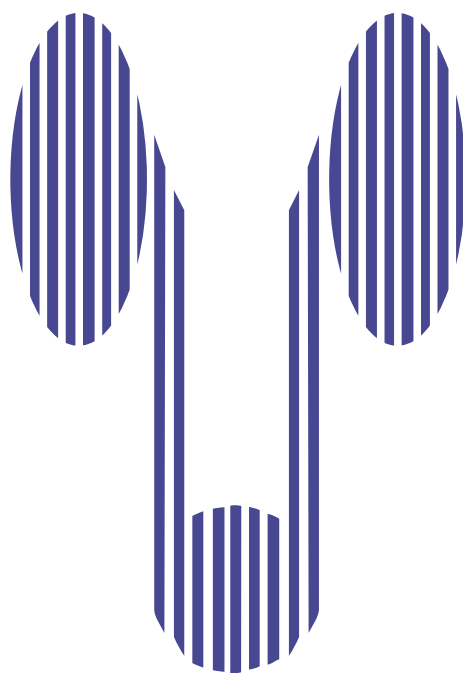


# International

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## **EDITOR'S COMMENT**

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The May – June 2003 issue of the International Braz J Urol presents interesting contributions from different countries, and as always the Editor will highlight some important papers.

Doctors Marcovith and Smith from Long Island Jewish Medical Center, New Hyde Park, New York, USA, provided on page 195 a thorough presentation and discussion on how to choose extracorporeal shock wave lithotripsy (SWL) and percutaneous nephrolithotomy (PNL) for treating renal pelvic stones. The authors stated that the most important to consider is that there is a rational approach to the selection of SWL or PNL. Each modality has advantages and disadvantages, and the application of either one should be based on well-defined factors. These variables include stone factors such as number, size, and composition; factors related to the stone's environment, including the stone's location, spatial anatomy of the renal collecting system, presence of hydronephrosis, and other anatomic variables, such as the presence of calyceal diverticula and renal anomalies; and clinical or patient factors like morbid obesity, the presence of a solitary kidney, and renal insufficiency. The morbidity of each procedure in relation to its efficacy should be taken into account. This article synthesized the current knowledge, and provided guidelines that represent state-of-the-art recommendations for treatment of stones of the renal pelvis using these 2 modalities.

Doctor Prando from Vera Cruz Hospital, Campinas, São Paulo, Brazil, proposed on page 208 a radiological classification of renal angiomyolipomas after studying an important series of 127 tumors. The author, based on the presence and amount of identifiable fat within the lesion, classified the renal angiomyolipomas in 4 distinct radiological patterns: pattern-I, predominantly fatty (usually less than 2 cm in diameter and intrarenal), corresponding to 54% of the cases; pattern-II, partially fatty (intrarenal or exophytic = 29%); pattern-III, minimally fatty (most exophytic and perirenal = 11%); and pattern-IV, without fat (most exophytic and perirenal = 6%). This classification would have important implications for management and selection of therapeutic alternatives. Doctor Rosenfield from Yale University School of Medicine, New Haven, Connecticut, USA, provided an excellent Editorial Comment on this manuscript.

Doctors Dall'Oglio and colleagues, from Federal University of São Paulo, Brazil, analyzed on page 221 the evolution of 5 cases of disruption of vesicourethral anastomosis during the post-operative period in a consecutive series of 1,600 radical retropubic prostatectomies, performed by a single surgeon. The management was conservative in all the cases with an average catheter permanence of 28 days. Two cases were secondary to bleeding, 1 followed the change of vesical catheter

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

and 2 were by unknown causes after removing the Foley catheter. Only one patient evolved with urethral stenosis, in the period ranging from 6 to 120 months. The authors concluded that this rare complication (0.3%) is not related to the surgeon's experience, and conservative treatment has shown to be effective.

Doctors Suaid and co-workers from University of São Paulo, Brazil, estimated the costs of benign prostatic hyperplasia (BPH) treatment in Brazil (page 234). The authors found that the estimated population for medical treatment was 5,397,321 individuals, with a cost corresponding to US\$ 1,916,489,055.00. The estimated population for surgical treatment was 2,040,299 men, what would represent a cost of US\$ 353,291,204.00 based on the Brazilian Unified Health System table and of US\$ 1,904,279,066.00 based on the Brazilian Medical Society table, with hospital expenses included. These figures induce us to predict that the treatment of BPH in the near future can become a public health problem for Brazilian society, since the current estimate costs would be around 2.26 – 3.83 billion dollars, added by the yearly increase in the risk population (25%) for the group under medical treatment and over the non-operated amount of the surgical group.

Doctors Rubeinstein and McVary, from Northwestern University, Chicago, Illinois, USA, in the best of my knowledge, provided our readers with the most complete and up-to-date presentation on transurethral microwave thermotherapy (TUMT) for benign prostatic hyperplasia (BPH) available in the literature (page 251). In this review, the authors discussed the current indications and outcome of TUMT, including the history of the procedure, the mechanism of action, the indications for TUMT, the pre-operative considerations, the patient selection, the results in terms of efficacy, by comparing TUMT vs. Sham, TUMT vs. Alpha-blocker and TUMT vs. TURP. Finally, the complications are presented, as well as other uses and future directions of the procedure. The authors concluded that TUMT is a safe and effective minