of inflammatory conditions as a common association with hemospermia and this is demonstrated in recent studies where current laboratory techniques detected a pathogen in 75% of cases of hemospermia (1).

In summary, current evidence suggests that, for patients with persistent hemospermia, endorectal coil MRI should be performed when TRUS is unsatisfactory or nondiagnostic.

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Gynecologic-Tract Sparing Extra Peritoneal Retrograde Radical Cystectomy with Neobladder

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ABSTRACT

Objective: We report on a series of female patients with transitional cell carcinoma of the bladder who underwent extra-peritoneal retrograde radical cystectomy sparing the female reproductive organs with neobladder creation.
Materials and Methods: 14 female patients between the ages of 45 and 72 years who underwent gynecologic-tract sparing cystectomy (GTSC) with neobladder between 1997 and 2002 were retrospectively reviewed. Our surgical technique is also described. Radical cystectomy is accomplished by a retrograde method sparing the uterus, adnexa, vagina and distal urethra. An orthotopic neobladder was constructed using small bowel or sigmoid colon, brought extraperitoneally, and anastomosed to the distal urethra.
Results: Operating time ranged from 4.5 to six hours with a mean of 5.3 hours. Ten patients were able to void satisfactorily while four required self-catheterization for complete emptying of the bladder. Seven patients were continent day and night and another 7 reported varying degrees of daytime and nighttime incontinence. One patient died of metastases and another of pelvic recurrence. There were no urethral recurrences. Patient satisfaction with the procedure was high.
Conclusions: Gynecologic-tract sparing cystectomy with orthotopic neobladder is a viable alternative in female patients with muscle invasive traditional cell carcinoma of the bladder, providing oncological safety with improved quality of life. Our extraperitoneal technique, which is an extension of our successful experience with retrograde extraperitoneal radical cystectomy in men, minimizes intraoperative complications and simplifies the management of post-operative morbidity with the neobladder.

Key words: *female; bladder neoplasm; carcinoma, transitional cell; cystectomy; urinary diversion*
Int Braz J Urol. 2008; 34: 180-90

INTRODUCTION

Over the past decade, radical cystectomy with orthotopic neobladder has become a popular treatment for muscle-invasive bladder cancer in females (1). This change has occurred due to a better understanding of the anatomy of the bladder neck, urethra, and continence mechanism in females and improvements in surgical technique. Recently there has been considerable interest in preservation of the gynecological tract to maintain sexual function without compromising oncological principles. It is clearly established that the continence mechanism in females depends on the striated sphincter and sexual function on the maintenance of adequate vaginal length and intact nerve supply to clitoris. Furthermore, an intact uterus with its adnexa allows reproductive function to be preserved in young patients who undergo radi-

cal cystectomy. The issue of oncological safety of a urethra-sparing cystectomy has been addressed by several authors (2,3) and is feasible and safe. We undertook refinements in our extra-peritoneal retrograde technique of cystectomy in males and extended it to females to preserve the gynecologic tract. The authors report their experience of extra-peritoneal retrograde radical cystectomy sparing the female reproductive organs (gynecologic tract) with orthotopic neobladder.

MATERIALS AND METHODS

Of the 237 patients who underwent radical cystectomy at our institution for muscle invasive transitional cell carcinoma of the bladder between January 1997 to December 2002, 178 patients were males and 59 were females. Of the 59 female patients, 14 underwent gynecologic-tract sparing cystectomy (GTSC) while the other 45 had ileal conduits. Age ranged from 45 to 72 years. All patients had biopsy proven muscle-invasive transitional cell carcinoma of the bladder with no evidence of lymphadenopathy or extravesical spread on clinical evaluation and imaging studies. Patients with diffuse carcinoma-in-situ or tumors involving the bladder neck were excluded, as were patients with a poor performance status. Other exclusion criteria were patients who were unable to perform self-catheterization due to obesity; problems with manual dexterity or lack of suitable assistance were also excluded. Patient motivation was assessed and only patients who understood the implications of a neobladder and were willing to self catheterize were included. All patients were continent prior to cystectomy. Patients in whom close follow-up was difficult were also excluded. Informed consent was obtained from all patients. All patients had a serum creatinine of less than 1.8 mg%. A thorough pre-operative gynecological checkup including a vaginal Pap smear to rule out any co-existing gynecological condition was done in all patients. All 14 patients underwent gynecologic-tract sparing cystectomy and creation of a neobladder as described below. Post-operatively the urethral catheter was removed at 3 weeks and patients were started on a regimen of clean intermittent self-catheterization 5-6 times per day, which was later discontinued in patients who voided satisfactorily.

Patient voiding patterns and continence were assessed by means of a questionnaire and personal interviews as well as a voiding diary. As no quality of life questionnaire had been validated for use in the subset of Indian female patients, we created a physician-administered questionnaire in the regional language. A patient was considered continent if she required no more than one pad for the loss of small quantities of urine during the night (from going to bed to getting up in the morning) or the day. Post-void residual urine was assessed by means of self-catheterization after spontaneous voiding.

Surgical Technique

Our technique of gynecologic-tract sparing cystectomy (GTSC) and neobladder was based on our experience gained in the performance of radical cystoprostatectomy by the retrograde method in male patients as reported previously (4). Bowel preparation is started on the morning of the day before operation and includes the administration of two liters of polyethylene glycol solution and oral antibiotics. A site for a stoma is marked in conjunction with the stoma therapist in case it becomes necessary to create a conduit. The patient is placed in the supine position on the table with her legs slightly abducted on the table allowing access to the urethral meatus. A 18F Foley catheter is passed and the balloon inflated to 20 cc. Betadine soaked pack is inserted in the vagina. Abdomen is opened through an infra-umbilical midline incision and the transversalis fascia incised. The peritoneum is swept cephalad and extra peritoneal space is explored. Bilateral pelvic lymphadenectomy is performed from the common iliac artery bifurcation all along the external iliac artery and vein to the femoral canal distally and obturator nerve medially. Frozen section examination is used only when the tissue appears highly suspicious. Further, if frozen section reveals positive nodes the lymphadenectomy is extended to the level of the inferior mesenteric artery. The bladder is retracted cephalad and fibrofatty tissue is removed from the retropubic space to expose the bladder neck (Figure-1). The dorsal venous

complex is ligated and divided and the endopelvic fascia incised on both sides. By sharp dissection, the urethra is dissected from its attachments to the vagina 2 cm below the bladder neck and is hooked with a right angle clamp (Figure-2). The anterior wall of the urethra is incised 1-2 cm below the bladder neck, the catheter removed, clamped proximally to prevent balloon deflation, and divided and then the posterior wall of urethra is divided. Six to eight 3-0 vicryl sutures are placed in the distal cut end of the urethra with the needles on the luminal surface and retained for later anastomosis to the neobladder. The proximal urethral end is held with the catheter and by gentle traction, the urethra with the bladder neck is dissected off the vaginal vault. Continued traction on the catheter prevents leakage of urine from the bladder into the operative field. There is generally fibro-fatty tissue between the vagina and bladder neck, which requires sharp and blunt dissection. Carefully without injuring the vault of vagina and paravaginal tissues, the bladder is lifted off the anterior vaginal wall and uterus (Figure-3). The vascular pedicles to the bladder are ligated and divided in retrograde fashion. Bladder with its fascia is next lifted off the peritoneum over the uterus, or in patients who have had a previous hysterectomy over the vault of the vagina and the rectum. The dissection proceeds further proximally and paravesical tissues and obliterated hypogastric pedicles are ligated and cut. The ureters are divided last and the cut ends are sent for frozen section examination. The urachus is ligated and divided and the specimen removed. In many instances, it is possible to remove the bladder without opening the peritoneum; if peritoneum is adherent to the dome of the bladder or when the tumor involves the dome of the bladder, it may be excised with the specimen. After the specimen is removed, wedges of tissue from the bladder neck and urethral cut margin are sent for frozen section examination. The peritoneum is opened for a short distance if not previously done and a segment of ileum extending 60 cm proximally from a point 15 cm proximal to the ileocecal junction is isolated on a vascular pedicle and

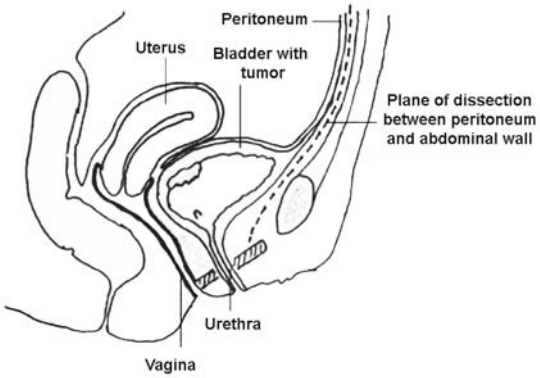

Figure 1 *– Relevant anatomy showing initial plane of dissection.*

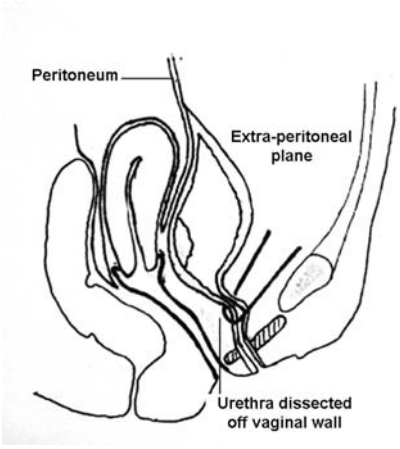

Figure 2 *– Anterior dissection dissecting urethra from anterior vaginal wall.*

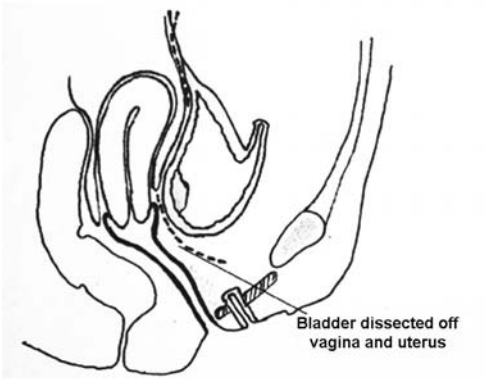

Figure 3 *– Dissection proceeding, lifting bladder from vagina and uterus.*

bowel continuity restored by end-to-end anastomosis, after ensuring that the segment reaches the urethra. The peritoneum is closed around the pedicle of the ileal segment, thus isolating it from the peritoneal cavity. The neobladder is then created as described by Hautmann. Briefly, the bowel is detubularised and sutured in a W configuration to create a plate and the ureters are implanted creating serosa-lined extra-luminal tunnels. In all cases, ureteric length was sufficient to allow easy reimplantation. In one patient a sigmoid colon neobladder, as described by Reddy (5) was created because of a previous medical history of ileocecal tuberculosis.

The neobladder is anastomosed to the urethra using the pre-placed vicryl sutures over a 20F Foley catheter, and lies extraperitoneally (Figure-4). Drains are placed and the incision closed.

During dissection of the urethra, care is taken not to dissect anterior and distal to the level of the transection, to ensure preservation of the pubo-urethral and urethropelvic ligaments. While dissecting lateral to the bladder it is advisable to avoid injury to paravaginal tissues so that the branches of the pelvic nerve plexus, which course laterally to the vagina, can be preserved.

RESULTS

Follow-up ranged from 18 to 71 months with a mean of 32.5 months. Operative time was between 4.5 and 6 hours with a mean of 5.3 hours. In one patient who had undergone a previous hysterectomy for menorrhagia the vagina was preserved. In all other patients the vagina, uterus and adnexa were preserved. Blood loss ranged from 300-1500 cc and three patients received transfusions. No patient suffered early or late complications requiring intervention. There was no perioperative mortality.

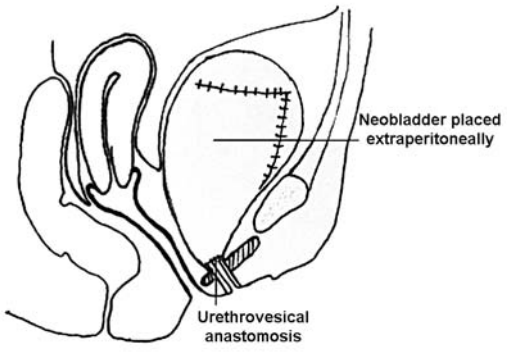

***Figure 4** – Neobladder in extraperitoneal pelvic space.*

One patient with T3bN2 grade tumor died of metastases 13 months after surgery. Another patient with T2bN1 grade tumor was diagnosed as having a pelvic recurrence and died at 26 months. The recurrence was on the lateral pelvic wall and distant from the urethra. Of the remaining 12 patients, 10 are alive and well with no evidence of disease, while 2 are lost to follow up. None of these had urethral recurrences. Details of patients are given in Table-1.

Ten patients were able to void satisfactorily, with post-void residual volumes ranging from 0-100 cc. Four of these patients required self-catheterization twice daily to empty completely the bladder and six voided with insignificant post-void residue. Remaining four patients are unable to void, requiring regular self-catheterization to empty their neobladders.

Seven of the 14 patients are continent by day and night. Of the remaining 7 patients, 3 have significant daytime and nighttime incontinence, 2 report nighttime wetness only which is managed using pads, and 2 have significant daytime-only incontinence.

Asymptomatic bacteriuria occurred in 9 patients. Two patients had recurrent episodes of clinically significant urinary tract infection that required institution of long-term antibiotic prophylaxis. One patient developed a rise of serum creatinine to 2.3 mg% from a baseline level of 1.6 mg%. Renal function in all other patients remained stable on follow-up.

Patient satisfaction after the operation was high, with most patients happy that they had opted for a neobladder as against an ileal conduit.

COMMENTS

Orthotopic neobladder has become an increasingly popular form of urinary diversion in male patients with muscle invasive bladder cancer who are candidates for radical cystectomy. However, female

Table 1 *– Summary of patients.*

Pte	Age	Neo-bladder	Pathology	Daytime Continence	Nighttime Continence	Voiding	CISC	Comments	Follow-up (months)
1.	68	Ileal	T2N0	no	no	Spontaneous	Yes	NED	65
2.	62	Ileal	T1N0	yes	yes	Hypercontinent	Yes	NED	36
3.	72	Ileal	T3N2	yes	no	Spontaneous		Died of mets at 13 months	13
4.	65	Ileal	T3N1	no	yes	Spontaneous	Yes	NED	29
5.	65	Ileal	T3bN1	yes	yes	Spontaneous		NED	29
6.	58	Ileal	T2N1	yes	no	Spontaneous	Yes	NED	27
7.	45	Ileal	T4N0	yes	yes	Hypercontinent	Yes	NED	27
8.	63	Ileal	T2N0	no	no	Spontaneous		NED	23
9.	62	Ileal	T2N1	yes	yes	Hypercontinent	Yes	Died at 26 months	26
10.	70	Ileal	T2N0	yes	yes	Hypercontinent	Yes	NED	20
11.	68	Ileal	T2N0	no	yes	Spontaneous		NED	18
12.	65	Ileal	T2N0	yes	yes	Spontaneous	Yes	NED	17
13.	64	Ileal	T2bN0	no	no	Spontaneous		NED	12
14.	55	Sigmoid	T3N0	yes	yes	Spontaneous		NED	12

NED = no evidence of disease; CISC = clean intermittent self catheterization.

patients with the same disease have traditionally been offered continent cutaneous stomas or ileal conduits. Although the literature on quality of life following radical cystectomy is divided on the relative benefit of cutaneous diversion vs. orthotopic diversion, some authors have shown that quality of life is better preserved after orthotopic diversion (4). The reasons why orthotopic diversion was not previously offered are two-fold. Traditionally radical cystectomy in female patients included total urethrectomy as a part of optimum oncological clearance. However, pathological studies in female radical cystectomy specimens have demonstrated that the urethra is rarely involved in the absence of extensive carcinoma in situ (6). In a literature review, Stein et al. identified bladder neck involvement and anterior vaginal wall involvement as risk factors for urethral involvement (7), this has allowed a subset of female patients to be identified in whom the distal 2 cm of the urethra can be preserved at radical cystectomy, allowing an orthotopic reconstruction to be performed. Subsequent experience with female neobladders has confirmed the oncological safety of sparing the urethra. Recent understanding of the continence mechanism and voiding in females has led to an increasing number of investigators creating neobladders with excellent results (6-8). Furthermore, Chang et al. (9) reported preservation of the anterior wall of vagina to provide better support to the distal urethra leading to better continence and decreased incidence of prolapse of the neo bladder and lower incidence of neo bladder-vaginal fistula. Additionally vaginal length helped better sexual function.

In the past, radical cystectomy in females included an anterior exenteration i.e. removal of the bladder, urethra, uterus, fallopian tubes, ovaries and anterior wall of the vagina. Recently the oncological

necessity for removal of the internal genital organs has been questioned. Groutz et al. examined the cystectomy specimens of 37 patients with bladder cancer and found uterine involvement by transitional cell carcinoma in only 1 patient (10). Chang et al. (11) looked at the involvement incidence of the internal genitalia in 40 anterior exenteration specimens; traditional cell carcinoma was identified in 2 of them, and in both gross involvement had been identified during operation. In one patient uterus showed the presence of a low-grade stromal sarcoma. They concluded that in the absence of clinical suspicion removal of the uterus and its adnexa rarely improves cancer control. More recently in a series of 609 female radical cystectomies, Ali-El-Dein et al. (12) reported a 2.6% rate of concomitant gynecologic organ involvement by bladder cancer and a 0% rate of primary genital cancer. The preservation of the uterus and its adnexa is desirable in a younger patient who wants to retain reproductive function. Moreover, Chang et al. (9) suggested that preservation of the uterus and its supports may prevent the dead space that otherwise would be filled by small bowel which in some may produce anterior enterocele following cystectomy as was reported by Anderson et al. (13). Horenblas et al. (14) reported on "sexuality preserving cystectomy" in 3 female patients with bladder cancer, using a retrograde method. No patient had a local recurrence, and all patients achieved satisfactory daytime and nighttime continence. One patient developed a vaginal urinary fistula and was converted to a continent catheterizable stoma. Vaginal lubrication and orgasmic feeling were reported to be normal after surgery. Preservation of branches of the pudendal nerve to the clitoris is essential for normal sexual sensation, and the uterus has been reported to have a role in orgasmic sensation (15). Several authors have described radical cystectomy by a retrograde technique. Hautmann (16) has used this approach in female patients during anterior exenteration while sparing the anterior vaginal wall and urethra preparatory to neobladder creation. More recently, Dhar et al. have reported nerve sparing radical cystectomy and orthotopic bladder replacement in female patients (17).

The oncological outcome in our group of patients was satisfactory, with 2 deaths out of 14 at a mean of 32 months. Notably no patient suffered a recurrence in the region of the urethra. As most urethral recurrences in male patients following radical cystectomy have been shown to occur within 19 months (18), this seems to indicate that urethral recurrence in the future will be unlikely. As shown by Stein et al. (6), patients with an uninvolved bladder neck rarely have urethral involvement. However, for greater safety they advise intraoperative frozen section biopsy of the distal surgical margin, which we follow. While the utility of sparing the uterus and ovaries in older female patients may be questioned, it is emphasized that the aim of sparing the uterus in this group is not reproductive ability but voiding function by preventing sagging of the pouch.

In our series 72% (10/14) patients were able to void spontaneously, while 28% (4 /14) unable to void. Four out of the 10 patients who were able to void were advised self-catheterization twice daily for complete bladder emptying. None of these patients reported urinary leakage and all expressed satisfaction that they were able to perform their daily activities without fear of wetting. Compliance with self-catheterization was adequate and pouch infections were not a problem. 64% of patients were continent by day: the remainder had low-volume leaks that could be easily managed by pads. A similar number who had nocturnal leakage of urine could manage their low-volume incontinence using pads. Though a 36% incontinence rate may seem high, management with pads is low cost and acceptable compared with the external appliances required with an ileal conduit, which in a developing country are unaffordable to many and not easily available in many areas. A majority of patients expressed satisfaction with the functional outcome.

We in the past reported our extra peritoneal retrograde approach for radical cystectomy in males (19) with the aim of complete closure of the peritoneal hiatus thus separating the GI tract from neobladder or ileal conduit. Bowel handling is minimized and the need to pack the bowels into the upper abdomen using towels is obviated. The morbidity is reduced and the management of urinary leak is simplified. Moreover, the left ureter does not cross the sigmoid mesentery reducing the incidence of left uretero ileal anastomotic stricture and improved preservation of the left upper tract. We extended the same technique of extra peri-

toneal retrograde approach for radical cystectomy in females followed by neobladder. This approach in 14 patients gave us excellent results in terms of minimal post-operative morbidity and long-term benefits. Retrograde approach for cystectomy has been reported by others using the trans-peritoneal route. However, we have been using the extra-peritoneal route as described previously and we are quite satisfied with the oncological safety and benefit of a peritoneal surface separating the GI tract from the neobladder resulting in reduction in morbidity, leak, and early return of peristalsis. Uretero-enteric anastomotic stenosis or neobladder-vaginal fistula has not been observed in our series mainly because of intact vaginal vault and no crossing of the left ureter.

CONCLUSION

We have here described a technique of performing radical cystectomy with orthotopic neobladder in selected female patients by a retrograde method with preservation of the internal genital organs. Early results are promising with regard to voiding function and patient satisfaction.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

Cystectomy has been the mainstay of aggressive bladder cancer treatment for years. Classic radical cystectomy in women involves en bloc removal of the bladder, uterus, ovaries, anterior vaginal wall and urethra. Acceptable oncological and functional results of orthotopic urinary diversion in men and better understanding of the female continence mechanism have, in the past decade, led to the fact that orthotopic neobladder has been established as an oncologically and clinically safe and good acceptable option of urinary diversion in appropriately selected women. With proper patient selection, preservation of the female urethra has been shown to be safe, although it was an initial oncological concern. Over the years, we have learned that bladder neck involvement, increased grade and stage, and lymph node involvement by tumor are a major risk factor for urethral involvement. However, gynecological-tract sparing cystectomy furthermore remains permanently discussed. The potential menace of insufficient cancer control and secondary malignancies of preserved gynecologic organs persists. In this group of patients the oncological outcome was satisfactory.

On the other hand, in properly selected female patients, preserving the uterus, ovaries and anterior vaginal wall may improve the functional results. By preserving the anterior vaginal wall and pubo-urethral ligaments, the occurrence of neobladder descent and pelvic prolapse is decreased. The preservation of the uterus may be beneficial to prevent a chronic retention (hypercontinence) by providing proper back support to the neobladder.

Finally, more importantly, the nerves, which are essential for a normal sexual response, are usually removed and damaged in standard cystectomy, and the surgery leads to the loss of proper sexual function.

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EDITORIAL COMMENT

The authors describe their technique in women with bladder cancer of retrograde radical cystectomy with sparing of the anterior vaginal wall and, when present, the uterus and ovaries, followed by an extraperitonealized orthotopic neobladder. Increasingly, efforts are made to avoid the traditional anterior pelvic exenteration, where radical cystectomy in the female is combined with total hysterectomy and bilateral salpingo-oophorectomy. Transitional cell carcinoma involves the uterus, vagina, or cervix in less than 3% of women with bladder cancer, all of whom have grossly locally advanced disease (1-3). The preservation of the vagina and uterus can have tremendous benefits to the clinical outcome and health-related quality of life (HRQOL) of the patient. Too often the sexual concerns of women are overlooked. Sexual dysfunction following radical cystectomy in the female is correlated with the magnitude of vaginal preservation. Furthermore, the risk of potentially devastating postoperative complications such as neobladder vaginal vault prolapse, enterocele formation, and neobladder-vaginal fistula, that occasionally mandate conversion to cutaneous diversions, may be reduced with preservation of the uterus and vagina (4). Similarly, extraperitonealization of the orthotopic neobladder may reduce the incidence of both bowel and urinary complications, or at the very least, reduce their severity when they occur. The authors' technique carries the promise of improved perioperative outcomes with the potential for better long-term HRQOL than standard procedures.

However, we must consider the findings of this study in the context of its own limitations: the absence of a comparison group and the use of physician-centered outcomes. I agree that intuitively, the major considerations in this technique, namely preservation of the gynecologic organs and extraperitonealization of the diversion, likely enhance patient-centered outcomes. Yet as we advance clinical care, we are obligated to validate our progress. Beyond utilization of comparison groups, we have yet to elucidate the HRQOL measures that calibrate a patient's satisfaction following radical cystectomy and urinary diversion. Many analyses have attempted to compare continent to incontinent diversions, with mixed results (5-9). The author's difficulty identifying an appropriate questionnaire with which to assess their patients highlights the difficulty in measuring HRQOL in this population. Can one instrument compare HRQOL across urinary diversions and patient gender?

The authors present a technique that may improve both perioperative and long-term clinical outcomes following radical cystectomy for bladder cancer. Yet the article also underscores the need for studies that employ experimental methods and appropriate measures of surgical results.

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EDITORIAL COMMENT

Two elements stand out in this study on cystectomy in females.

In the first place the preservation of all internal genital organs and secondly the retrograde extraperitoneal approach.

Standard cystectomy in females comprises of the complete removal of internal genitals together with a part of the vagina. While this may have been oncologically sound in older days, it seems over treatment at this moment. Involvement of the genital tract by urothelial cancer in contemporary series is a very rare event. In all cases, preoperative staging reveals invasion of the genital tract by urothelial cancer. This has been documented by a variety of authors as described in this paper. In addition, risk factors for urethral involvement and therefore a contraindication for this type of surgery have been defined with great certainty. Despite these rational arguments in favor of this type surgery, daily practice remains so far largely unchanged.

I see at least one reason. Bladder cancer, especially muscle invasive bladder cancer, has a poor long-term survival even in the most favorable conditions. Local recurrences should be avoided at all cost, as they portend a lethal end in almost all cases. Fear of local recurrences has withheld many colleagues to embark on this type of surgery. While this may seem reasonable, recent reports like this one testify to the safety of "sexuality preserving cystectomy". In a comparison, done at our institute, no more local recurrences were found in the group of patients treated with a "sexual preserving cystectomy" compared to patients undergoing a standard cystectomy (submitted for publication). With a follow up of more than 10 years now, I consider this type of surgery in well selected patients oncologically safe.

Also interesting is the extraperitoneal approach used by the authors. Some details caught my attention.

In the first place the closure of the peritoneum around the mesentery of the neobladder. While no scientifically sound comparison was done between this method and the standard closure, this could very well be a factor of importance in decreasing the postoperative complications.

The retrograde fashion leads to early dissection of the bladder neck. The authors use the inflated balloon to decrease the risk of tumor spill. I would suggest two other measures in order to further decrease this risk: closure of the bladder neck around

the balloon and early transection or clipping of the ureters.

Although the authors should be applauded for adding new proof of safety for this type of surgery, I am somewhat concerned about the functional results.

In the first place no information on sexual functioning is given. This was apparently not assessed. In the second place the incontinence rate of more than 35%. This needs to be analyzed as, also in underdeveloped countries, this rate of incontinence is in need of improvement.

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Small Intestinal Submucosa for Patch Grafting after Plaque Incision in the Treatment of Peyronie's Disease

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ABSTRACT

Objective: Report the results using porcine small intestinal submucosa (SIS) as a graft material in the surgical management of Peyronie's disease (PD).
Materials and Methods: We performed a retrospective chart review of men with PD who underwent surgical correction of the curvature by plaque "H" incision and patch grafting with 4-ply SIS (Cook, Bloomington, IN) by a single surgeon at our institution. Degree and direction of curvature, sexual function, and co-morbidities were assessed pre- and postoperatively.
Results: Thirteen patients were identified. Mean age was 57 ± 8, range 42-70 years. Median follow-up was 14 months, range 3-89 months. At presentation, all reported penile curvature. Also reported were difficulty with vaginal penetration (determined by question number 2 of the sexual encounter profile questionnaire – SEP2),
palpable plaque, hourglass deformity, difficulty with firmness, and difficulty with sustaining erection (determined by SEP3) in77%, 69%, 77%, 62%, and 46% of patients, respectively. Mean and median degrees of curvature of the primary deformity were 71 and 67.5 degrees, respectively. Three patients had secondary curves of less than 30 degrees in a different direction. Mean and median plaque size were 3.5 and 2.7 cm^2, respectively. Seven patients had one graft and six patients had two grafts placed with a mean size of 15 ± 0 cm^2.
Conclusions: For the patient with PD, SIS grafting can achieve a functionally straight erection with durable results yet with relatively high rates of erectile dysfunction. SIS is a viable graft material for use in the surgical treatment of PD.

Key words: *penis; Peyronie's disease; surgery; graft; small intestinal submucosa*
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INTRODUCTION

Peyronie's disease (PD) is a condition of plaque formation in the tunica albuginea of the corpora cavernosa with resultant curvature of the penis (1). The disease has two phases; an early acute phase associated with painful erections and progression of deformity, and a later chronic phase in which the pain ceases and the deformity is stabilized. Conservative medical therapy is the initial treatment of choice for patients with acute phase disease. A variety of medications has been utilized including vitamin E, para-aminobenzoate potassium, tamoxifen, colchicine, and verapamil. In addition to oral therapy, intralesional

injections and various forms of energy have been applied for the treatment of PD (2). Few medical therapies have been proven effective in large scale trials. Surgical correction is the treatment of choice when the deformity precludes intercourse, but should not be considered until the disease has reached its stable, chronic phase.

Surgical options for the management of PD can be divided into 3 types: procedures that shorten the convex, uninvolved side of the tunica albuginea, procedures that lengthen the concave, diseased side, and implantation of a penile prosthesis (3). Ellipsoid resection and closure of the tunica albuginea on the healthy convex side, as first described by Nesbit, was the previous standard for surgical care (4). Subsequently, successful variations including a Heineke-Mikulicz procedure and multiple parallel plications have been reported (5,6). These procedures are limited by a shorter postoperative penile length that precludes their use in patients with large plaques, severe deformities, or small penises (3). For these patients, superior results may be obtained using tunical lengthening procedures where incision or excision of the tunical plaque is followed by interposition of a graft material to bridge the resulting defect in the tunica. Plaque incision utilizing autologous materials such as saphenous vein as patch grafts for the incised defect has been reported to result in high rates of patient satisfaction (7,8). Drawbacks to autologous grafting are the increased morbidity of a secondary tissue harvest site and increased OR time required for tissue procurement and preparation.

Non-autologous "off the shelf" biomaterials are an attractive alternative to autologous tissue for patch grafting (3). At our institution we favor porcine small intestinal submucosa (Stratasis, Cook Urological, Spencer, IN), a xenographic biomaterial retaining matrix elements that support host cell migration and differentiation. There have been some preliminary reports describing the use of SIS in Peyronie's disease repair (9-12). We present our institution's experience with SIS grafts in 13 patients.

MATERIALS AND METHODS

Institutional review board approval was obtained for a retrospective chart review of men who underwent surgical correction of Peyronie's disease with plaque incision and patch grafting with 4-ply porcine small intestinal submucosa (Stratasis, Cook Urological, Spencer, IN) at our institution by a single surgeon between March 1999 and August 2006.

Thirteen patients were identified. Subjective difficulty with vaginal penetration, firmness, and sustaining erection as well as age, erectile dysfunction, use of pro-erectile medications, presence of palpable plaque, plaque location, hourglass deformity, foreshortened penis, degree and direction of curvature, flaccid and stretched penile length, and comorbidities (hypertension, diabetes mellitus, Dupuytren's contracture, plantar fasciitis, lower urinary tract symptoms) were included in the preoperative analysis. Sexual function was determined by SEP2.

Technique - The plaque incision and grafting procedure was carried out as detailed in prior reports (9). Briefly, subcoronal degloving incision was used with subsequent degloving of the penis down to dartos fascia to expose the anterior lamella of Buck's fascia. The area of maximal curvature was identified via artificial erection (Penrose tourniquet placement at the base of the penis and continuous corporal infusion of sterile saline). The circumflex veins were suture ligated or cauterized using bipolar current. If the plaque was dorsally located, the neurovascular bundle on the dorsal surface was mobilized under loupe magnification down to the penoscrotal junction. A relaxing incision was made in the plaque at the point of maximum curvature in the shape of the letter "H". A graft of 4 layers SIS that was oversized to be 120% of the size of the defect was hydrated in normal saline and sewn in using 5-0 PDS running sutures. Assessment of curvature was repeated. Persistent curvature was managed by a second H-incision and SIS graft or by penile plication (by the 16-dot technique of Lue) (6). The dartos was closed with a 3-0 vicryl suture and the skin with 3-0 chromic followed by a compressive Coban dressing for 48 hours.

Follow-up data was collected by the operating surgeon at follow-up office visits. Postoperative penile curvature, length, potency, use of erectile dysfunction medications, pain, and palpable plaque were recorded. Subjective (by patient) and objective (by physician) cosmetic and functional outcomes were recorded.

RESULTS

Patient demographics are shown in Table-1. Mean age was 57 ± 8 years (range = 42-70 years). The median length of follow-up was 14 months (range 3-89 months). Table-2 lists presenting symptoms and sexual function. Ten patients (77%) presented with difficulty invaginal penetration (as determined by the sexual encounter profile question 2 [SEP2]), 8 patients (62%) had difficulty maintaining firmness, and 6 patients (46%) had difficulty sustaining erection (as determined by the sexual encounter profile question 3 [SEP3]). Pre-operatively, 5 patients (38%) were potent, 7 patients (54%) were potent with phosphodiesterase-5 inhibitors, and 1 (8%) was impotent, as determined by SEP 2 and 3.

The plaque was palpable in 9 patients (69%), and 10 patients (77%) had hourglass deformity. Penile curvature was dorsal in 8 patients (62%), ventral in 2 patients (15%), and toward the left in 3 patients (23%). Three patients (23%) had secondary curves of less than 30 degrees in a different direction. The degree of primary curvature ranged from 45 to 90 degrees, with mean of 71 and median of 68. Nine plaques (69%) were located in the mid-shaft, with 2 (15%) in the proximal and 2 (15%) in the distal portion of the phallus. Mean and median plaque size were 3.5 and 2.7 cm^2, (range = 1 - 8) respectively.

Table 1 – *Patient demographics.*

Age (years)	57 ± 8	Range 42 - 70
Median follow-up (mo)	14	
Characteristics of curvature		%
Dorsal	8	(62)
Ventral	2	(15)
Left	3	(23)
Secondary curve present	3	(23)
Mean degree curvature	71	range 45 - 90
Median degree curvature	68	
Characteristics of plaque		%
Proximal	2	(15)
Mid-shaft	9	(69)
Distal	2	(15)
Mean size (cm^2)	3.5	range 1 - 8
Median size (cm^2)	2.7	
Palpable plaque	9	(69)
Waist deformity	10	(77)
Number of grafts placed		
1	7	(54)
2	6	(46)
Mean graft size (cm^2)	15 ± 10	range 1.5 - 36
Concomitant penile plication	11	(85)

Table 2 – *Presenting symptoms.*

Difficulty with vaginal penetration	10 (77%)
Difficulty maintaining firmness	8 (62%)
Difficulty sustaining erection	6 (46%)
Potency (SEP 2/3)	
Without ED medication	5 (38%)
With ED medications	7 (54%)
Not potent	1 (8%)

ED = erectile dysfunction; SEP = sexual encounter profile questionnaire.

At operation, 7 (54%) patients had one graft and 6 (46%) patients had 2 grafts placed. Mean size of graft was 15 ± 10 cm^2 (range = 1.5 - 36). Eleven patients (85%) required concomitant penile plication for residual curvature.

Postoperative results are listed in Table-3. As determined by combined stimulation test (intracaver-

Table 3 – *Postoperative data.*

Residual bend	
None	7 (54%)
Residual bend present	6 (46%)
5 degree	3 (23%)
10 degree	1 (8%)
15 degree	2 (15%)
Potency (SEP 2/3)	
Without ED medication	4 (31%)
With ED medications	2 (15%)
Not potent	7 (54%)
Waist deformity	2 (15%)
Recurrent plaque	4 (30%)

ED = erectile dysfunction; SEP = sexual encounter profile questionnaire.

nosal injection of alprostadil), seven patients (54%) had a completely straight phallus and six (46%) had residual bends of less than 15 degrees (three 5 degree, one 10 degree, two 15 degree). At follow-up, 4 patients (31%) were potent, 2 patients (15%) were potent on medication, and 7 patients (54%) were impotent (as determined by SEP 2 and 3). Two patients (15%) had hourglass deformity and there was recurrent plaque in 4 patients (30%).

COMMENTS

Plaque incision and grafting is the procedure of choice for the treatment of severe Peyronie's disease. This precludes intercourse when patients have large plaques, severe curvature, or a short phallus, which makes the loss of penile length with plication procedures unacceptable. Autologous grafts such as saphenous vein have been used as patch grafts with satisfactory results. However, non-autologous grafts have the advantage of not requiring a second harvest site, decreasing operative time and patient morbidity as well as preserving graft material, such as saphenous vein, should the patient require coronary artery bypass surgery in the future.

SIS is an extracellular matrix that is 80 to 100 μm thick and composed of mainly Type I collagen. The matrix retains angiogenic and other growth factors even after processing, and induces a rapid infiltration of native cells and neovascularization, acting as a scaffold for cell differentiation and maturation (13). A study using SIS in the fascia lata of dogs demonstrated that as early as 6 weeks after grafting, the SIS is completely replaced with a well vascularized connective tissue, a well organized collagen framework and fiber orientation identical to that of the original tissue (14). Furthermore, SIS grafting of the tunica albuginea in rabbits has shown no significant inflammatory response, corporeal fibrosis, or loss of cavernous smooth muscle content (15).

Knoll first described the successful use of SIS for the correction of Peyronie's disease in 12 patients, with good functional results and no complications or patient complaints at 11 months mean follow-up except for one recurrence requiring reoperation (9). All patients achieved potency both preoperatively and postoperatively, with one requiring intracavernous injection therapy. In a later report at 20 months mean follow-up with 97 patients, Knoll described only 6% with residual curvature of less than ten degrees and 84% of patients retaining the same degree of potency as preoperative with no penile shortening, pain, infection, hematoma, or bulging of graft site (16).

In our series of 13 patients, all deformities were straightened either completely or with minimal residual curvature. Our results are similar to Knoll, being durable with no recurrent Peyronie's disease after 14 months median follow-up, although 4 patients (30%) had recurrent plaque and 2 (15%) had residual hourglass deformity. No patients experienced infection, bulging, or immunologic reaction at the graft site. One patient had a hematoma at the surgical site that resolved spontaneously without significant sequelae.

John et al. published a case report series of 4 patients with less encouraging results, with 3 of their 4 patients suffering recurrent curvature; however, the grafts used were oversized by only 10% rather than 20% (10). The single non-recurrence was only 20 degrees, with the others being 45, 80, and 90 degrees, suggesting that the 10% oversizing may not have been sufficient to compensate for graft contracture in the more severe bends. Additionally, one recurrent bend had been previously straightened with polytetrafluoroethylene mesh and another was grafted with 1-ply rather than 4-ply SIS, making it difficult to draw comparisons with our series.

Breyer et al. also reported a much higher recurrence (37%) and complication rate (37%) using SIS grafting in 19 PD patients after 15 months mean follow-up (11). Their study used 1-ply rather than 4-ply SIS, which may explain their higher recurrence rate, as compared with our and Knoll's series (9) (both using 4-ply SIS). Also, many of Breyer's complications were minor, including hematoma (26%) and infection (5%). Furthermore, although 37% had recurrent curvature, only one required subsequent plication (5%). We feel that 1-ply SIS is too thin and contracts more, and thus only 4-ply should be used for PD grafting. Further study is clearly needed.

Most recently, Kovac and Brown compared outcomes at 22 months mean follow-up after dermal, pericardial, and SIS grafting for PD in a 36 patient

series (12). They reported better maintenance of preoperative length and rigidity in patients with SIS versus dermal or pericardial grafts as well as significant improvements in ED as determined by the Sexual Health Inventory for Men (SHIM) score (17 postoperative vs. 10.1 preoperative). This is comparable with Knoll, who reported 84% maintenance of potency, as well as Breyer, who reported no increase in ED as determined by the SHIM score.

In contrast, patients in our series had a relatively high rate of postoperative erectile dysfunction as determined by SEP 2 and 3. One patient was impotent preoperatively but a penile implant was not a covered benefit of his insurance, and he underwent grafting in order to straighten his penis in order to have intercourse with a vacuum device. Seven patients (54%) originally potent with oral phophodiesterase-5 inhibitors suffered from ED post-operatively. Possible explanations for postoperative ED rates higher than prior reports on grafting are: the large size of grafts and number of grafts needed to correct severe (60-90 degree) curvatures, ventral position of plaque, our surgical technique, and the graft itself (not precluding venous leak). Preoperatively, one of the patients had a ventral plaque, which has been shown to have the greatest likelihood of postoperative venous leak (17). The other 6 patients had curvatures of > 60 degrees, with four having 90 degree bends. Additionally, five of the patients required 2 grafts to repair the defect. Importantly, the use of various instruments (e.g, International Index of Erectile Function, SHIM score, SEP 2/3) among series to help assess ED may also contribute to differences in reported ED rates, as these instruments were not designed specifically for PD patients.

Our findings with respect to postoperative ED are similar to those of Leungwattanakij et al. who used processed cadaveric pericardium instead of SIS. Five out of 8 patients reported difficulty with erections due to venous leakage at 30 months mean follow-up (18). The authors postulated that patients with large plaque size, ventral plaque, and severe curvatures (> 60) may be more likely to have postoperative cavernosal insufficiency leading to ED.

In our study, concomitant penile plication was performed in 11 of 13 cases. In order to prevent the need for plication in addition to the incision and grafting procedure, we have since modified our surgical technique. The SIS graft is oversized by 130% instead of 120%, and the H incision is broader and larger. Moreover, we have started to excise a small, linear segment of the plaque before placement of the graft, a technique that other authors have found to negate the need for a secondary plication (19).

Weaknesses of our study include a retrospective design, small sample size, and the use of subjective assessments of satisfaction and erectile function. Future studies on graft materials for the surgical correction of PD should utilize objective means of characterizing penile blood flow, such as power Doppler ultrasonography of the penis, and objective measures of rigidity and tumescence, such as Rigiscan® nocturnal penile tumescence.

CONCLUSIONS

The results of our experience using SIS in the repair of Peyronie's disease demonstrate its efficacy in achieving a functional, straight erection with durable results. The advantages of SIS include ease of use and favorable biochemical characteristics as well as ready availability and lack of need for native tissue harvest with its attendant morbidity. Our study showed a relatively higher rate of venous leak erectile dysfunction than previously described, particularly in men with greater penile curvature at baseline. Larger studies investigating the true rates of erectile dysfunction using SIS as well as comparisons with other materials are warranted.

CONFLICT OF INTEREST

Dr. Steven B. Brandes is from Pfizer Speaker's Bureau and is also a consultant and speaker for American Medical Systems.

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EDITORIAL COMMENT

As authors described in this paper, surgical approaches for the correction of PD can be divided into three basic categories; tunical plication, plaque excision (incision) and grafting procedures, and penile prosthesis implantation. Regarding to grafting materials, saphenous vein grafts are the most widely used with acceptable outcome in long-term. However, ideal "off the shelf" biomaterial is warranted because harvesting autologous material can cause the pain at donor site and longer operative time. Various off-the-shelf materials including SIS are currently reported (1).

Authors reported on 13 patients with PD who treated with SIS grafting. Seven patients (54%) had a completely straight phallus and six (46%) had residual bend less than 15 degree after 14-month follow-up. Although only one patient had erectile dysfunction preoperatively, 7 patients were impotent postoperatively. From these results, SIS grafts would allow for satisfactory clinical results despite relatively high rate of erectile dysfunction.

However, long-term outcome of surgery for penile curvature is quite important to evaluate the durability of the procedure and treatment strategies. Unfortunately, longer follow-up with adequate number of patient treated with off-the-shelf material are still lacking. Additionally, since it is recognized that the majority of men with PD have vascular comorbidities that contribute to sexual dysfunction (2), surgery is not an exclusive factor that causes postoperative erectile dysfunction. Better understanding of the natural history of PD and long-term outcome of each surgical procedure are still needed.

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Concurrent Management of Bilateral Ureteropelvic Junction Obstruction in Children Using Robotic-Assisted Laparoscopic Surgery

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ABSTRACT

Introduction: Bilateral ureteropelvic junction (UPJ) obstruction occurs infrequently. When surgical management is deemed necessary, staged pyeloplasties traditionally have been recommended to minimize the morbidity associated with performing procedures concurrently. With the advent of robotic-assistance, concurrent surgical management can more readily be performed laparoscopically. In this report, we evaluated the safety and outcome of managing patients with bilateral UPJ obstruction with concurrent robotic-assisted laparoscopic pyeloplasty.
Materials and Methods: We performed a retrospective review of five patients with bilateral ureteropelvic junction obstruction who underwent concurrent bilateral robotic-assisted pyeloplasties at our institution between October 2003 and April 2007. Technical consideration for patient positioning, robotic set-up, port placement, and the use of a hitch stitches was assessed. The operative time, complications, analgesic needs, length of hospitalization, and overall success of the procedure were evaluated.
Results: Operative time ranged from 235 to 541 minutes (mean = 384). Estimated blood loss was 5-100 cc (mean = 48.0). Length of hospitalization ranged from 1.3 to 3.6 days (mean = 2.4). Ureteral stents were removed 3-8 weeks postoperatively. There were no complications. All kidneys demonstrated decreased hydronephrosis on postoperative ultrasound or improved drainage parameters on diuretic renography or IVP.
Conclusions: Simultaneous bilateral robotic-assisted laparoscopic pyeloplasties utilizing 4-port access is feasible and safe. It provides an effective method of managing patients with bilateral UPJ obstruction, avoiding the burden and morbidity of performing staged surgeries.

Key words: *pediatrics; hydronephrosis; laparoscopy; robotics; pyeloplasty*
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INTRODUCTION

In children, bilateral ureteropelvic junction obstruction is present in approximately 10-40% of UPJ obstructions (1,2). Most bilateral cases are asymmetrical, with one side being more severely affected than the other. When surgical intervention is deemed necessary, staged pyeloplasties traditionally have been recommended. While the success of performing concurrent bilateral open pyeloplasties has been reported (3), many surgeons remain hesitant to perform this procedure because of the morbidity associated with operating on both kidneys concurrently and the potential for acute bilateral renal obstruction.

As a result, staged pyeloplasty is often considered safer. However, it requires the need for the patient to undergo two separate operations, which are separated by a potentially prolonged recovery period.

Laparoscopic surgery has achieved increasing popularity in the management of ureteropelvic junction (UPJ) obstruction in children. Its less invasive nature provides for more rapid recovery and improved cosmesis. Successful concurrent bilateral pyeloplasties utilizing free-hand laparoscopy have been reported (4). However, it remains technically challenging. Robotic-assisted surgery has significantly decreased surgeon learning curves as compared to free-hand laparoscopy, while at the same time achieving postoperative outcomes comparable to open pyeloplasty (5). Thus, it may be of benefit in the concurrent surgical management of bilateral UPJ obstruction. In this study, we evaluated the safety and outcome of performing concurrent robotic-assisted laparoscopic pyeloplasties.

MATERIALS AND METHODS

After Institutional Review Board approval was obtained a retrospective review was initiated. Between October 2003 and April 2007, five patients underwent concurrent robotic-assisted bilateral pyeloplasties for the management of bilateral ureteropelvic junction obstruction at our institution. All patients had preoperative radiologic imaging including ultrasonography, diuretic renography, or intravenous pyelogram indicative of the diagnosis of bilateral ureteropelvic junction obstruction. The indications for surgery included increasing degree of hydronephrosis, pain, urinary tract infection, and parental preference.

Surgical Technique

Preoperatively, patients received a clear liquid diet for 24 hours and a rectal suppository the night before the procedure. After the induction of anesthesia, the patient was placed in supine position and a 30-degree wedge was placed under the patient elevating the more affected side. The patient was then carefully secured to the operating table, prepped and draped.

To insert the trocars, the table was rotated to place the patient in a flat supine position in order for the ports to be placed safely into the peritoneum. A 12 mm camera port was inserted in the umbilicus. Three 5 or 8 mm working ports were then inserted; the first in the midline 10 cm above the umbilicus and the other two in the mid-clavicular line in the right and left lower quadrant (Figure-1). After placing the ports, the patient was maximally rotated to the contralateral side, which helped to shift the bowel away from the renal fossa. The robotic system was then engaged.

The procedure was performed as previously described by Lee et al. (5). In brief, the peritoneum was incised along the avascular white line of Toldt. After reflection of the colon and incising through anterior lamina of Gerota's fascia, blunt dissection was performed to expose the renal pelvis, UPJ and proximal ureter. A hitch stitch was utilized to elevate the renal pelvis for easier dissection and suturing (Figure-2). An incision through the renal pelvis was then made above the UPJ. After excising the UPJ segment, the ureter was transposed over any existing crossing vessel and anastomosed back to the pelvis after it was spatulated. A running suture of 5-0 vicryl or monocryl was used in all cases. A kidney internal splint/stent (KISS) or a double-J stent was placed, depending on the surgeon's preference.

After completion of the anastomosis, surgery was performed on the contralateral kidney. All the ports were wrapped in sterile towels to maintain sterility during the changeover. Either of two methods was used to set up the robotic system for the contralateral pyeloplasty. The first involved moving the robot to the opposite side, which necessitated powering down the robot and re-arranging the room set up. The second involved rotating the patient 180-degrees, with careful monitoring of the endotracheal tube and the patient during the change of position. Over time, we preferred the later method, which was more practical. Careful discussion and planning with the anesthesiologists (such as placement of extension tubing and longer monitoring cables) prior to start of the procedure allowed the patients to be moved safely and efficiently during the changeover. The exact same set-up and surgical procedure was performed as previously described. At the end of the procedure, all ports sites were closed.

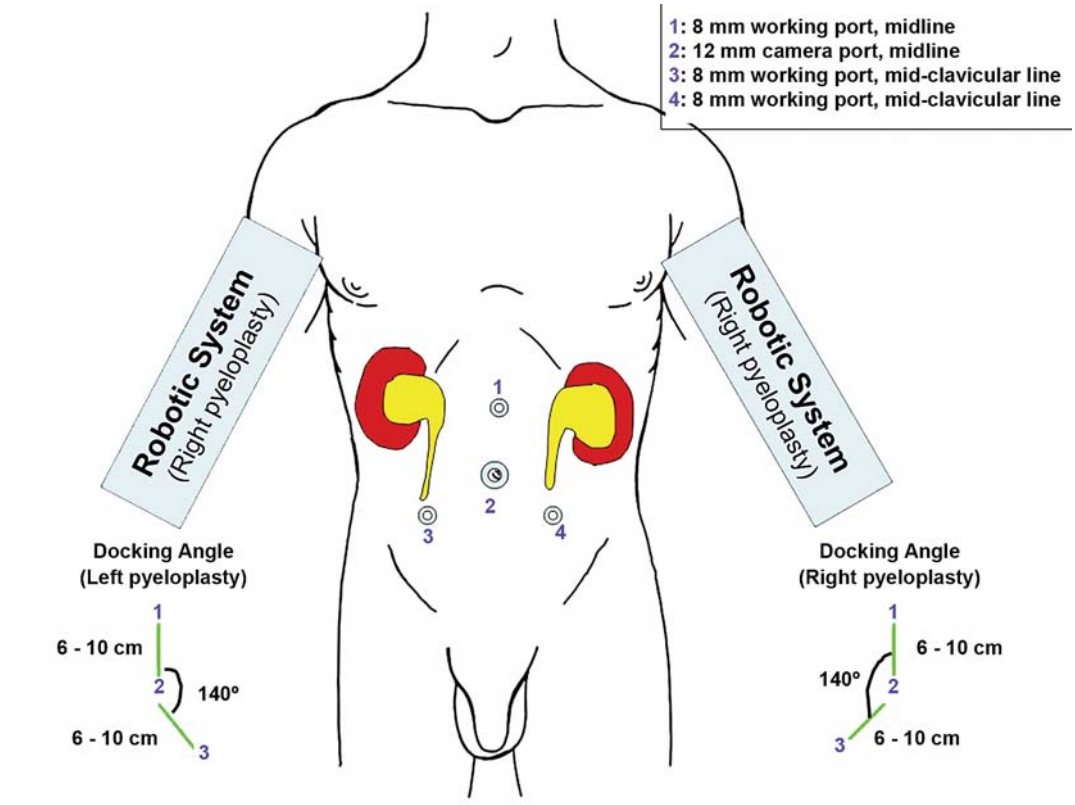

Figure 1 *– Surgical cart and port placement.*

The stents were removed per the surgeon's preference. Follow-up imaging with renal ultrasonography were performed on all patients. If improvement in the degree of hydronephrosis was observed postoperatively and the patients were asymptomatic, only an ultrasonography was performed during subsequent follow-up visits. If there were any concerns regarding the degree of hydronephrosis observed postoperatively, a diuretic renography (MAG-3) or intravenous pyelogram was carried out to assess drainage.

RESULTS

The age of the patients was 3.4-14.0 years (mean - 9.5 years). All patients had a voiding cystouretrogram (VCUG) preoperatively to rule out concomitant reflux. No patient had preoperative drainage (i.e. nephrostomy). The operative time ranged from 235 to 541 minutes (mean = 384). Estimated blood loss ranged from 5 to 100 cc (0.2-2 cc/kg) with a mean of 48.0 cc (1.3 cc/kg). Total perioperative morphine

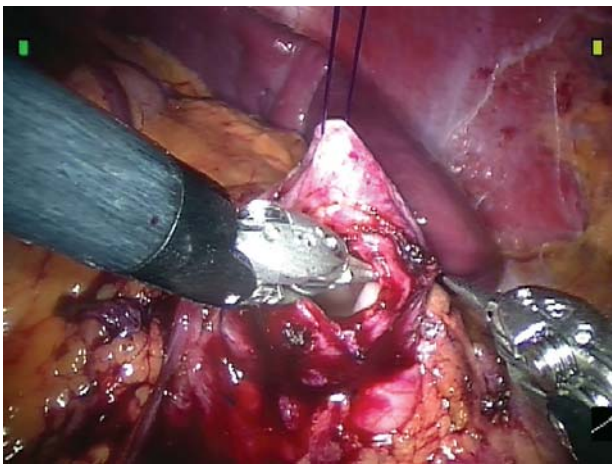

Figure 2 *– Renal pelvis hitch stitch to facilitate exposure and anastomosis with the ureter.*

equivalent requirement (i.e. codeine and fentanyl) ranged from 0.77 to 3.71 mg/kg (mean = 1.7). There were no intraoperative or postoperative complications. The length of hospitalization ranged from 1.3 to 3.6 days (mean = 2.4). All patients had ureteral stents placed bilaterally (3 with double-J stents, 2 with KISS). In 4 patients, the stents were removed sequentially 3 to 6 weeks postoperatively, with a 1-2 weeks interval in between each stent removal. In one patient, both stents were removed simultaneously at 8 weeks. All patients received prophylactic antibiotics until both stents were removed. Postoperative follow-up ranged from 2 to 43.7 months (mean = 11.4). Table-1 details the patients' intraoperative findings, conditions and radiologic evaluation at the time of last follow-up. Figure-3 illustrates typical pre- and postoperative radiologic findings in our patients with bilateral UPJ obstruction managed with concurrent laparoscopic pyeloplasties.

Table 1 – *Patient description.*

Patient	Preoperative Findings	Etiology	Follow-up Radiology
1	Presentation: Flank pain and nausea. Renogram: Left T 1/2 12 min with 40% residual. Right t 1/2 78 min with 76% residual	Right crossing vessel. Left intrinsic stenosis	41 months: US - Bilateral mild pelvicaliectasis. Patient asymptomatic
2	Presentation: Flank pain and nausea. US: Bilateral moderate to severe hydronephrosis	Bilateral crossing vessel	9 months: US - Right side with mild pelvicaliectasis. Left side with moderate pelvicaliectasis. Patient asymptomatic
3	Presentation: Flank pain and hematuria. US: Left moderate hydronephrosis. Right moderate to severe hydronephrosis	Bilateral intrinsic stenosis	6 months: Renogram - Renal function: Left 51%, Right 48%. Bilateral delay in spontaneous collecting drainage. Complete drainage after furosemide without obstruction bilaterally. Patient asymptomatic.
4	Presentation: Hydronephrosis after bilateral megaureter repair. US: Severe bilateral hydronephrosis	Bilateral crossing vessel	6 months: IVP - Right side with considerable calyceal dilation. Left side with residual pelvicaliectasis. Prompt drainage bilaterally. Patient asymptomatic
5	Presentation: Pyelonephritis. US: Left moderate hydronephrosis. Severe right hydronephrosis. Renogram: Left T 1/2 > 100 min with 87% residual. Right T 1/2 55 min with 70% residual	Bilateral crossing vessels. Right secondary intrinsic obstruction	2 months: Left minimal pelvicaliectasis. Right no hydronephrosis. Patient asymptomatic

IVP = intravenous pyelography; US = ultrasonography.

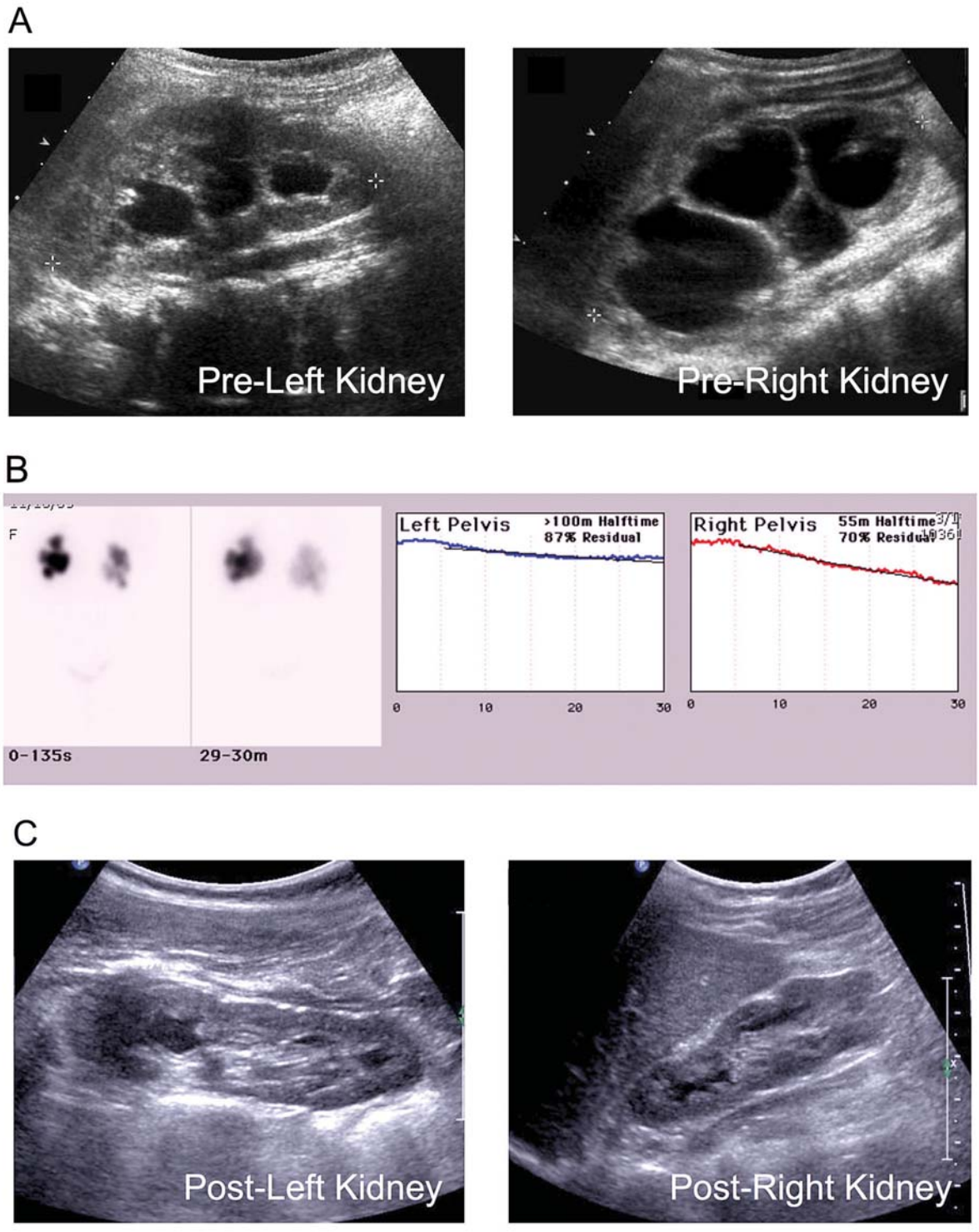

Figure 3 *– Ultrasound findings. A) Preoperative ultrasound reveals moderate hydronephrosis of the left and severe hydronephrosis of the right kidney. B) Preoperative diuretic MAG-3 renogram demonstrating significant residual of the radionuclide in both kidneys after furosemide administration. C) Postoperative ultrasound demonstrates no hydronephrosis in the right kidney and minimal pelvicaliectasis in the left kidney 2 months after surgery.*

COMMENTS

The efficacy and safety of robotic-assisted unilateral pyeloplasty is well documented. To our knowledge this is the first reported series regarding concurrent robotic-assisted laparoscopic bilateral pyeloplasties. We found that performing these procedures concurrently can be time saving. The operative time was reasonable, considering our mean time for performing a unilateral robotic laparoscopic pyeloplasty was 219 minutes (5). The most experienced robotic surgeon at our institution performed his first bilateral robotic-assisted case in 235 minutes, compared to 268 minutes in a published series utilizing free-hand laparoscopy. With increased experience we believe the time savings of simultaneous bilateral robotic-assisted pyeloplasty versus free-hand laparoscopy will continue to increase (5). We observed that by re-positioning the patient rather than the robotic system we could decrease the changeover time to 10-20 minutes. In addition, we decreased the operative times by inserting all 4 trocars at the beginning of the surgery, avoiding the need to place new ports when operating on the contralateral kidney. This also helped to decrease the operative times by avoiding the need to change around the robotic instruments to pass and cut sutures, provide suction/ irrigation, and remove materials.

We also found that this procedure may have significant benefits compared to staged open procedure. The use of perioperative morphine equivalent in this case series (mean of 1.7 mg/kg) is only marginally higher than a recently published cohort from our institution who underwent unilateral open pyeloplasty (mean 1.5 mg/kg). Since the patients in this series only underwent one procedure rather two, this suggests that concurrent bilateral pyeloplasties subjected patients to less pain than staged unilateral surgical interventions. The mean length of hospitalization (2.4 days) for patients undergoing bilateral laparoscopic pyeloplasties is identical to those undergoing unilateral laparoscopic pyeloplasty and is less than that for open surgery (3.5 days) (5). Of note, the length of hospitalization consistently decreased over time, presumably secondary to increased surgeon experience with robotic-assisted surgery in unilateral pyeloplasty procedures and the postoperative monitoring of such patients. Additionally, the patient benefits from improved cosmesis associated with minimally invasive surgery. Most importantly, the entire procedure with all the necessary re-positioning maneuvers was done without any intraoperative complications. However, future larger scale studies with long term patient follow up will be required to completely evaluate the safety of concurrent robotic-assisted laparoscopic bilateral pyeloplasty as compared to a staged approach.

Moreover, our short-term follow up data suggests that concurrent robotic-assisted bilateral laparoscopic pyeloplasties may have postoperative outcomes comparable to that of unilateral open and conventional laparoscopic procedures. In follow-up, all patients in this series were asymptomatic. Their postoperative radiological evaluation demonstrated significant improvement in the degree of hydronephrosis on US or in the drainage parameters seen on diuretic renography or IVP. The level of imaging improvement in conjunction with clinical improvement was used to determine success. Stenting patterns were similar to the unilateral laparoscopic pyeloplasty cases. Placement of the stents and their staged removal avoided the potential complication of simultaneous bilateral renal obstruction. It could be argued that unlike the staged open procedure, where stenting is not routinely performed, concurrent surgery requires two additional procedures for the removal of the double-J stents. We feel however, that the additional procedures (stent removal) while requiring anesthesia when performed on children, have minimal risks and morbidity. Alternatively, KISS stents that can be removed in the clinic without anesthesia can be utilized, as was the preference of one of the surgeons in this study. At our institution, an ultrasound is performed 1-3 months after stent removal to asses the level of hydronephrosis. If significant improvement is observed, a follow-up ultrasound is performed at 6-12 months postoperatively. If the initial postoperative ultrasound does not show improvement, a follow up ultrasound is performed three months after the initial postoperative ultrasound. If this repeat ultrasound does not demonstrate significant improvement, a furosimide-MAG3 renogram is performed. Prospective studies regarding the impact on the quality of life of this type of surgical management will be required to more definitely assess the utility of simultaneous bilateral pyeloplasties.

CONCLUSION

Robotic-assisted surgery offers an advantage in the management of bilateral renal pathologies such as bilateral UPJ obstruction. The results of this small cohort in conjunction with our institution's increasing experience with robotic-assisted surgery demonstrates that robotic-assisted simultaneous bilateral pyeloplasties are feasible, and may have postoperative outcomes comparable to unilateral open and conventional laparoscopic pyeloplasty. The use of the four ports, patient positioning and the hitch stitch will help to make the procedure effective and allow it to be performed in a time saving manner.

ACKNOWLEDGEMENTS

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CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

In the last decade, interest has been evolving in the search for implementation of minimally invasive surgical techniques in pediatric population harboring urological pathologies. As a result of this process, the adoption, evolution and diversification of the laparoscopic approach in children has been inevitable, contributing to better esthetic results, increased magnification and improved intraoperative visualization, reduced postoperative pain, and shorter hospital stays.

Initially used as a diagnostic modality in the treatment of cryptorchidism, pediatric laparoscopic

surgery is currently performed for complex ablative (e.g. nephrectomy, adrenalectomy, etc.) as well as reconstructive procedures such as ureteropelvic junction obstruction (UPJO). Laparoscopic pyeloplasty can be done either trans or retroperitonealy. Advocates of the retroperitoneal approach suggested an easier dissection, but there is less working space in the retroperitoneum, often making the procedure difficult in smaller children and infants, and there is some question as to whether crossing vessels are more easily missed. In addition, a bilateral retroperitoneal approach implies intraoperative repositioning of the patient and lack of possible use of common ports for both sides.

The introduction of robotic surgery could offer real advantages including a greater ability for intracorporeal suturing, enhanced stereoscopic visualization with true depth-of-field vision, and shortening of the learning curve for laparoscopy.

The study presented in this issue deals with the feasibility and safety of performing bilateral robotic-assisted laparoscopic repair of UPJO. The authors should be applauded for their contribution in popularization and diversification of robotic-assisted surgery in pediatric urology. The description of the technical approach is clear and detailed, and the use of common ports for both sides, introduced at the beginning of the procedure, is reasonable and appears to contribute to better esthetic results and decreased repositioning time. There is no doubt that feasibility and safety has been proven, however, the small number of patients and the short term follow-up do not allow concluding the late outcome of the procedure. Lessons learned from adult series have suggested that although failures become evident within the first 12 months, they can occur as late as 3 years after intervention (1). As such, pediatric patients should be followed up at least that long to ensure a lasting result. With laparoscopic pyeloplasty reported success rate of more than 90%, comparable with the results of the gold standard open pyeloplasty, it is not surprising that endopyelotomy lost the game and is in course of being abandoned as a first line treatment, unless performed in very selective situations. Failures of laparoscopic pyeloplasty may sometimes occur, however infrequently and the experience gained with adults has revealed that recurrent UPJO can be endoscopically resolved, with a high success rate. The minimal invasiveness of the endoscopic approach in such cases also appears to be appealing in the pediatric population, obviating the need for another open or laparoscopic repair. It was performed successfully at any age and it should be kept in mind as a possible alternative in children (2).

Overall, the early results with robotically assisted laparoscopic pyeloplasty are encouraging and warrant further evaluation in pediatric urological surgery. It appears that the robot is most helpful to those early in their training, and its major value will be in increasing access to minimally invasive procedures in centers lacking experience in complex laparoscopic techniques. However, its cost effectiveness remained to be determined in relation to the type of procedure and the individual institutional surgical volume.

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The Malone Antegrade Continence Enema (MACE) Principle In Children: Is It Important If the Conduit Is Implanted In the Left or the Right Colon?

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ABSTRACT

Objective: The aim of the study was to determine which was the optimal side for the conduit to be placed (right or left colon) for antegrade continence enema implantation.
Materials and Methods: Between July 1999 and March 2006, 31 patients underwent the construction of a catheterizable conduit using the Malone principle (MACE) In 22 cases the conduit was re-implanted in the right colon and in 9 cases in the left colon. There were 20 male patients and 11 female patients, with a mean age of 10.23 years. The follow-up period varied from 3 from 83 months (average 25 months). Right and left implantation of the conduit in the colon were compared with regards to the presence of complications, volume of the solution utilized, frequency of colonic lavage, time needed for performing the enema, and degree of satisfaction.
Results: One patient with the conduit in the right colon, using the appendix, lost the mechanism after two month follow-up. Thirty patients remain clean and are all capable of performing self-catheterization. No statistically significant differences were found between the groups regarding the variables studied: complications ($p = 1.000$), solution volume ($p = 0.996$), time required ($p = 0.790$) and patient's rating ($p = 0.670$). The lavage frequency required for patients with the conduit in the right colon may be lower.
Conclusion: The MACE principle was considered effective for treating fecal retention and leaks, independent of the implantation site. The success of this surgery appears to be directly related to the patient's motivation and not to the technique utilized.

Key words: *fecal incontinence; enema; surgery*
Int Braz J Urol. 2008; 34: 206-13

INTRODUCTION

Different diseases can cause intestinal dysfunction and continuous feces soiling. And for the treatment to be adequately performed, it is of utmost importance that a cause be found and eventually treated. Independent of its origin, intestinal incontinence, especially when it has become chronic, could carry significant emotional and social problems. Therefore, the management of children with continuous fecal soiling is essential to improve quality of life (1).

Retrograde enema was the treatment of choice until recently when there was a major step forward made by Malone et al. in 1990 (2) with the description of the continent cecal access for antegrade enema. The technical procedure utilized the Mitrofanoff (3) principle for the creation of a continent conduit with the appendix, which is easily catheterizable from a stoma.

In cases where the appendix has previously been removed or is required for urological use, the need to construct a new conduit occurs. This has been achieved by utilizing a cecal flap (4), a sigmoid flap (5) or a segment of the small intestine or colon that has been reconfigured (6) by means of the Yang-Monti principle (7,8).

After the reimplantation of these conduits in the left colon began, doubts emerged regarding the optimal place for reimplanting them: the right colon or the left colon. Calado et al. (5) believed that the left colon was the more physiologically appropriate location, with a decrease in the risk of water absorption as well as a decrease in the time required for enema administration and washout, thereby increasing patient satisfaction and compliance. The enema performed in right colon often is long and tedious for handicapped patients, as the volume of washout from the cecum to the rectum is large, especially in neuropathic bowels prone to dolichosigmoid (5).

The aim of the study was to determine which was the optimal side for the conduit to be placed (right or left colon) for antegrade continence enema implantation.

MATERIALS AND METHODS

Between July 1999 and March 2006, 31 patients with intestinal dysfunction and continuous feces soiling underwent the construction of a catheterizable conduit using the MACE principle (2).

The criteria for indicating surgical treatment were fecal incontinence not responsive to more conservative measures (dietary modifications and medical treatment); patients who remained clean by performing enemas via the rectal route; the patients and their parents should be motivated to perform the antegrade enema.

There were 20 male patients and 11 female patients, with a mean age of 10.2 years (range: 4 to 17 years). Fourteen children had imperforate anus, twelve had myelomeningocele, three had medullar trauma, one had spina bifida, and one had complex perineal trauma (Table-1).

For the 22 patients with the mechanism reimplanted in the right colon (Table-2), the conduit utilized was the cecal appendix, which was kept in its original position and subjected to an anti-reflux procedure consisting of suturing the walls of the cecum around the appendix. In 16 patients, this conduit was brought to the exterior at the umbilicus and in six, at the right iliac fossa. In five of these children, the appendix was divided into two parts (Figure-1), with concomitant division of its irrigation, in order that its proximal part was utilized for intestinal catheterization and its distal part as a Mitrofanoff conduit (3) for performing intermittent urinary catheterization.

In the nine patients with reimplantation of the mechanism in the left colon (Table-2), the conduit was constructed by utilizing a segment of the sigmoid with its base against the mesenteric margin (5). This was tubularized around a urethral probe and was subjected

Table 1 *– Patients with fecal incontinence.*

Diseases	N
Imperforate anus	14
Myelomeningocele	12
Medullar trauma	3
Spina bifida	1
Complex perineal trauma	1
Total	31

Table 2 *– Patients with serious fecal incontinence according to the surgical technique utilized.*

Technique Utilized	N
Appendix with anti-reflux mechanism	22
Tubularized sigmoid	9
Total	31

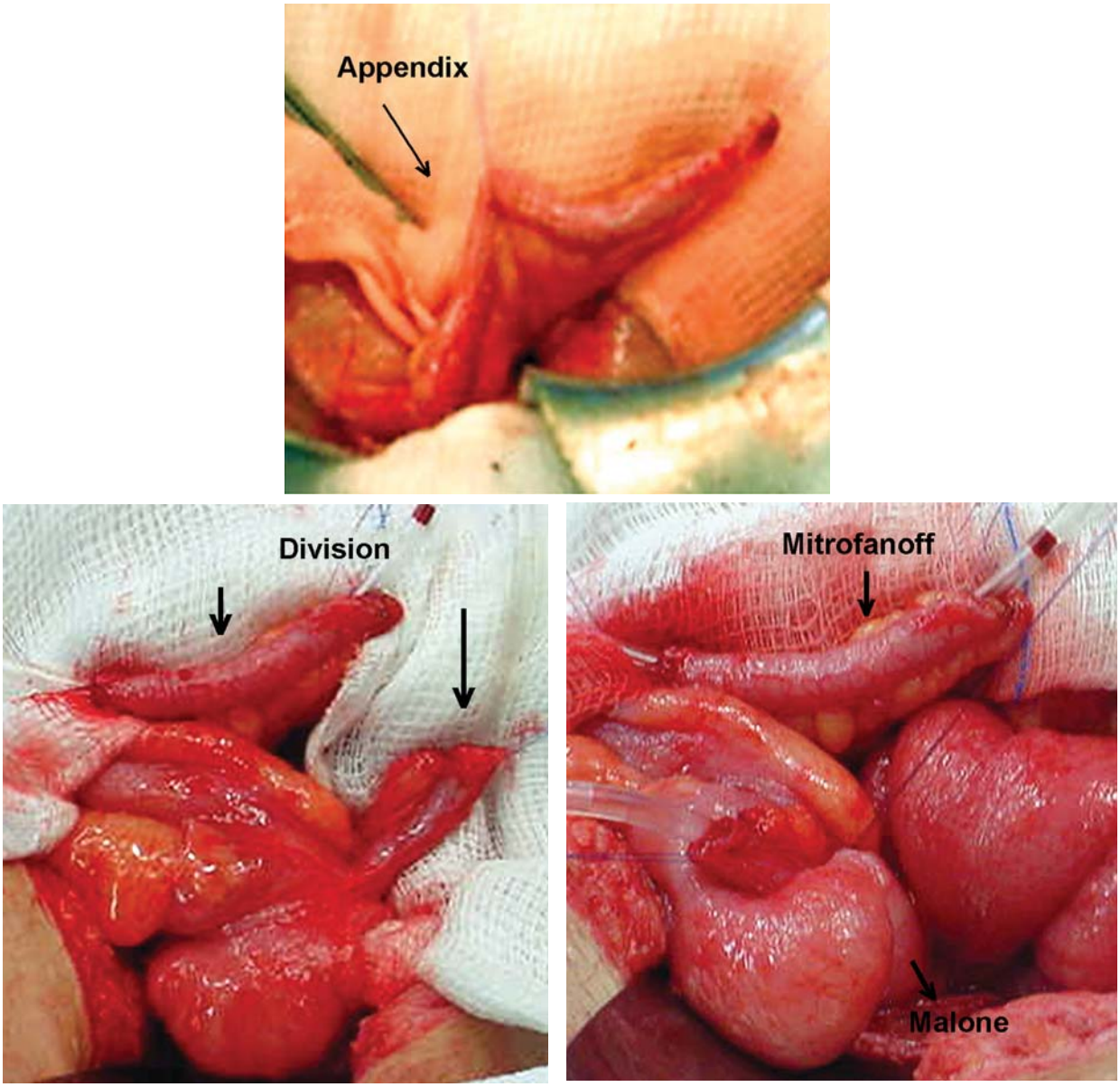

Figure 1 *– The appendix was divided into two parts in order that its proximal part was utilized for intestinal catheterization and its distal part as a Mitrofanoff conduit for performing intermittent urinary catheterization.*

to an anti-reflux procedure involving the walls of the sigmoid. It was brought to the exterior at the left iliac fossa.

During the same operation, 16 patients simultaneously also underwent other procedures:

- 10 patients: bladder enlargement, construction of a conduit for urinary continence catheterization (Mitrofanoff (3)) and plastic surgery on the bladder neck;
- 2 patients: construction of a conduit for urinary continence catheterization (Mitrofanoff (3));
- 1 patient: sigmoidoplasty to reduce its caliber;
- 1 patient: plastic surgery on the bladder neck;
- 1 patient: reconstruction of the intestinal transit;
- 1 patient: correction of an incisional hernia.

Following the surgery, all the patients were given training, in order to learn how to operate the mechanism. The volume utilized for the enema was

adjusted individually, so that it would be sufficient for cleaning the colon, without rectal leaks during the day. The solution used depended on the patient's preference (tap water for 14 patients, glycerinated solution for 13 patients and saline solution for 4 patients).

The mean follow-up duration was 25 months (range: 3 to 83 months).

Right and left implantations of the conduit in the colon were compared with regard to the presence of complications, volume of the solution utilized, frequency of enema, time needed for performing the enema, and degree of satisfaction (the patients were asked to give a score on a scale from 1 to 10 to rate the improvement in their quality of life following the construction of the mechanism for performing antegrade enema).

The quantitative variables were represented by mean, standard deviation, median, minimum and maximum, and the qualitative variables by absolute frequency (n) and relative frequency (%). The non-parametric Mann-Whitney test for independent samples was applied to make comparisons between groups of patients with regard to the variables of solution volume, time needed and patient's rating. Associations between the presence of complications and the side of implantation were evaluated by means of Fisher's exact test. The significance level was set at 0.05 (α = 5%).

RESULTS

One patient had loss of the mechanism after two months follow-up, following presentation of an abscess in the pathway of the appendix that evolved with fibrosis of the conduit. Thirty patients are currently using their conduits: 21 implanted in the right colon and nine in the left colon. All these patients are clean and capable of performing self-catheterization (Table-3).

Complications

No statistically significant differences were found between the groups (p = 1.000). Six patients (27.3%) with the conduit re-implanted in the right colon and constructed using the appendix presented complications:

- stenosis of the stoma in the skin (four patients);
- loss of the mechanism after two months follow-up, following presentation of an abscess in the pathway of the appendix that evolved with fibrosis of the conduit (one patient);
- discharge of secretions (one patient).

Three patients (33.3%) with the conduit re-implanted in the left colon and constructed using a sigmoid flap presented complications:

- peristomal infection (two patients);
- difficulty in probing because of angling of the conduit, which necessitated surgical reintervention (one patient);

Volume of the Solution Utilized

No statistically significant differences were found between the (p = 0.996). The patients with the conduit re-implanted on the right side used a mean enema volume of 13.34 mL/kg. The patients with the conduit re-implanted on the left side used a mean enema volume of 13.35 mL/kg.

Frequency of Enema

The patients with the conduit on the left side required daily enema. On the other hand, the enema frequency required for patients with the conduit on the right side may be lower, given that six of our patients (27%) performed intestinal cleaning only on alternate days.

Time Needed for Performing the Enema

No statistically significant differences were found between the groups (p = 0.790). The mean time needed for performing the enema was 51.4 minutes (range: 30 to 60 minutes) for the patients with the conduit constructed using the appendix and re-implanted on the right side, and 49.2 minutes (range: 15 to 90 minutes) for the patients with the conduit constructed using the sigmoid and re-implanted on the left side.

Degree of Satisfaction

No statistically significant differences were found between the groups (p = 0.670). The patients were asked to give a score on a scale from 1 to 10 to rate the improvement in their quality of life following the construction of the mechanism for performing antegrade enema. The patients with the conduit in the

Table 3 – *Left colon versus right colon.*

Variables Analyzed		Right Colon (N = 22)	Left Colon (N = 9)	p Value
Complications				1.000
Absent		16 (72.7%)	6 (66.7%)	
Present		6 (27.3%)	3 (33.3%)	
Solution volume (mL/kg)				0.996
mean (± SD)		13.34 (4.91)	13.35 (5.62)	
median		12.77	13.16	
minimum - maximum		5.0 - 23.8	4.5 - 21.7	
Time needed (min)				0.790
mean (± SD)		51.4 (12.3)	49.2 (26.5)	
median		60	50	
minimum - maximum		30 - 60	15 - 90	
Patient's rating				0.670
mean (± SD)		8.9 (1.6)	9.2 (0.7)	
median		10	9	
minimum - maximum		5 - 10	8 - 10	
Frequency of lavage	N = 15	1x/day		NR
	N = 6	Alternate days	1x/day	
	N = 1	2x/day		

SD = standard deviation.

right colon gave a mean score of 8.9 and the patients with the conduit in the left colon gave a mean score of 9.2.

COMMENTS

The MACE procedure has been used in patients with fecal incontinence caused by chronic retention of feces, independent of its etiology, when these patients are resistant to the medical treatment (5,6,8-10). In our study, imperforate anus and myelomeningocele were the principal diseases presented by the patients.

The procedure, described by Malone et al. (2) in 1990, consists of dissection and isolation of the cecal appendix, suture of the appendix tip into the skin as an appendicostomy, and the implantation of the bottom of the appendix into the cecum in an antireflux tunnel. The appendicostomy is therefore fixed in the inferior right quadrant or in the umbilical region, therefore permitting the introduction of a catheter to perform enemas in an antegrade direction. The original procedure was posteriorly modified,

maintaining the appendix in its original position and fixing the cecum in the abdominal wall, thus avoiding twisting of the conduit and reducing the time needed to perform the surgery (11).

Mouriquand et al. (6) proposed the use of an isolated intestinal segment of ileum reconfigured using the Yang-Monti (7,8) technique with the implantation of the conduit in the left colon. They reported that this placement of the conduit in the left colon combined with regular performance of enema resulted in the accumulation of feces only in the left colon, reduced time required to perform the enema, and increased child compliance.

Complications involving this procedure are not rare, and the most important ones involve the stoma (12). In the present study, when the conduit utilized was the appendix, stenosis of the skin was the principal complication, and this was corrected by means of dilatation or new maturation of the stoma in the skin. When the conduit utilized was a sigmoid flap, the peristomal infection rate increased, which was expected because of the manipulation involved in opening and suturing colonic loops.

The volumes utilized for performing enemas through conduits implanted on the right and left sides were similar, which has led us to the hypothesis that the volume needed for cleaning the colon is independent from the size of the colon, which is distally situated from the implantation site of the conduit.

If the feces only accumulate in the left colon as stated by Mouriquand et al. (6), one can imagine that even if the conduit is re-implanted in the right colon, it would clear no significant amount of additional feces from the right colon. Thus, the enema volume required for a right-sided conduit could be similar to the volume required for a left-sided conduit.

The enema solution chosen most often by our patients was plain tap water, followed by glycerinated solution and physiological solution. With these solutions, no metabolic disturbances were observed, whereas many have been reported when the solution utilized was phosphated.

There were no differences regarding the time required for performing the enema. The patients took a mean time of 50 minutes (range: 15 to 90 minutes), independent of the conduit reimplantation site.

The patients with the conduit on the left side required daily colon cleaning. On the other hand, the lavage frequency required for patients with the conduit on the right side may be lower, given that six of our patients (27%) performed intestinal cleaning only on alternate days.

The authors consider that if the appendix is already available, the MACE procedure can be performed with little mobilization of the organ and the results could be as good as, if not better, than if the conduit was re-implanted directly in the left colon. This has the additional advantage that there is no need to use intestinal segments to perform the catheterization conduit. The appendix should be utilized even when urinary continence derivation is simultaneously necessary, since the proximal appendix can be utilized for intestinal catheterization and the distal appendix can be utilized as a Mitrofanoff conduit (3) for performing intermittent urinary catheterization, as was done in five of our cases, with good results.

The success of this surgery appears to be directly related to the patient's motivation and not to the technique utilized. Thirty patients in this study are currently using their conduits: 21 implanted in the right colon and nine in the left colon. All these patients are clean and are capable of performing self-catheterization. To obtain this high rate of adherence to treatment, all the patients must have been aware that, after the mechanism for antegrade enemas had been constructed, a certain time was needed for adjusting the volume of liquid to be utilized and the frequency of the enemas, until the continence they required was obtained. Through such awareness, abandonment of the use of the conduit was avoided.

When the patients were asked to give a rating from 1 to 10 regarding the improvement in their quality of life following the surgical procedure, the result was a score of 8.9 for the conduits implanted on the right side and 9.2 for the conduits implanted on the left side, thus showing a high satisfaction rate, independent of the implantation site in the colon.

Fecal continence promotes independence among children, and it improves their self-esteem and quality of life. The method utilizing the MACE principle is relatively safe and if we have correctly

interpreted the results of this limited series, the surgical technique should be the simplest one to perform. Moreover, our patients demonstrated a high degree of satisfaction with the procedure independent of which side it was implanted in.

The success of the Malone procedure seems to depend mainly on selection of the patients. The patients and their parents should be motivated to perform the antegrade enema as a routine task and should be conscious that there is an adaptation period before the expected continence is obtained. Fecal continence promotes the children's independence, improves self-esteem, and improves the quality of life.

The construction of colonic conduit for antegrade enema is not the cure for fecal incontinence but could be an optimal therapeutic option for the patients with chronic and irreversible constipation with soiling. The surgical technique should be the simplest one to perform and our patients demonstrated a high degree of satisfaction with it, independent of which side it was implanted in.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

The authors have performed a review of their surgical experience with a left- and right-sided Malone antegrade continence enema (MACE) procedure. Their data shows no significant difference in evacuation time, continence, or satisfaction between the two groups.

Interestingly, a significant number of patients with a right MACE were able to irrigate only on alternate days and remain continent as opposed to those with a left MACE. In our institution, a right-sided MACE is nearly always our first choice when using the appendix in its orthotopic location. A Monti-MACE can be implanted wherever it is deemed appropriate from a vascular pedicle standpoint given the restraints of the urinary reconstruction to be performed. A theoretical concern with a left MACE in a myelomeningocele patient with a dilated colon would be proximal constipation that may not be adequately treated by the enema regimen.

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Does Vaginal Anti-Incontinence Surgery Affect Sexual Satisfaction? A Comparison of TVT and Burch-Colposuspension

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ABSTRACT

Objective: To evaluate the sexual satisfaction rates of women who underwent tension-free vaginal tape (TVT) procedure for stress urinary incontinence and compare it with the results of Burch-colposuspension.
Materials and Methods: A self-administered questionnaire was given to 81 patients who had undergone TVT or Burch-colposuspension at our institution to determine sexual satisfaction rates and reasons for dissatisfaction. Forty-seven patients in TVT group and 22 patients in Burch-colposuspension group were considered eligible for the study. The mean follow-up period and age of patients in TVT and Burch-colposuspension groups were 34 months, 51.5 years and 89 months, 52.9 years, respectively. The difference between the ages in the two groups was not statistically significant, while the difference between mean follow-up periods was significant ($p = 0.000$).
Results: When evaluating sexual satisfaction, 73% in the TVT group and 86% in the Burch-colposuspension group did not report any difference in sexual satisfaction following surgery, while in the TVT group, 23% expressed negative and 4% positive changes, and in the Burch-colposuspension group 9% expressed negative and 5% positive post surgical changes. The differences in sexual satisfaction rates between the two groups were not considered significant. The majority (54%) of those who expressed a negative change suffered from dyspareunia.
Conclusions: Although sexual satisfaction seems to be more adversely affected by TVT compared to Burch-colposuspension, the difference was not statistically significant. Further studies are required concerning different anti-incontinence techniques in order to arrive at more precise conclusions.

Key words: *urinary incontinence, stress; surgical procedures, operative; sexual dysfunction, physiological*
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INTRODUCTION

Sexual dysfunction in women is a fairly common problem and one that occurs in as many women as in men. It is an important health problem that affects the quality of both women and their partners' lives (1,2). Although the available literature on this subject has been increasing, less is known about female sexual dysfunction than male sexual dysfunction (3). It has been observed in various studies that the anterior and distal parts of the vagina, which is the most innervated, play an important role in sexual function (4,5).

Many surgeons currently prefer to use tension-free vaginal tape (TVT) procedure to treat stress urinary incontinence (SUI). However, the effect on sexual function of vaginal surgery for incontinence has not yet been clearly established and only limited

data on this subject are reported in the literature (6-9). Altered sexual function might be attributed to vaginal surgery, which may cause vaginal narrowing or can damage the highly innervated anterior vagina (5).

The aim of this study was to use a questionnaire to evaluate any changes in sexual satisfaction of women who underwent a TVT procedure for SUI. The results of this evaluation were compared with the results from those women who had undergone surgery using a suprapubic anti-incontinence technique (Burch-colposuspension).

MATERIALS AND METHODS

Eighty-one patients who had undergone TVT procedure (between 1999 and August 2000) or Burch-colposuspension (between July 1994 and June 1998) at our institution were contacted by phone. Sixty-nine patients (85%) who were sexually active pre-and postoperatively, had a partner, and a successful surgical outcome were invited for a hospital consultation. Forty-seven patients in the TVT group and 22 patients in the Burch-colposuspension group were considered eligible for the study. The mean age of the patients who underwent TVT was 51.5 years (median 51, range 38-68) whereas the mean age of the patients who underwent Burch-colposuspension was 52.6 years (median 52, range 36-67). Concomitant rectocele or cystocele repair was performed in 3 patients. All Burch-colposuspension surgery was performed under general anesthesia, whereas TVT was performed with either local or general anesthesia. The mean follow-up period of patients in TVT and Burch groups were 34 months (range 20-45) and 89 months (range 55-111), respectively (Mann Whitney-U, $p = 0.000$).

Since no validated questionnaire in our language was available at that time, a questionnaire containing 8 questions was developed in our department to evaluate sexual satisfaction of the patients and their partners after the operation (Figure-1).

Chi-square, Fisher's exact, and Mann-Whitney U tests were performed for statistical analysis. The Fisher's exact test was only used, instead of Chi-square test, when the expected number of patients in either category was less than five.

RESULTS

When evaluating sexual satisfaction, 34 of 47 patients (73%) in TVT group and 19 of 22 patients (86%) in Burch-colposuspension group did not report any difference after the operation. It was affected negatively or positively in 11 (23%) and 2 (4%) patients in the TVT group, and in 2 (9%) and 1 (5%) patients in the Burch-colposuspension group, respectively. The differences of sexual satisfaction rates between the two groups were not significant (Fisher's exact test; $p = 0.137$) (Table-1). In the TVT group, of the 11 patients expressing negative effect, 5 were suffering from dyspareunia, 2 from sexual desire disorders, while 2 had vaginal dryness and 2 had orgasmic disorders. Both of the negatively effected patients in the Burch group also had dyspareunia (Table-2). None of the patients had declared any of these problems prior to the surgery.

When evaluating the sexual satisfaction of the partners, 45 of 47 patients' partners (95.7%) in the TVT group and 22 of 22 patients (100%) in the Burch-colposuspension group did not report any difference. Only one partner (2 %) in the TVT group mentioned that his sexual life deteriorated after the operation.

Thirty-six of 47 patients (76.5%) in the TVT group and 19 of 22 (86.3%) in the Burch-colposuspension group were satisfied with the operation, and 37 patients (76.5%) in TVT group and 19 (86.3%) in Burch-colposuspension group declared that, in the same circumstances, they would have undergone the surgery again and could recommend it to their relatives or friends.

COMMENTS

Sexual dysfunction in women is a fairly common problem and age, level of education, physical and mental health status seem to affect this situation. It is a health problem that affects both women's as well as their partners' quality of life (1). Urinary incontinence itself is also an important parameter that negatively affects all of the sexual functional parameters (10). Women who experience leakage during intercourse hope that their sexual function will improve follow-

1) Are you sexually active or not?
a. Yes b. No

2) Do you have a sexual partner?
a. Yes b. No

3) Compare your present sexual satisfaction during intercourse with that before the operation.
a. Better b. Same c. Worse

4) If it is worse, what problems are you experiencing with your sexual life?
A. How is your sexual desire?
a. Better b. Same c. Worse
B. Do you feel any dryness during the intercourse?
a. Yes b. No
C. Do you feel any pain during the intercourse?
a. Yes b. No
D. Do you have orgasm during the intercourse?
a. Yes b. No

5) For partner,
Compare the present sexual satisfaction during intercourse with that before the operation.
a. Better b. Same c. Worse

6) Are you satisfied with the outcome of the operation?
a. Yes b. No

7) Would you want your partner to undergo this operation again if it were indicated?
a. Yes b. No

8) Would you recommend this operation to your relatives or friends?
a. Yes b. No

Figure 1 *– Questionnaire that was designed for the evaluation of the sexual function after anti-incontinence surgery.*

ing surgery for SUI, and this affects their decision to undergo surgery (2).

However, surgery for pelvic prolapsus and SUI may cause sexual dysfunction due to vaginal narrowing and/or may alter vaginal innervation and cause sexual dysfunction (11). On the other hand, it is reported that abdominal surgery performed for urinary incontinence does not affect sexual function. However, by elevating the anterior vaginal wall and tilting the axis of vagina, sexual function may improve (12). For this reason, we compared the results of those patients who had undergone Burch-colposuspension while evaluating sexual function of the patients who had undergone TVT operation at our department. Patients who still had leakage were excluded from the study, because leakage during intercourse, itself is a factor that causes sexual dysfunction. One of the limitations of our study is the significant difference in follow-up period of the TVT and Burch-colposuspension groups. Therefore, further prospective randomized studies evaluating the sexual satisfaction rates are needed to compare different surgical techniques for the treatment of SUI.

Table 1 – *Satisfaction rates of the continent and sexually active women in TVT and Burch-colposuspension groups.*

	TVT (47)	Burch (22)	p Value*
Sexual satisfaction during intercourse after surgery			
Worse	11 (23%)	2 (9%)	
Better	2 (4%)	1 (5%)	
Same	34 (73%)	19 (86%)	0.1374*
Sexual satisfaction of the partner after surgery			
Worse	1 (2%)	-	
Better	2 (4%)	-	
Same	44 (94%)	22 (100%)	0.6811*
Satisfied with the outcome of the operation	35 (74.5%)	19 (86.6%)	0.355**
Accept to undergo operation again	36 (76.5%)	19 (86.6%)	0.523**
Recommend it to their relatives or friends	36 (76.5%)	19 (86.6%)	0.523**

** = chi square; ** = Fisher exact test.*

Table 2 – *The reasons for dissatisfaction after TVT and Burch-colposuspension.*

	TVT	Burch
Sexual desire disorders		
Hypoactive sexual desire disorder	2	-
Sexual aversion disorder	-	-
Sexual arousal disorder	-	-
Lubrication or vaginal dryness	2	-
Orgasmic disorder	2	-
Sexual pain disorder		
Dyspareunia	5	2
Vaginismus	-	-
Other sexual pain disorder	-	-
Total	11	2

Lemack et al. evaluated the sexual function of 56 women after anterior vaginal wall surgery for SUI and found that the sexual lives of 18% of the women worsened following surgery (7). They also observed that postmenopausal women on hormone replacement therapy were more likely to be sexually active following surgery (46%) than those who were not on hormone replacement therapy (17%) (7). In one of the prospective studies, Rogers et al. reported that sexual function did not improve after anti-incontinence surgery despite improvement of incontinence (13).

Many studies evaluating the sexual function after TVT showed conflicting results, with a reported sexual dysfunction after surgery ranging from 3 to 20% of cases (8,14-19). We believe that the limitations of current methods of sexual function evaluation and different study design and patient selection criteria prevent a reliable comparison of results. Maatia et al. evaluated the sexual function of 43 sexually active women who underwent TVT and noted that 72%

of women did not experience any difference, while sexual function in 5% of the patients had improved and 14% worsened(8). In this study, worsening of sexual satisfaction following surgery was not found to be due to surgical procedures but decreased libido and vaginal atrophy was due to decreased postmenopausal estrogen levels (8). Berglund et al. reported that there was no significant difference in sexual activity before and after surgery in women who had undergone surgery for SUI (20). Recently Shah et al. showed that overall sexual function did not change in women undergoing placement of a mid to distal polypropylene urethral sling (19). Wang et al. investigated the change of the patients' sexual function after the surgery for SUI, and compared the laparoscopic Burch-colposuspension with TVT (21). In this study they found that surgery adversely affected the patients' sexual life, with TVT having a lesser negative affect than Burch-colposuspension. In our study, when evaluating sexual satisfaction, 73% of women who underwent TVT operation did not experienced any difference. In 4% of patients, sexual satisfaction was improved, while in 23% of patients, it had worsened. In the Burch-colposuspension group the number of the patients who were adversely affected and reported a worsening of sexual satisfaction after the operation was lower (9%) and not considered statistically significant. A total of 11 patients reported sexual dysfunction after vaginal-incontinence surgery (TVT) and, of these patients 45% described dyspareunia post-operatively while 18% had orgasmic disorder, 18% suffered from lubrication or vaginal dryness and 18% had decreased sexual desire. In the Burch-colposuspension group, 2 patients whose sexual lives had deteriorated after the operation reported dyspareunia. Recently, the study reported by Ghezzi et al. showed no significant difference in the incidence of dyspareunia (18). The relationship between dyspareunia and vaginal surgery is still unclear. Some authors have indicated that symptomatic vaginal narrowing is rare even in those patients undergoing simultaneous posterior repair (7,12,22,23), while others have stated that the vaginal narrowing is primarily experienced when the posterior wall defect has been corrected with anti-incontinence surgery (6,24). Haase et al. evaluated the influence of the operations for stress incontinence on sexual life and found that dyspareunia was observed in all of the patients in which posterior wall repair was performed during the operation (6). We also performed rectocele repair in 2 patients and cystocele repair in a patient concomitantly while performing TVT operation. None of these patients reported dyspareunia. Lemack et al. noted that the number of patients who suffered from dyspareunia preoperatively (29%) decreased postoperatively (20%) (7).

Another limitation of our study was that we were not able to use a validated questionnaire. Since there was not a validated Turkish version of one of the sexual function questionnaires, we created a questionnaire, which contained 8 questions in this study. To compare the success of anti-incontinence surgery and to evaluate the sexual function of women after these operations, validated questionnaires are important to standardize the studies. The Turkish version of the Female Sexual Function Index (FSFI) has recently been validated by the Turkish Andrological Society. Despite this limitation, we believe that our results provide a useful insight for clinicians when managing and counseling the patients who have undergone vaginal surgery for SUI.

CONCLUSIONS

Although sexual satisfaction seems to be more adversely affected by TVT compared to Burch-colposuspension, the difference was not statistically significant. Further studies are warranted concerning the different incontinence techniques in order to provide more precise conclusions.

CONFLICT OF INTEREST

None declared.

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Histopathological Characterization of a Syngeneic Orthotopic Murine Bladder Cancer Model

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ABSTRACT

Purpose: We developed and characterized by histopathology and immunohistochemistry a syngeneic murine bladder tumor model derived from the MB49 tumor cell line.
Materials and Methods: Bladder tumor implantation was achieved by intravesical instillation of 5 x 10^5 MB49 tumor cells in C57BL/6 mice. A chemical lesion of the bladder was performed in order to promote intravesical tumor implantation. The bladder wall lesion was accomplished by transurethral instillation of silver nitrate ($AgNO_3$). After 15 days, the animals were sacrificed, examined macroscopically for intravesical tumor and bladder weight. Histology and immunohistochemistry were performed using cytokeratin 7 (CK7), carcinoembrionic antigen (Dako-CEA), p53 and c-erbB2 oncoprotein (Her2/neu).
Results: Twenty-nine out of 30 animals (96.7%) developed intravesical tumors in a 15-day period. Macroscopically, the mean bladder weight was 0.196g (0.069-0.538g), 10 to 15 times the normal bladder weight. The immunohistochemical analysis showed significant membrane expression of CEA and CK7: a similar finding for human urothelial cancer. We also characterized absence of expression of p53 and anti-Her2/neu in the murine model.
Conclusions: High tumor take rates were achieved by using the chemical induction of the bladder tumor. Although electric cauterization is widely described in the literature for syngeneic orthotopic animal models, the technique described in this study represents an alternative for intravesical bladder tumor implantation. Moreover, the histopathology and immunohistochemical analysis of the murine bladder tumor model derived from the MB49 cell line showed a resemblance to human infiltrating urothelial carcinoma, allowing clinical inference from experimental immunotherapy testing.

Key words: *bladder cancer; intravesical instillation; tumor cell line; mice/c57bl; experimental neoplasm*
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INTRODUCTION

Animal models provide a system for understanding basic biological questions. With animal models, adequate control of experimental design is possible so that rigorous experiments can be performed to test various hypotheses . In the case of testing therapeutic mechanisms, it is important to select a model that is most analogous to the clinical setting so that observations can be readily transferred to clinical studies for validation (1).

A murine bladder tumor model may offer some of these characteristics, while having many controlled variables under laboratory conditions (2). This permits inference from experimental data, which can be helpful for clinical purposes. The murine bladder

tumor models may be a xenograft model (in immunodeficient mice) (3), a chemically induced bladder cancer model (4), or a syngeneic animal model (5).

The use of immunodeficient mice in bladder cancer research has allowed the implantation of human carcinomas in an animal model. In addition, it has demonstrated the importance of the immune system, in particular as regards T lymphocytes, in anti-tumor activity (6).

The chemically induced models were achieved by administering carcinogens such as N-[4-(5-nitro-2-furyl)-2-thiazolyl] formamide (FANFT) in C3H/He mice (7) or 7,12-dimethylbenzanthracene in mice strain C57BL/6 (8). Although adequate for immunotherapeutic testing, a long period of time was required for carcinogen-induced bladder tumor growth.

The syngeneic animal models were developed with the objective of improving immunotherapeutic studies (9). It is characterized by the transplantation of carcinogen-induced bladder cancer into syngeneic immunocompetent mice (5,10). This murine bladder tumor model has been considered appropriate for this purpose, as it permits the possibility of mimicking intravesical conditions. Moreover, research can be improved by testing local tumor response to drugs in an immunocompetent host (11). Implantation of syngeneic tumor cells can be made subcutaneously (heterotopic model) or by intravesical instillation (orthotopic model), in the anatomical site.

In this study, our aim was to characterize the syngeneic orthotopic murine bladder cancer model derived from the MB49 tumor cell line by histopathology and immunohistochemistry. We focused on the urothelial histogenesis of the murine tumor in order to demonstrate its similarities to the human bladder tumor. Therefore, our findings may support its use as an useful experimental bladder tumor model for drug testing and new immunotherapeutic alternatives. In addition, we demonstrate the feasibility of the implantation of the tumor cell line MB49 by the chemical lesion of the bladder using silver nitrate, as described previously by Luo et al. (12). Silver nitrate was chosen for this purpose due to its controlled and stable characteristics. Similar effects may be achieved using ethanol and poly-L-lysine, but this was not tested in this series.

The markers used for immunohistochemistry testing were cytokeratin 7, carcinoembrionic antigen, p53 and c-erbB2 oncoprotein, all commonly used for evaluating human bladder tumor.

MATERIALS AND METHODS

Animals - Eight- to 10-week-old female C57BL/6 mice, weighing 15-20g, were provided by the Bioterism Center of the university and maintained at our animal care facility for 1 week prior to use. The mice were housed five per cage in a limited access area at a controlled room temperature, with food and water ad libitum. The experiments were approved by the institution's Ethics Board Council.

Preparation of tumor cells - Syngeneic bladder tumor cell line MB49 was kindly provided by Dr. Yi Lou (University of Iowa, USA). The cells were maintained in vitro culture (DMEM, 10% FBS, 1% penicillin/streptomycin, at 37°C and 5% CO_2). Tumor cells were harvested by trypsinization and suspended in DMEM without L-glutamine, FBS, and antibiotics. Viability was determined by trypan blue exclusion and only tumor cell suspensions with more than 90% viable cells were used for tumor implantation.

Intravesical tumor implantation - Mice were anesthetized by the intraperitoneal administration of ketamine/xylazine solution at a dose of 0.1 mL/10g body weight. Subsequently, a 24-gauge Teflon i.v. catheter (Nipro^R) was inserted through the urethra into the bladder using an inert lubricant (sterile contact gel) (Figure-1). Then, in order to prepare the bladder for tumor implantation, a brief acid exposure, followed by alkaline neutralization, promoted a chemical lesion on the bladder wall, performed by intravesical instillation of 8µl 1M silver nitrate ($AgNO_3$). This promoted an adequate and controlled diffuse bladder wall lesion. After 10 seconds, the content was washed out by transurethral infusion of phosphate-buffered saline. The first catheter was removed and a new 24-gauge catheter was inserted in the urethra for intravesical instillation of MB49 cells. A cell suspension of MB49 tumor cells (5 x 10^5 cells in 0.1 mL 50% normal mouse serum) was instilled and retained for 2 hours by stitches.

Figure 1 *– A 24-gauge catheter inserted in the urethra for intravesical instillation (female C57BL/6 mice).*

The mice were evaluated on a daily basis for viability and gross hematuria. After 15 days, the animals were sacrificed by CO_2 inhalation, examined macroscopically for intravesical tumor and individually verified the bladder weight.

Histology and immunohistochemistry: After gross examination, the bladders were fixed in buffered formalin 10%, routinely processed and paraffin included and stained by hematoxylin and eosin . Immunohistochemistry was performed to characterize the immunophenotype and the antibodies used were cytokeratin 7 (CK7 OV-TL 12/30, 1:100), carcinoembrionic antigen (Dako-CEA, II-7 1:200), p53 (DO7, 1:100) and c-erbB2 oncoprotein (Her2/neu, 1:100), all produced by Dakocytomation, Glostrup, Denmark. Three-micrometer sections from the paraffin block containing tumor were placed on adhesive-coated slides. In a heat antigen retrieval process the slides were placed in a citrate buffer (1mM, pH 6.0) and heated for 30 min. in the steamer. The slides were incubated overnight at 4ºC with the above antibodies. Labelled Streptavidin Biotin (LSAB; Dako Cytomation, CA,) at first biotinylated link universal for 35 min at room temperature, then the slides were rinsed with Tris-buffer for 5 min., incubated for a further 35 min. with streptavidin-HRP. The slides were rinsed in tap water for 5 min. Color was developed by incubating the slides in 0.06% diaminobenzidine in PBS for 15 minutes, and the slides were rinsed in Tris-buffer and tap water, counterstained with Harris hematoxylin, dehydrated, cover slipped, and reviewed under light microscope. Tissue sections of a bladder urothelial carcinoma known to express p53 and Her2-neu, as well as pulmonary adenocarcinoma positive for cytokeratin 7 and CEA were used as positive controls. For each case a negative control was applied by following all steps of IHC except for replacement of the primary antibody by PBS.

RESULTS

All the animals survived the surgical intervention, no transmural bladder injury or bladder perforation was observed. All animals, after 7 days, presented evident gross hematuria (Figure-2), that persisted until the sacrifice on day 15. There was no obstruction of the urinary flow, except for the gross and intense hematuria. Considering all the animals (30) that received intravesical instillation of MB49

Figure 2 *– Gross hematuria in a mouse, 7 days after the intravesical instillation of MB49 cells.*

cells, 29 (96.7%) developed intravesical tumors after the 15-day period. At that time there was massive growth of a solid tumor inside the bladder.

Macroscopically the mean bladder weight was 0.196g (0.069-0.538g) in the tumor group, while a C57BL/6 mouse bladder weighs between 0.010g to 0.015g approximately. The tumor was represented by an usually solitary solid mass, growing inside the bladder, deeply red, soft and extremely bloody. There were areas of necrosis and superficial ulceration. Microscopically, there was a high grade urothelial solid carcinoma composed of proliferation of large, cubic cells, arranged in solid nests, with round, hypercromatic nuclei and one or more nucleoli. Scattered giant, bizarre cells were seen in the tumor. The mitosis rate was high (50/HPF). Superficial ulceration and foci of necrosis were identified. In all cases the tumor was invasive through the bladder wall, reaching the muscularis propria. No vascular invasion or perineural infiltration was seen. The transition to normal urothelium was evident, and no in situ carcinoma was identified (Figure-3).

The immunohistochemical analysis showed strong, membrane expression of CEA and CK7: a similar profile that we commonly see for urothelial cancer that affects humans. Although p53 expression is very common in urothelial cancer, due to p53 mutation, in the murine model it does not seem to be a part of the carcinogenesis since we were unable to detect p53 staining. Also, we used antibody anti-Her2/neu, an oncogene super expressed in 30 to 60% of human urothelial carcinomas. There was no Her2/neu expression in the cases we have evaluated. The molecular evaluation of those two abnormalities among others should be the subject of our next study.

COMMENTS

As demonstrated above, the histological and immunohistochemical characteristics described in the murine bladder tumor model derived from the MB49 cell line mimics one of the main aspects of the human infiltrating urothelial carcinoma, which is defined as a urothelial tumor that invades beyond the lamina propria. By producing a pathologically similar cancer to the human urothelial carcinoma, evidence from experimental research may become closer to data from human testing.

Considering the immunoregulatory mechanisms that participate in bladder tumor-host interaction (12), a wide field of research is open for investigation. Consequently, adequate local and systemic experimental environment model is required, allowing a significant conclusion to be obtained for further studies.

A murine bladder tumor model may offer some of these characteristics, while having many controlled variables under laboratory conditions. These factors permit inference from experimental data, which can be helpful for clinical purposes, specially considering safety issues.

Despite the technical difficulty of orthotopic tumor implantation, improvements have been made to avoid the variability of tumor cell adhesion to the bladder wall (5). Soloway et al. simulated a transurethral fulguration by cauterizing the murine bladder wall, creating conditions for tumor cells implantation (10). The development of this technical modification enhanced the model's applicability by transforming the orthotopic syngeneic bladder tumor model into a reliable tool for investigating tumor growth mechanisms and intravesical drug testing. Furthermore, the model closely resembles the clinical situation, making it very suitable for bladder cancer research.

The use of immunohistochemistry for accurate diagnosis of cancer has long been demonstrated (13). Determination of cytokeratins, in this situation, may be helpful in tumors poorly differentiated and for identifying the primary site of metastatic carcinomas (14). Moreover, IHC provides information on tumor progression, giving p53 expression among other markers, a significant prognostic value (15,16).

The murine bladder tumor model not only creates adequate conditions for understanding tumor adhesion, proliferation and invasiveness, but also allows the development of a cancer with many similar histopathological characteristics to the human urothelial carcinoma, making it a valuable tool for anti-tumor drug testing, based on immune, viral or gene therapy(9,17,18).

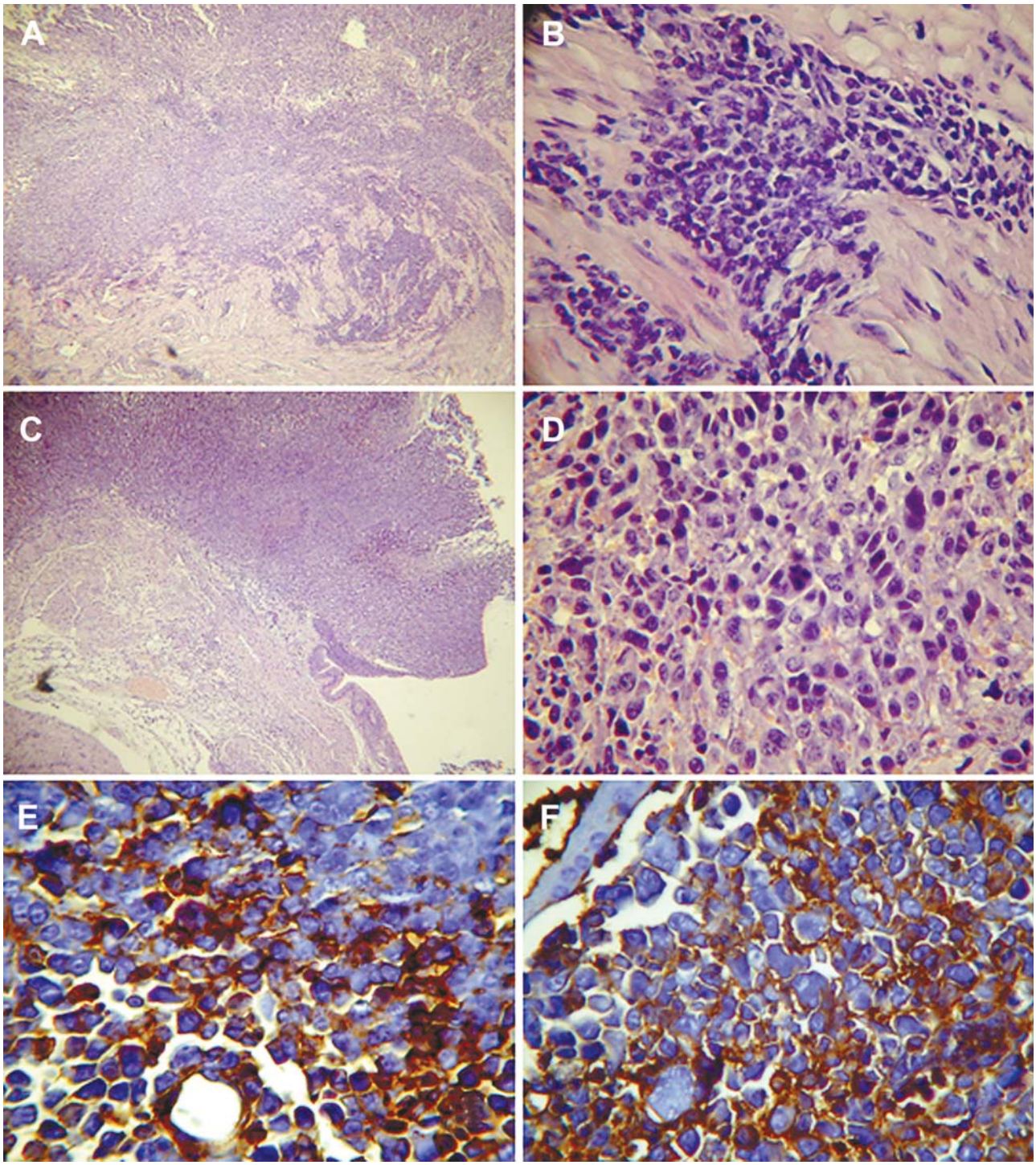

Figure 3 – *A) High grade urothelial carcinoma, extensively infiltrative in the muscularis propria, HE X40 and B) X400. C) High grade urothelial carcinoma characterized by a exophytic growth through the vesical lumen, diffusely infiltrative in the lamina propria. Note the clear distinction between normal urothelium and tumor, HE, X40. D) High grade carcinoma characterized by large cubic cells, with intense nuclei polymorphism and high mitotic activity, HE, X400. E) Membrane immune expression of cytokeratin 7, X400, and F) CEA, X400.*

CONCLUSIONS

The tumor implantation procedures described herein provide a reproducible experimental bladder cancer model. The orthotopic murine model has an important role improving our knowledge of therapeutic mechanisms of superficial bladder cancer in the proper anatomical site.

In conclusion, the histopathology and immunohistochemical profile of the murine bladder tumor model derived from the MB49 cell line resembles the human infiltrating urothelial carcinoma, allowing us to make inferences about its behavior and response to different treatment regimes.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

The study presented by Chade et al. shows a nice modification of the previously published orthotopic MB-49 bladder tumor model.

The main difference to the model optimization published by Günther et al. (1999) is the initial bladder lesion before tumor cell instillation. In the previous model by Günther et al. mice were placed with their backs on the ground plate of the cautery unit. To optimize contact, electrocardiogram electrode contact gel was used. The soft-tipped end of a spring-wire guide of a 24-gauge central venous catheter was inserted into the bladder via a Teflon catheter and gently pushed forward until it reached the bladder wall. The guide wire was attached to a cautery unit and a monopolar coagulation was applied for 5 s at the lowest setting (5 W). After removal of the guide wire, 0.05 mL of the tumor cell suspension was instilled. Chade et al. induced instead of physical alteration of the bladder wall a chemical lesion with intravesical silver nitrate.

Furthermore, in the original description catheters were after tumor cell instillation pinched off with a clamp, kept locked with a Luer-Lock closing cone, and left in place until the mice awakened. Using this method, a dwell time of approximately 3 h. was given.

Here, a dwell time of 2 hours was performed by temporary stitches (presumably of the urethra).

The effectivity of the described technique is comparable to the previous model. The tumor take was almost 100% and all animals developed gross hematuria. However, the number of animals with pulmonary metastases, which was 20-70% before, was not mentioned here.

Chade et al. examined the Her2/neu, p53, CK7, and CEA expression in this model. Interestingly, p53 and Her2/neu staining was negative. One has to be aware that this can also be due to antibody-related problems since immunohistochemistry staining procedures are frequently more difficult in mouse tissue than in human tissue. We have previously examined Ki-67 (TEC-3) expression and found in the tumors up to 70% positive cells (unpublished data).

In general, the molecular comparison between human bladder cancers and mouse models is very interesting since the results of therapeutic applications

may be easier to interpret. As the authors point out further molecular evaluations are planned. It would be highly interesting to perform these evaluations also in an humanized immune incompetent (SCID or Nude) mouse model. However, we were until now not able, to transfer the intravesical model into SCID mice since most mice died after bladder wall coagulation. Maybe the technical modification of Chade et al. would lead to better results.

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EDITORIAL COMMENT

Bladder cancer is well suited for experimental therapies due to the isolated bladder cavity in which therapies can be given locally. By transurethral noninvasive surgery, bladder tumors can easily be monitored and biopsies taken for further analyses. These features are beginning to attract a number of drug developers within a variety of fields including chemo-, immuno- and gene therapy. Bladder cancer is one of few cancers that have excellent orthotopic murine experimental models that are closely mimicking the clinical situation (1,2). Hence, in these orthotopic models, tumor biology can be studied and tumor therapy can be given locally by instillation via cauterization of urethra just as in the patients. In the current issue, Chade et al. are describing a novel system to enhance tumor take in experimental bladder cancer using silver nitrate ($AgNO_3$) as well as giving further insights into the biology of murine bladder tumors by performing a histopathological evaluation.

The most common murine bladder cancer cell lines are the mouse bladder-49 (MB49) and the mouse bladder tumor-2 (MBT2) cells (1-3). These two cell lines can be used in syngeneic C57BL6 and C3H mice, respectively. The cell lines are utilized to create subcutaneous, orthotopic or metastatic tumors. In one of the first orthotopic models electrocautherization was used for tumor take. The electric pulse created a burn wound to which MB49 cells attached and formed tumors. In this model, the effect of Bacillus Calmette-Guérin (BCG) therapy has been extensively evaluated and immunological mechanisms found in this model have later been proven transferable to human systems (1,4). However, the electrocautherization model has a few drawbacks. The main issue is that it can be difficult to obtain the technical equipment necessary. Further, this model does not give 100% tumor take which increases the number of mice needed per treatment group and may mask the true result in some treatment groups where differences are slim. Many groups have tried to obtain similar or better tumor take by chemical pretreatment of the bladder surface prior instillation of tumor cells. Agents tested are for example ethanol and poly-L-lysine (PLL) (2). Ethanol functions as an irritant and theoretically removes the mucin layer in the bladder thereby facilitating tumor take. The latter, PLL, is a polycathion that is thought to by its positive electrical charge become a bridge between the negatively charged urothelium and the tumor cells thereby aiding tumor attachment. PLL has so far been the only agent that repeatedly gives tumor take in all mice. In this issue, Chade et al has further improved the management of the orthotopic model via the use of $AgNO_3$ pretreatment of the bladders to irritate the bladder wall prior tumor cell instillation. The tumor take is similar to that of PLL but the model as such saves time since this agent only needs a few seconds of incubation compared to PLL that needs to be incubated in the bladder for 10-20 min. prior tumor

instillation. It will be of interest to evaluate effects of different therapies in this improved model.

The MB49 tumor cells have many similarities to its human equivalent in terms of antigens and immune escape mechanisms. The latter include infiltration of T regulatory cells in the growing tumor, expression of TGF, attraction of IL10-producing suppressor cells other than T regulatory cells etc (5-7). This makes the MB49 model excellent for evaluation of novel immunotherapies. The MB49 cells have expression of the male antigen HY and this antigen has been used as a pseudo tumor antigen when the cells are used in female mice (8). However, when antigen-directed approaches are evaluated, true tumor antigens need to be targeted. Carcinoembryonic antigen (CEA) is one of the first identified tumor antigens. It is expressed in about half of all human tumors, especially in adenocarcinomas (9,10). The results from Chade et al demonstrate that MB49 cells express CEA as do human bladder cancer. This antigen is often used in tumor immunotherapy and the MB49 model can, hence, serve as a model system not only for bladder cancer but for all CEA positive tumors.

The murine experimental MB49 model gives new insights to tumor progression, survival and immune escape in human bladder cancer. Currently, there are several novel therapies such as immune and gene therapy that are proven potent in the MB49 model and now translated into clinical Phase I and II trials. It is important to further investigate murine experimental models to simplify the techniques as well as to further enlighten biological phenomena that may be translated into human cancer and get us closer to better and more refined drugs.

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EDITORIAL COMMENT

An animal model that closely resembles human bladder cancer is needed for preclinical studies on the pathogenesis of bladder cancer and the development of therapeutic strategies for treating this disease. This paper describes a syngeneic murine bladder tumor model that is developed by intravesical implantation of MB49 cells, a commonly used murine bladder cancer cell line of the C57BL/6 origin. The authors have established the experimental conditions that result in a high incidence of orthotopic tumor in mice (96.7%; 29 out of 30 mice on day 15). By using a small volume of silver nitrate to traumatize the urothelium, the authors have demonstrated the feasibility of this method for intravesical bladder tumor implantation. The implanted animals developed a solid tumor inside the bladder that mimics human urothelial invasive carcinoma in histopathology. Immunohistochemical analysis showed the strong expression of cytokeratin 7 and carcinoembrionic antigen on the surface of MB49 tumor cells, which is similar to human urothelial cancer. These surface markers facilitate the identification of primary tumor when metastasis occurs. Although this model is feasible and provides a high rate of tumor intake, this model needs to be improved for its variability in tumor growth. Nevertheless, this model provides a useful means for the therapeutic studies of bladder cancer including immunotherapy, chemotherapy, and gene therapy.

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International Braz J Urol 34 (2): 230-232, March - April, 2008

Re: Comparison of Vasovasostomy with Conventional Microsurgical Suture and Fibrin Adhesive in Rats

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Int Braz J Urol. 33: 829-36, 2007

To the Editor,

We read with great interest the paper by Wilson F. Busato Junior and colleagues (1). In this elegant study two techniques of vasovasostomy have been tested in a laboratory setting. One group of rats underwent "conventional" one-layer anastomosis on the left vas deferent, after transection on the right side; another group was evaluated for a simplified anastomosis performed with one anchor point plus fibrin glue, and the last group served as control after a sham operation. The authors concluded that the two techniques are similar ($p > 0.05$) and the operative time is the only relevant difference.

As a first point to debate we would emphasize that the results of this study cannot be considered out of an experimental concern. This is because the anastomosis was performed using perfect stumps of deferens and they were immediately reattached after cutting. Thus, it does not reproduce the real clinical condition in which a scar tissue can be found at the cut ends.

Another issue refers to the way of apposing the divided ends of the vasa. The authors applied a direct end-to-end anastomosis in both procedures. However, in a clinical context, it might be helpful a modified approach based on preparing the vas ends. As reported by Fox, the convoluted portion of the vas is always thinner and more difficult to suture than the straight part. Therefore, in all cases in which the stumps are of different size, it is advantageous to transect obliquely the deferent in order to augment the diameter of its lumen (2). This technique has shown ensuing paternity in one third of patients either after primary or revised vasovasostomy.

Finally, the authors suggest that the fibrin-supplied vasovasostomy since requires less operative time may became a simplified procedure suitable also for a general urologist. Nevertheless the microsurgical vasovasostomy performed at microscope is widely considered improved over other methods using less magnification (3). Thus, in our opinion the vasovasostomy should preferably address to urologists trained in microsurgery (clinical or experimental) or practiced in dedicated centers.

In any case, we congratulate the authors for a well drawn study dealing with appropriate number of animals according to modern ethical rules (4).

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Re: Sperm Defect Severity Rather than Sperm Source is Associated with Lower Fertilization Rates after Intracytoplasmic Sperm Injection

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Int Braz J Urol, 34: 49-56, 2008

To the Editor,

I sincerely hope that I may be permitted to comment on a very important issue in the male factor infertility aspect: the male gamete and its role in the outcome of intracytoplasmic sperm injection (ICSI). We read with interest the article published by Verza and Esteves entitled: "Sperm defect severity rather than sperm source is associated with lower fertilization rates after intracytoplasmic sperm injection" (1).

In the past, we had the opportunity to publish 2 articles regarding this issue (2,3). One of these articles we reported that the pregnancy rates is significantly lower in patients with non-obstructive azoospermia compared to patients with obstructive azoospermia (1). In the other article, we detected higher fertilization and implantation rates seen in azoospermic patients from congenital causes of obstruction. In addition, epididymal sperm results in higher pregnancy rates and lower miscarriage rates compared to testicular spermatozoa (3).

In fact, various factors may influence the outcome of ICSI in azoospermic patients. These include parameters linked to male partner - such as serum FSH and testicular histology - that may reflect upon the quality of the surgically retrieved sperm cells.

The authors evaluated one very interesting issue that has been left apart from the other articles published regarding the outcome of ICSI with the use of sperm from different etiologies. The quality of the semen is very important and not only the origin of the sperm retrieved. In the past, Nagy et al demonstrated that, irrespective the source of the semen, the outcome using ICSI is the same (4). Additionally, Svalander et al., demonstrated that sperm morphology according to the strict criteria is not related to the ICSI outcome (5). However, this is not completely true. In clinical practice, the quality of the semen does matter. The worst the semen quality, the worst outcome result. This emphasizes the role of the urologist in order to improve semen quality instead of referring this patient for assisted reproduction without any sort of urological treatment before. Our role of urologists is to try to improve semen quality, for instance, operate varicoceles, perform vasectomy reversals, etc.

Once again, as a urological community, we thank such important article.

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UROLOGICAL SURVEY

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STONE DISEASE

Secondary signs of non-enhanced CT prior to laser ureterolithotripsy: is treatment outcome predictable?

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J Endourol. 2008; 22: 415-8

Purpose: To correlate the presence of secondary signs of non-enhanced computed tomography (NECT) in renal units harboring ureteral calculi with intraoperative findings and treatment outcome after holmium:yttrium-aluminum-garnet laser (Ho:YAG) ureterolithotripsy.
Subjects and Methods: Two-hundred patients were prospectively included after ureteral calculi were detected on NECT. All patients underwent Ho:YAG ureterolithotripsy at the Medical University of Vienna. All CT studies were reviewed by one specialized uroradiologist blinded to pre- and postoperative parameters for secondary signs as renal enlargement, perinephric stranding, ureteral dilation, periureteral edema, and ureteral rim sign. The impact of secondary signs on intraoperatively-verified impaction and treatment outcome was evaluated.
Results: Of the 200 patients 85 (42.5%) harbored proximal and 115 (57.5%) harbored distal ureteral calculi. The stone-free rates for proximal and distal calculi were 80% and 97%, respectively. Although proximal stone location and intraoperatively-verified impaction correlated significantly with stone-free rates ($P < 0.0001$, $P = 0.01$), the presence of secondary signs could not predict intraoperatively-verified stone impaction or stone-free rates (renal enlargement: $P = 0.2$, $P = 0.5$; perinephric stranding: $P = 0.7$, $P = 0.5$; ureteral dilation: $P = 0.7$, $P = 0.7$; periureteral edema: $P = 0.8$, $P = 0.06$; ureteral rim sign: $P = 0.8$, $P = 0.3$).
Conclusion: Preoperative secondary signs seen on NECT in patients harboring ureteral calculi do not correlate with intraoperative findings of impaction, and do not predict treatment outcome after Ho:YAG ureterolithotripsy.

Editorial Comment

Previous studies have demonstrated that patients with secondary signs of obstruction on CT scan imaging are more likely to require surgical intervention. It would be helpful if CT scan findings could predict the success rate with ureteroscopic lithotripsy. As such, the success rates are high and complication rates uncommon with Holmium laser lithotripsy, therefore the likelihood of identifying preoperative prognostic factors is low.

The low level of success with proximal ureteral stones could be related to the reliance on semi-rigid ureteroscopy in this study - the addition of flexible ureteroscopes and stone retrieval devices may have helped improve success rates. As such, the impact of proximal ureteral stone location and endoscopic evidence of impaction may warrant further evaluation using these two modalities.

The authors report that over one-third of patients had stone impaction at the time of ureteroscopy, as defined by adherence to the ureteral wall necessitating detachment with the Holmium laser. In our experience, the risk of impaction appears related to the duration of symptoms and obstructions. Indeed, it is surprising that such a high rate of impaction was detected as the median time to intervention was only 2 days after imaging.

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Quantitative assessment of citric acid in lemon juice, lime juice, and commercially-available fruit juice products

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Background and Purpose: Knowledge of the citric acid content of beverages may be useful in nutrition therapy for calcium urolithiasis, especially among patients with hypocitraturia. Citrate is a naturally-occurring inhibitor of urinary crystallization; achieving therapeutic urinary citrate concentration is one clinical target in the medical management of calcium urolithiasis. When provided as fluids, beverages containing citric acid add to the total volume of urine, reducing its saturation of calcium and other crystals, and may enhance urinary citrate excretion. Information on the citric acid content of fruit juices and commercially-available formulations is not widely known. We evaluated the citric acid concentration of various fruit juices.
Materials and Methods: The citric acid content of 21 commercially-available juices and juice concentrates and the juice of three types of fruits was analyzed using ion chromatography.
Results: Lemon juice and lime juice are rich sources of citric acid, containing 1.44 and 1.38 g/oz, respectively. Lemon and lime juice concentrates contain 1.10 and 1.06 g/oz, respectively. The citric acid content of commercially available lemonade and other juice products varies widely, ranging from 0.03 to 0.22 g/oz.
Conclusions: Lemon and lime juice, both from the fresh fruit and from juice concentrates, provide more citric acid per liter than ready-to-consume grapefruit juice, ready-to-consume orange juice, and orange juice squeezed from the fruit. Ready-to-consume lemonade formulations and those requiring mixing with water contain </= 6 times the citric acid, on an ounce-for-ounce basis, of lemon and lime juice.

Editorial Comment

Citrate is the most abundant urinary organic ion and a potent inhibitor of crystallization, nucleation and crystal growth and aggregation. It acts by binding free calcium, binding to the calcium oxalate crystal surface, and blocking crystal-epithelial cell interactions. It may also impact urinary pH. This evaluation of the citric acid concentration of various fruit juices answers important questions that will help with the dietary counseling of our patients with stone disease.

As with most good studies, it also provokes further questions worthy of investigation. How does the bioavailability of the dietary citrate sources differ, and how does each source impact urinary citrate and pH? Is there variability in citrate contents based on the climate or soil composition where the fruits were grown? Though citrate levels are lower for orange juice, potassium levels are higher - would the added alkali load with orange juice enhance urinary citrate excretion and offset its lower citrate level?

For now, it is important we emphasize for patients that fresh or concentrated lemon or lime appears to be their best shot at squeezing their risk of stone recurrence.

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ENDOUROLOGY & LAPAROSCOPY

3-year actuarial biochemical recurrence-free survival following laparoscopic radical prostatectomy: experience from a tertiary referral center in the United States

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J Urol. 2008; 179: 917-21; discussion 921-2

Purpose: We performed a prospective analysis of pathological and oncological outcomes following laparoscopic radical prostatectomy at a medical center in the United States.
Materials and Methods: A total of 528 men underwent laparoscopic radical prostatectomy between April 2001 and August 2005. We excluded 4 open surgical conversions (0.8%) and 16 men (3.0%) without followup. The remaining 508 men had a mean preoperative prostate specific antigen of 6.0 ng/mL (range 0.3 to 27) and Gleason score of 6.3 (range 6 to 10). Stage was cT1b in 1 case (0.2%), cT1c in 350 (68.9%), cT2a in 135 (26.6%), cT2b in 21 (4.1%) and cT2c in 1 (0.2%). Of the patients 89% underwent cavernous nerve preservation. Biochemical recurrence was defined and timed at the first prostate specific antigen of 0.2 ng/mL or greater if at repeat testing it remained 0.2 ng/mL or greater.
Results: Mean followup was 13.2 months (median 12, range 2 to 52). Pathological stage was pT0N0/Nx in 2 men (0.4%), pT2N0/Nx in 414 (81.5%), pT3aN0/Nx in 72 (14.2%), pT3bN0/Nx in 17 (3.3%) and pT2-3N1 in 3 (0.6%). Positive margin rates increased with higher stage (8.2% in pT2 and 39.3% in pT3 cases, $p < 0.0001$). Three-year actuarial biochemical recurrence-free survival was 98.2% for pT2N0/Nx and 78.7% for pT3N0/Nx/N1 disease ($p < 0.0001$), and it was 94.5% overall. Multivariate analysis controlling for age, preoperative prostate specific antigen, postoperative Gleason score and stage, and margin status showed that only Gleason score (greater than vs. less than 7) and stage (pT3 or any N1 vs. pT2) predicted biochemical progression.
Conclusions: Laparoscopic radical prostatectomy can provide excellent cancer control outcomes for clinically localized prostate cancer with high actuarial biochemical recurrence-free survival rates at 3 years.

Editorial Comment

Since the first laparoscopic radical prostatectomy (LRP) was described by Schuessler et al. in 1997 and then by Guillonneau et al. in 1999 this surgical technique has evolved, as well, as the laparoscopic instruments and better understanding of the "laparoscopic" anatomy allowed several other investigators to demonstrate no difference of oncological outcomes between the open and laparoscopic approach in their reports. In a couple of years we will celebrate the 10th anniversary of LRP performed by high volume tertiary care centers. I foresee that the oncological outcomes will be similar as the open surgical technique. Furthermore, we do need reports from trials that can compare different surgical approaches for the treatment of Prostate Cancer. Moreover, the ideal prostate cancer marker should be identified in the near future to prevent overtreatment of the disease and also to decrease disease specific mortality.

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Comparison of laparoscopic and open partial nephrectomy for tumor in a solitary kidney

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J Urol. 2008; 179: 847-51; discussion 852

Purpose: We compared the postoperative and renal functional outcomes of patients undergoing open or laparoscopic partial nephrectomy for tumor in a solitary functioning kidney.
Materials and Methods: Between 1999 and 2006, 169 open and 30 laparoscopic partial nephrectomies were performed for 7 cm or smaller tumors in a solitary functioning kidney. Data were collected in an institutional review board approved registry and median follow-up was 2.0 years. Preoperative and postoperative glomerular filtration rates were estimated with the abbreviated Modification of Diet in Renal Disease equation.
Results: By 3 months after open or laparoscopic partial nephrectomy, the glomerular filtration rate decreased by 21% or 28%, respectively ($p = 0.24$). Postoperative dialysis was required acutely after 1 open partial nephrectomy (0.6%) and 3 laparoscopic partial nephrectomies (10%, $p = 0.01$), and dialysis dependent end stage renal failure within 1 year occurred after 1 open partial nephrectomy (0.6%) and 2 laparoscopic partial nephrectomies (6.6%, $p = 0.06$). In multivariate analysis warm ischemia time was 9 minutes longer ($p < 0.0001$) and the chance of postoperative complications was 2.54-fold higher ($p < 0.05$) with laparoscopic partial nephrectomy. Longer warm ischemia time (more than 20 minutes) and preoperative glomerular filtration rate were associated with poorer postoperative glomerular filtration rate in multivariate analysis. Notwithstanding the association with warm ischemia time, the surgical approach itself was not an independent predictor of postoperative glomerular filtration rate ($p = 0.77$).
Conclusions: While laparoscopic partial nephrectomy is technically feasible for tumor in a solitary kidney, warm ischemia time was longer and complication rates higher compared with open partial nephrectomy. In addition, although average loss of renal function at 3 months is equivalent (after accounting for warm ischemia time), a greater proportion of patients required dialysis temporarily or permanently after laparoscopic partial nephrectomy in this initial series. Therefore, open partial nephrectomy may be the preferred nephron sparing approach at this time for these patients at high risk for chronic kidney disease.

Editorial Comment

The authors should be congratulated for this enlightening, instructive manuscript.

Laparoscopic partial nephrectomy is a complex procedure with a steep learning curve but it has been demonstrated by several investigators including the present authors that it is a technically feasible surgery for small tumors even in solitary kidneys.

The warm ischemia time (WIT) was longer and complication rates higher compared with open partial nephrectomy but the loss of renal function was equal in 3 months for both groups.

Nonetheless, this minimally invasive approach is another viable treatment option that can be reserved for patients that can tolerate a slightly longer WIT (9 min. longer than open surgery).

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IMAGING

Focal prostatic atrophy: mimicry of prostatic cancer on TRUS and 3D-MRSI studies

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Objective: It is well known that histologically focal prostatic atrophy (FPA) is one of the most frequent mimics of prostatic adenocarcinoma. The purpose of our study was to show that FPA may also simulate prostate cancer on transrectal ultrasound studies (TRUS) and on 3D-magnetic resonance spectroscopic imaging of the prostate (3D-MRSI).
Materials and Methods: From 2004 to 2006, 625 men suspected of prostate cancer, underwent TRUS guided biopsy (n = 513, group I) or TRUS-guided biopsy directed with 3D-MRSI of the prostate (n = 142, group II). The latter group was formed only by patients with elevated PSA levels and prior negative prostate biopsies. All sites showing FPA on histopathologic analysis were correlated with findings observed on gray scale and color Doppler-TRUS studies or on 3D-MRSI of the prostate.
Results: From a total of 513 patients biopsied and studied by gray scale and color Doppler-TRUS(Group I) , 48 patients (9.3%) presented histological diagnosis of FPA associated with sonographic abnormalities in the peripheral zone of the prostate. Thirty-two patients presented hypoechoic nodules with absent flow and 16 patients had hypoechoic nodules with increased flow. From a total of 142 patients submitted to TRUS-guided biopsy directed with 3D-MRSI (Group II), 16 (11.2%) presented histological diagnosis of FPA associated with abnormalities strongly suspicious for prostate cancer on conventional MRI and/or on 3D-MRSI. These abnormalities were: focal area of low signal intensity on T2-w image or clusters of voxels with choline + creatine/ citrate ratio above 3 SDs.
Conclusion: Similarly to the histopathologic findings focal prostatic atrophy may mimic cancer on gray-scale and color Doppler-TRUS studies and on 3D-MRSI studies. Radiologists should be aware of this entity which together with prostatitis, represent an important cause of false-positive result on prostatic biopsy directed with endorectal MRSI (11.2%).

Editorial Comment

Prostatic atrophy is one of the most frequent mimics of prostatic adenocarcinoma. There are still controversies regarding the causal linkage of FPA to the prostate cancer and to other pre-neoplastic lesions. On conventional and color Doppler transrectal ultrasound and on magnetic resonance spectroscopic imaging studies (MRSI), FPA may also simulate prostate cancer. The vast majority of our cases that simulate prostate cancer were related to sub-type hyperplastic prostatic atrophy. We might speculate why FPA manifests as false-positive MRSI findings: in the hyperplastic sub-type, the number of cellular membranes are increased. This could explain the elevation of choline level without modification of the polyamine level. It has been shown that there is a positive and significant association between extent of FPA in biopsies and serum total or free PSA elevation. For this reason, pathologists should include the presence of FPA in the pathology report of a prostatic biopsy, particularly in those patients with absence of cancer. When extensive FPA is the only finding in patients with several negative prostatic biopsies, this lesion may be the source for PSA elevation.

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The 20-core prostate biopsy protocol--a new gold standard?

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Purpose: We investigated the ability of a 20-core prostate biopsy protocol to enhance the prostate cancer diagnosis rate.
Materials and Methods: We compared the diagnosis rate of prostate biopsies in 2 groups of consecutive patients, including group 1-10 cores and group 2-20 cores. The prostate specific antigen range in the 2 groups was 3 to 30 ng/mL and biopsies were performed because of increased prostate specific antigen (more than 3 ng/mL) and/or abnormal digital rectal examination. To analyze the results we divided each group into 3 subgroups according to prostate specific antigen, including group 1-3 to less than 6 ng/mL, group 2-6 or greater to less than 10 ng/mL and group 3-10 or greater to up to 30 ng/mL. Multivariate analysis was performed to assess the difference in the diagnosis rate among the subgroups according to the number of cores taken.
Results: The percent of positive biopsies was 39.7% in group 1 and 51.7% in group 2. Multivariate analysis confirmed that the number of biopsies taken was a factor that independently and significantly correlated with the prostate cancer diagnosis. The 20-core biopsy protocol was more efficient than the 10-core protocol in the 3 subgroups with 47.2% vs. 28.1% of patients diagnosed in group 1 (OR 3.26, p = 0.001), 40.5% vs. 36.1% in group 2 (OR 2.37, p = 0.009) and 69.8% vs. 39.7% in group 3 (OR 2.01, p = 0.015).
Conclusions: The 20-core biopsy protocol was more efficient than the 10-core biopsy protocol, especially in patients with prostate specific antigen between 3 and 6 ng/mL. Nevertheless, it is mandatory to confirm whether detected tumors are clinically significant on pathological examination of the radical prostatectomy specimens.

Editorial Comment

The authors of this manuscript demonstrated that the 20-core biopsy scheme was more efficient for diagnosing prostate cancer than the 10-core biopsy scheme in 3 distinct subgroups of PSA levels .Unfortunately they did not evaluate these two different protocols according to the patient age and prostate volume. As we know, prostate volume is a relevant variable in the planning of the optimal number of cores in the first scheme of biopsy. In our experience, there is no magic number of cores to be taken that could be adequate for all patients. We think that the location from where these cores were taken is more important than the total number of cores. Several reports in the literature has been shown that for prostate less than 40 cc, a scheme with 12 cores is usually adequate. However, this scheme is usually inadequate for prostate larger than 80 cc. Another important issue to consider is whether additional cores are or are not routinely obtained from suspicious hypoechoic lesion or area with clear abnormal flow on color Doppler examination. In a review of 589 consecutive TRUS-guided biopsy , where we prospectively removed 12 cores from prostates < than 40 cc; 14 cores from prostates with 41-60 cc; 16 cores from prostates with 61-80 cc and 18 cores from prostates > than 80 cc), there was no proportional increase in the prostate cancer detection rate. The two best results were obtained with 12 cores/ < 40 cc (44.8%) and 16 cores/ 61-80 cc) = 36.5%. The detection rate obtained with the scheme with 18 cores/ > 80 cc was only 29%. Additional cores obtained in all patients from suspicious lesions on gray-scale and/or color-Doppler were not included in these results. The presence of suspicious hypoechoic was not statistically significant but the use of color Doppler increased the overall diagnosis rate in 8% of patients (isoechoic cancer). Color-Doppler ultrasound was particularly useful for the detection of cancer in patients with larger glands.

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UROGENITAL TRAUMA

Retrograde urethrocystography impairs computed tomography diagnosis of pelvic arterial hemorrhage in the presence of a lower urologic tract injury

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Background: There is controversy about the appropriate sequence of urologic investigation in patients with pelvic fracture. Use of retrograde urethrography or cystography may interfere with regular pelvic CT scanning for arterial extravasation.

Study design: We performed a retrospective study at a regional trauma center in Toronto, Canada. Included were adult blunt trauma patients with pelvic fractures and concomitant bladder or urethral disruption who underwent initial pelvic CT before operation or hospital admission. Exposure of interest was whether retrograde urethrography (RUG) and cystography were performed before pelvic CT scanning. Main outcomes measures were indeterminate or false negative initial CT examinations for pelvic arterial extravasation.

Results: Sixty blunt trauma patients had a pelvic fracture and either a urethral or bladder rupture. Forty-nine of these patients underwent initial CT scanning. Of these 49 patients, 23 had RUG or conventional cystography performed before pelvic CT scanning; 26 had cystography after regular CT examination. Performing cystography before CT was associated with considerably more indeterminate scans (9 patients) and false negatives (2 patients) for pelvic arterial extravasation (11 of 23 versus 0 of 26, $p < 0.001$) compared with performing urologic investigation after CT. In the presence of pelvic arterial hemorrhage, indeterminate or false negative CT scans for arterial extravasation were associated with a trend toward longer mean times to embolization compared with positive scans ($p = 0.1$).

Conclusions: Extravasating contrast from lower urologic injuries can interfere with the CT assessment for pelvic arterial extravasation, delaying angiographic embolization.

Editorial Comment

This article brings up important points about the proper technique for performing retrograde urethrography for suspected traumatic urethral disruption injuries and for cytography for suspected bladder injuries. In this day and age, we only perform CT cystograms (instead of conventional cystography) to evaluate the patient with a pelvic fracture and gross hematuria. It was not clear from the article their criteria for deciding on bladder imaging, yet in our experience, the yield is small unless there is gross hematuria and a pelvic fracture.

The other point that this article raises, is that patients die after blunt trauma because of the “fatal triad”, namely being cold, coagulopathic and acidotic. In the initial time period after injury, adequate resuscitation and control of bleeding is key, to prevent the patient from spiraling downward. A bladder and/or urethral injury will not harm the patient or push him over the edge in the first few hours after a trauma. There is strong support for damage control of urologic injuries. It is reasonable that in a patient with a pelvic fracture who is hemodynamically unstable, the bleeding takes precedence and evaluating the urethra and bladder can wait.

As to pelvic fractures in general, the keys are to decrease the volume of the pelvis and so decrease the potential space for blood to collect. A small increase in radius increases volume by a great amount. By placing an external fixator a pelvic ring disruption, the true pelvis is reduced and cancellous bone re-approximated and in so doing allows venous bleeding to tamponade. Significant arterial bleeding, however will not stop with just true pelvis volume reduction. Arterial bleeding requires angiography and embolization. The most common arteries injured with pelvic fracture are the superior gluteal and the pudendals. Clearly, having significant

contrast extravasated from the bladder evaluation can potentially interfere with visualization of small pelvic arterial bleeders on subsequent angiography -however, the article is somewhat deceptive in that there was no statistical difference in the time to embolization in their two study populations. Perhaps, the study did not have the power to prove such- or the contrary, it may make no difference clinically.

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Three-dimensional analysis of pelvic volume in an unstable pelvic fracture

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Background: A model was developed to predict changes in pelvic volume associated with increasing pubic diastasis in unstable pelvic fractures.
Methods: Intact and postfracture pelvic volumes were calculated in 10 cadavers using computerized axial tomography (CT). The true pelvis was assumed to be either a sphere, a cylinder, or a hemi-elliptical sphere. Using the appropriate equations for calculating the volume of each of these shapes, pelvic volume was predicted and then compared with the measured values.
Results: The observed volume changes associated with increasing pubic diastasis were much smaller than previously reported. The mean difference between the measured and predicted volume was 20.0 +/- 9.9% for the sphere, 10.7 +/- 6.5% for the cylinder, and 4.5 +/- 5.9% for the hemi-elliptical sphere. The differences between these means were statistically significant ($p < 0.001$).
Conclusions: This data suggests that the hemi-elliptical sphere best describes the geometric shape of the true pelvis and better predicts quantitative changes in pelvic volume relative to an increasing pubic diastasis as the radius has little effect on the change in volume. Due to the small changes in volume observed with increasing diastasis, factors other than the absolute change in volume must account for the clinically observed effects of emergent pelvic stabilization.

Editorial Comment

This article is a complement to the above article on pelvic fracture. Reducing the absolute pelvic volume by pelvic reduction and stabilization is critical to helping venous bleeders to tamponade. Traditionally, the true pelvis is thought to be a sphere in shape, where an increase in pubis diastasis results in a marked volume increase, proportional to the radius cubed. They contend from their cadaveric experiments that the true pelvis is actually a hemi-elliptical sphere. Therefore, pelvic rind disruptions only increase the volume by the radius squared. This study suggests that reduction and stabilization of the pelvic ring disruption is more important then the reduction in volume.

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PATHOLOGY

The Impact of ISUP 2005 Consensus on Gleason Grading in Contemporary Practice

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Background: International Society of Urological Pathology (ISUP) in 2005 attempted to achieve a consensus in the application of Gleason grading system in contemporary practice. We investigated how the ISUP consensus impacted the Gleason grading in a center with a large urological pathology practice.
Design: We compared the Gleason score (GS) distribution and the GS concordance on biopsy and radical prostatectomy (RP) in two patient cohorts (before and after the ISUP consensus) in our institution. Both cohorts had similar demographic, preoperative clinical, and RP characteristics. The first cohort consisted of 908 consecutive patients with matched biopsies and RP, performed from 07/2000 to 06/2004 in our institution, prior to the ISUP consensus. The second cohort consisted of 423 patients with matched biopsies and RPs, performed from 10/2005 to 06/2007, after the ISUP consensus. All biopsies and RPs were reported by one group of pathologists.
Results: The ratio of GS 3+4 vs. 4+3 for GS7 on biopsy and RP was similar in both cohorts. Biopsy GS 7 (3+4 vs. 4+3): 24% vs. 6% (2001-2004) and 35% vs. 8% (2005-2007). RP GS 7 (3+4 vs. 4+3): 39% vs. 9% (2001-2004) and 48% vs. 12% (2005-2007). Biopsy GS compared to RP GS were upgraded in 8% and 5% and downgraded in 29% and 30% in cohorts 2001-2004 and 2005-2007, respectively. The most common change from biopsy to RP in both patient cohorts occurred due to biopsy GS 6 upgrade to RP GS 7 (change in secondary grade from 3 to 4).
Conclusions: We document a trend for upgrading GS on both biopsy and RP in our practice after the ISUP consensus. The significance of this change for patient management and prognosis is uncertain. Although the overall GS concordance on biopsy and RP have not been significantly impacted by the ISUP consensus, the complete agreement for GS7 has improved after the ISUP consensus.

Editorial Comment

The Gleason grading system is the most commonly used grading system for prostate carcinoma in the United States. Due to its unique aspects is gaining worldwide acceptance. The Gleason grading system is solely based on the architectural pattern, cytologic features are not factored in, the overall grade is not based on the highest grade within the tumor, and the prognosis of prostate cancer is intermediate between that of the most predominant pattern of cancer and that of the second most predominant pattern (1-4).

At the International Society of Urological Pathology (ISUP) consensus conference in 2005, the Gleason grading system underwent its first major revision (5). Several important reasons were considered for the need of a revision of the system: 1). In the 1960s, there was no screening for prostate cancer other than by digital rectal examination, as serum PSA had not yet been discovered. In Gleason's 1974 study (1), most (86%) of the men had advanced disease with either local extension out of the prostate on clinical examination or distant metastases. Only 6% of patients had nonpalpable tumor diagnosed by transurethral resection and 8% of patients were diagnosed with a localized nodule on rectal examination; 2). The method of obtaining prostate tissue was also very different from today's practice. Typically, only a couple of thick-gauge needle biopsies were directed into an area of palpable abnormality. The use of 18-gauge thin biopsy needles and the concept of sextant needle biopsies to more extensively sample the prostate were not developed until the 1980s. Consequently, the grading of prostate cancer in thin cores and in multiple cores from different sites of the prostate were not issues in Gleason's era; 3). In the 1960s, radical prostatectomy was relatively uncommon, prostates were not as often removed intact, and glands were not processed in their entirety or as extensively and systematically to the degree currently seen. Further issues relating to radical prostatectomy specimens such as the grading

of multiple nodules within the same prostate or dealing with tertiary patterns were not addressed within the original Gleason system; 4). The Gleason system also predated the use of immunohistochemistry. It is likely that with immunostaining for basal cells many of Gleason's original 1 + 1 = 2 adenocarcinomas of the prostate would today be regarded as adenosis (atypical adenomatous hyperplasia). Similarly, many of the cases in 1967 diagnosed as cribriform Gleason pattern 3 carcinoma would probably be currently referred to as cribriform high-grade prostatic intraepithelial neoplasia, if labeled with basal cell markers.

Stratifying the Gleason score into prognostic groups 2-4, 5-6, 7, and 8-10, using the modified Gleason grading there is a tendency for a change toward a higher prognostic group in approximately 25% of the biopsies (6). This occurs due to some new pathology criteria used in the revised ISUP grading: a) inclusion of most cribriform patterns in grade (pattern) 4; b) considering ill-defined glands with poorly formed glandular lumina as pattern 4; c) ignoring in high-grade cancer lower grade patterns if they occupy less than 5% of the area of the tumor; d) including high-grade tumor of any quantity within the Gleason score; and, e) for tertiary Gleason patterns, both the primary pattern and the highest grade are recorded.

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A contemporary study correlating prostate needle biopsy and radical prostatectomy Gleason score

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Purpose: We determined whether contemporary practice patterns of Gleason grading for prostate needle biopsy and radical prostatectomy have evolved.
Materials and Methods: We correlated needle biopsy (assigned at Johns Hopkins Hospital and other institutions) and radical prostatectomy Gleason score for 1,455 men who underwent radical prostatectomy at Johns Hopkins Hospital from 2002 to 2003, and compared the results with those of a 1994 study of similar design.

Results: Outside institutions diagnosed Gleason score 2-4 in 1.6% (23 of 1,455) of needle biopsies vs. 22.3% (87 of 390) in 1994. Of needle biopsies labeled Gleason score 2-4, 30.4% revealed radical prostatectomy Gleason score 7-10. In 2002 to 2003 no Johns Hopkins Hospital needle biopsy was assigned Gleason score 2-4. Needle biopsies designated Gleason score 6 or less had 80.0% accuracy with regard to radical prostatectomy Gleason score vs. 63% accuracy in older data. For needle biopsy Gleason score 7 or greater, 35.5% (outside institution) and 24.8% (Johns Hopkins Hospital) of radical prostatectomies displayed Gleason score less than 7. Overall, outside and Johns Hopkins Hospital needle biopsy diagnoses showed 69.7% and 75.9% agreement with radical prostatectomy Gleason score, respectively. Direct comparison of Johns Hopkins Hospital and needle biopsy Gleason scores elsewhere revealed 81.8% agreement, with 87.1% for Gleason score 5-6, 68.1% for Gleason score 7 and 35.1% for Gleason score 8-10. For 59.4% of outside needle biopsies with Gleason score 8-10, Johns Hopkins Hospital Gleason score was 7 or less. Conversely, for 64.9% of Johns Hopkins Hospital needle biopsies with Gleason score 8-10, outside Gleason score was 7 or less. For needle biopsies with Gleason score 5-6, 7 and 8-10, the incidence of nonorgan confined disease at radical prostatectomy was 17.7%, 47.8% and 50.0%, respectively, for Johns Hopkins Hospital vs. 18.2%, 44.6% and 37.5% for outside institutions.
Conclusions: The last decade has seen the near elimination of once prevalent under grading of needle biopsy. All cases still assigned Gleason score 2-4 show Gleason score 5 or greater at radical prostatectomy and nearly a third reveal Gleason score 7-10, reaffirming that Gleason score 2-4 is a needle biopsy diagnosis that should not be made. As evidenced by variable over grading and under grading, as well as poor correlation with pathological stage, difficulties in the assignment of Gleason pattern 4 and overall Gleason score of 8-10 on needle biopsy remain an important issue.

Editorial Comment

This study underlines the issue related to the Gleason score 2-4 in biopsies. In an Editorial published in 2000 (1), Epstein favors that Gleason score 2-4 adenocarcinoma of the prostate on needle biopsy is a diagnosis that should not be made. His arguments are based on the following facts: 1) the vast majority of tumors graded as Gleason score 2-4 on needle biopsy, when reviewed by experts in urologic pathology, are graded as Gleason scores 5-6 or higher; 2) Gleason score has a poor reproducibility in its diagnosis even among urologic pathologists; 3) assigning a Gleason score 2-4 to adenocarcinoma on needle biopsies can adversely impact patient care, because clinicians may assume that low-grade cancers on needle biopsy do not need definitive therapy. Not assigning a Gleason score 2-4 to adenocarcinoma on needle biopsy it does not mean that low-grade prostate does not exist. Gleason score 2-4 adenocarcinomas are typically seen on TURP. Low-grade cancers are rarely seen on needle biopsy because they are predominantly located anteriorly in the prostate within the transition zone and they tend to be small. In a series of 2285 biopsies in consultation, Epstein assigned a Gleason score of 2-4 in only 26/2285 (1.1%) consult biopsies demonstrating cancer.

The 2005 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma recommended that, rather than stating categorically that a Gleason score 4 on needle biopsy should “never” be made, this diagnosis should be made “rarely, if ever”. While recommending that the diagnosis of Gleason score 4 on needle biopsy should be made “rarely, if ever” is similar to “never”, it does allow for the exceedingly rare case where low grade cancer has been sampled on needle biopsy. The consensus conference cautioned that although the potential exists for rendering a diagnosis of Gleason score 4 on needle biopsy, it is a diagnosis that general pathologists should almost never make without consultation to an experienced urologic pathologist.

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UROLOGICAL ONCOLOGY

Dihydrotestosterone levels and survival in screening-detected prostate cancer: a 15-yr follow-up study

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Eur Urol. 2008; 53: 106-11

Objectives: It has been hypothesized that dihydrotestosterone (DHT), the main intracellular androgen in the prostate, affects prostatic tumour progression. In this study, we evaluated serum DHT levels at the time of prostate-cancer diagnosis in relation to survival.
Methods: Sixty-five screening-detected patients diagnosed in 1988-1989 were followed for 15 yr. DHT levels at the time of diagnosis were determined through radio-immuno assay. Subjects were followed up through the nationwide tax register. Medical records of all dead subjects were reviewed, and cause of death was established by an endpoint committee. Data were analyzed through Kaplan-Meier estimation and Cox proportional-hazards regression.
Results: Seventeen of 41 deaths in the cohort during follow-up were attributed to prostate cancer. Patients with DHT above the median had a significant better prostate-cancer-specific survival than those with DHT below the median (log rank p = 0.0075). In the univariate analyses, one unit increase in DHT was associated with a hazard ratio (HR) of 0.14 (95% CI=0.02-0.93). In the multivariate model, including prostate-specific antigen level, the association between DHT and prostate-cancer-specific survival was not significant (HR=0.18; 95% CI=0.02-1.6). DHT level below the median remained significantly associated with decreased survival in the multivariate model (HR=0.23; 95% CI=0.06-0.90). No association was found between DHT level and hazard of dying from causes other than prostate cancer.
Conclusions: Although the prognostic value of DHT levels at diagnosis remains unclear, these results provides evidence of an association between low DHT and decreased survival in prostate cancer patients.

Editorial Comment

The association of androgens and prostate cancer is still debated. This trial analyzes the relation of dihydrotestosterone (DHT) levels and survival in prostate cancer patients. Testosterone is the principal androgen and the main intracellular androgen in the prostate is DHT. DHT arises from intracellular conversion of testosterone and binds to the intracellular androgen receptor with an affinity seven-fold higher than testosterone.

The authors found a correlation of decreased survival and low DHT serum levels in their cohort of 65 patients. Although this study is hampered by several flaws such as small patient numbers, this is still a very

interesting manuscript, and to my knowledge, the first to look into DHT serum levels and prostate cancer survival. Further studies should focus into this topic.

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The template of the primary lymphatic landing sites of the prostate should be revisited: results of a multimodality mapping study

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Eur Urol. 2008; 53: 118-25

Objectives: To map the primary prostatic lymphatic landing sites using a multimodality technique.
Methods: Thirty-four patients with organ-confined prostate cancer (cT1-cT2; cN0) underwent single-photon emission computed tomography fused with data from computed tomography (SPECT/CT) (n = 33) or magnetic resonance imaging (SPECT/MRI) (n = 1) 1h after ultrasound-guided intraprostatic injection of technecium (Tc-99m) nanocolloid. The presence of lymph nodes (LNs) containing Tc-99m was confirmed intraoperatively with a gamma probe. A backup extended pelvic lymphadenectomy (PLND) was performed to preclude missed primary lymphatic landing sites. The SPECT/CT/MRI data sets were used to generate a three-dimensional projection of each LN site.
Results: A total of 317 LNs (median, 10 per patient; range, 3-19) were detected by SPECT/CT/MRI, 314 of which were confirmed by gamma probe. With an "extended" PLND, two thirds of all primary prostatic lymphatic landing sites are resected compared with only one third with a "limited" PLND.
Conclusions: The multimodality technique presented here enables precise mapping of the primary prostatic lymphatic landing sites. PLND for prostate cancer should include not only the external and obturator regions as well as the portions medial and lateral to the internal iliac vessels, but also the common iliac LNs at least up to the ureteric crossing, thus removing approximately 75% of all nodes potentially harbouring metastasis.

Editorial Comment

This report from Berne, Switzerland focuses on the extend of retroperitoneal lymph node dissection in prostate cancer. The authors used Spect/CT and MRI data to localize the lymph nodes in prostate cancer and tried to remove these during radical prostatectomy. They found primary landing site lymph nodes up to the mesenteric vein and para-aorta. The authors conclude that upon classical lymph-node dissection (LND) only 38% of the relevant lymph nodes are removed. On the other hand, pararectal, pre-sacral and para-aortal LND would add to morbidity and would compromise the results of nerve-sparing RPE. Therefore, an extended LND is seen as a compromise in patients with risk of nodal disease, where the template of classical extended LND is encompassed by a template including the common iliac arteries up to where the ureters cross. By this extended template up to 75% of the relevant lymph nodes would be removed.

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NEUROUROLOGY & FEMALE UROLOGY

Dyspareunia response in patients with interstitial cystitis treated with intravesical lidocaine, bicarbonate, and heparin

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Objectives: To test the dyspareunia response of patients with interstitial cystitis/painful bladder syndrome treated with an intravesical therapeutic solution of lidocaine, heparin, and sodium bicarbonate.
Methods: We studied consecutive patients with interstitial cystitis/painful bladder syndrome who were sexually active and were treated with an intravesical therapeutic solution. All patients provided their medical history, underwent a physical examination, and completed the Pelvic Pain Urgency Frequency symptom scale, voiding diary, and the pain domain (questions 17 to 19) of the Female Sexual Function Index before and after therapy. The patients were treated with intravesical instillations three times weekly for 3 weeks. The patients returned for follow-up 3 weeks later. The patients rated their response using a Patient Objective Rating of Improvement of Symptom scale.
Results: A total of 23 patients (mean age 38 years) were included in this study. Of the 23 patients, 15 (65%) reported improvements of greater than 50% on the Patient Objective Rating of Improvement of Symptom scale. Before and after instillation, nocturia was 4 +/- 2 versus 2 +/- 1 ($P < 0.001$), the voided volume was 98 +/- 59 mL versus 169 +/- 80 mL ($P < 0.001$), the Pelvic Pain Urgency Frequency score was 21 +/- 6 versus 15 +/- 6 ($P < 0.001$), and the Female Sexual Function Index pain domain score was 1.9 +/- 0.9 versus 3.7 +/- 1.6 ($P < 0.001$), respectively. Of the 23 patients, 13 (57%) reported resolution of dyspareunia. Of the 13 patients with bladder tenderness only versus the 7 with multiple tender locations on the vaginal examination, 11 (85%) versus 2 (29%) had resolution of dyspareunia ($P < 0.01$) and 12 (92%) versus 2 (29%) had successful overall outcomes ($P < 0.01$).
Conclusions: The results of this study have demonstrated that an intravesical therapeutic solution provides relief of voiding symptoms, pain, and dyspareunia in patients with interstitial cystitis/painful bladder syndrome. A randomized, prospective trial is warranted.

Editorial Comment

The authors analyzed the rate of dyspareunia in a female patient population diagnosed with interstitial cystitis and subsequently treated with intravesical instillations of a lidocaine/sodium bicarbonate/heparin solution three times a week for three weeks in a row. The therapy seemed to have a certain level of durability in that a definite percentage of patients were asymptomatic for three weeks. The authors noted that patients had a much higher response rate if prior to treatment they were plagued with bladder tenderness only on physical examination as opposed to a diffusely painful vagina on digital palpation.

This interesting paper highlights the association of sexual problems in patients with interstitial cystitis. It is heartening that those patients who had basically only bladder tenderness on vaginal palpation experienced an 85% resolution of their dyspareunia with this instillation therapy. The authors note that alkalinizing the lidocaine will allow it to have a greater penetration of bladder epithelium. Alkalinization of lidocaine has also been reported to diminish pain during interdermal injections with local infiltrated anesthesia. I found it noteworthy that the total solution instilled in the bladder was only 14 cc while the lidocaine gel instilled in the urethra to anesthetize prior to catheterization was 10 cc in itself. The logistical efficacy of intravesical therapies for patients in the office cannot be understated. Those with an interest in this specific population and therapy should definitely review the article upon which this report is based (1).

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The expectations of patients who undergo surgery for stress incontinence

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Objective: The purpose of this study was to assess patient expectations of surgical outcome after preoperative counseling of surgical procedures in a randomized trial of 655 women in a comparison of the rectus fascial sling and Burch colposuspension.
Study Design: Women who selected surgery for treating stress incontinence and who consented to this randomized, surgical trial completed a preoperative questionnaire to assess expectations for the postsurgical effects of surgery on urinary incontinence-related symptoms, limitations, and emotions. Associations of expectations with a range of preoperative urinary incontinence measures were explored.
Results: The most frequent preoperative symptoms were urine leakage (98%), embarrassment (88%), frequency (74%), physical activity (72%), and urgency (70%). Sexual and social limitations were less frequent (< or = 44%). Treatment expectations were higher for women who reported more symptom bother. As expected, most women (98%) had an expectation that urine leakage would be completely or almost completely eliminated. However, most women (92%) who reported urgency or frequency (83%) expected significant improvement of these symptoms after surgery.
Conclusion: Patients who undergo stress incontinence surgery have high expectations regarding the outcome of incontinence surgery, which include the resolution of urgency and frequency.

Editorial Comment

The authors reviewed the expectations of patients with regards to the anticipated results of their upcoming anti-incontinence operation (be it a Burch urethropexy or a autologous fascial suburethral sling). The patients had a consultation with their surgeon as well as viewing a standardized video presentation on the future surgery. The discussion of expectations and explanation of risks and benefits of surgery was standardized among the 22 surgeons at all the participating study sites. Even after both a video presentation and verbal discussion, 92% of the patients still expected that their urgency symptoms would resolve and 74% that their urinary frequency would improve with an anti-incontinence operation. Expectations were not related to preoperative health, age, physical examination or history of previous surgery.

An interesting article that formalizes the anecdotal experience of urologic surgeons: no matter how intensive the preoperative counseling and explanation of risks and benefits, patients expect an anti-incontinence

operation will address all aspects of their voiding dysfunction. It has been noted in the past that a certain percent of patients will have their urgency addressed with an anti-stress incontinence operation (1). The segment in whom the urgency persists will definitely report a lower satisfaction with their surgery even with a technically perfect procedure (2).

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PEDIATRIC UROLOGY

Outcome analysis of severe chordee correction using tunica vaginalis as a flap in boys with proximal hypospadias

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Purpose: There is ongoing controversy regarding optimal treatment for severe ventral curvature. It has been suggested that ventral corporeal lengthening may be associated with recurrent curvature and erectile dysfunction. To further assess these issues we reviewed our experience with ventral penile lengthening for correcting the severe ventral curvature associated with proximal hypospadias.
Materials and Methods: We reviewed the records of 38 boys with severe hypospadias and congenital ventral curvature greater than 45 degrees who were treated at our institution from 1995 to 2004 with placement of a flap or graft in the corporeal bodies to straighten the phallus. Of the patients 21 had perineal and 17 had penoscrotal hypospadias, including 22 with associated penoscrotal transposition and/or bifid scrotum and 6 with ambiguous genitalia. Testosterone stimulation before surgery was given in 11 children at surgeon discretion.
Results: Median age at surgery was 15 months. The urethral plate was divided in 94.7% of patients. A tunica vaginalis flap was used alone in 23 cases and associated with dura, pericardium or small intestinal submucosa in 8, 2 and 1, respectively. The remaining 4 patients underwent ventral grafting alone, including lyophilized dura in 1, pericardium in 1 and dermis in 1. Urethral reconstruction was achieved by the transverse island flap technique or 1 of its modifications in 34 children. Four boys underwent a 2-stage procedure. Followup available on 35 of 38 patients was 1 to 11 years (median 5.3). Recurrent ventral curvature in 5 of 35 patients was mild in 1 and clinically significant, requiring re-intervention, in 4. Four of 9 patients (44.4%) who underwent corporeal grafting with lyophilized dura had recurrent ventral curvature vs. 1 of 23 (4.3%) who had a tunica vaginalis

flap (chi-square 5.14, p = 0.02). At last followup straight erections were documented by patients and/or parents in 30 of 35 children (85.7%). Conclusions: The short-term outcome of ventral penile lengthening using tunica vaginalis flap alone for correcting severe chordee is favorable with a 95% success rate. Dural grafts were associated with a higher risk of recurrent ventral curvature compared to tunica vaginalis flaps. Although most of our patients were not yet adults, when chordee and erectile dysfunction may become apparent, we believe that tunica vaginalis flap repair is a good option for correcting severe ventral curvature.

Editorial Comment

Important points made in the manuscript include that if grafting is the surgeon's choice, that the grafts should be 20-30% larger than the defect. The tunica vaginalis flap was easy to harvest and these authors had excellent success. Being a flap rather than a graft, it can be cut to the appropriate size. The blood supply has been shown to be reliable and the complications noted doing a one-stage repair are in line with what one would expect from one-stage repairs without the severe curvature correction. I find most mild chordee can be corrected dorsally but I agree with these authors that the tunica vaginalis flap is their procedure of choice to correct severe chordee on the ventral aspect of the penis.

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Long-term tolerability of tolterodine extended release in children 5-11 years of age: results from a 12-month, open-label study

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Objective: To evaluate the long-term tolerability of tolterodine extended release (ER) in children (aged 5-11 yr) with urgency urinary incontinence (UUI).
Methods: This was a multicenter, open-label extension of a 12-wk, double-blind, placebo-controlled study of tolterodine ER. Patients had UUI suggestive of detrusor overactivity (>/= 1 diurnal incontinence episode per 24h for >/= 5 of 7 d) and >/= 6 voids per 24h at baseline and had completed the 12-wk double-blind study. Patients received tolterodine ER (2mg once daily) for 12 mo. The primary end points were the incidence and severity of adverse events (AEs) and the incidence and reasons for withdrawals. Visits were scheduled at 3, 6, 9, and 12 mo, and investigators were instructed to report all AEs. At 6 and 12 mo, vital signs were recorded and a physical examination was performed.
Results: A total of 318 patients were enrolled (double-blind tolterodine ER, n = 221; placebo, n = 97). The majority of patients were white (90%), mean +/- SD age was 7.6 +/- 1.5 yr, and 54% were boys. Forty-nine percent of patients reported >/= 1 AE during the study, similar to that observed in the preceding 12-wk study (42%). The most frequent AEs were urinary tract infection (7%), nasopharyngitis (5%), headache (5%), and abdominal pain (4%); 111 (35%) patients withdrew. The most common reasons for withdrawal were lack of efficacy (12%), symptom improvement (8%), and withdrawn consent (6%). Ten patients (3%) withdrew because of AEs.
Conclusion: Long-term treatment with tolterodine ER was well tolerated in children with UUI.

Editorial Comment

This is the first large-scale prospective study for long-term safety and tolerability of tolterodine extended release, showing mostly mild side effects and 65% of the patients completing the entire 12 month treatment period. Few long-term drug studies are performed in children, which makes this study more significant. My regret for the study is that they did not include an efficacy arm so that a practitioner could have all the information necessary to make wise treatment choices for their patients that may need long-term care.

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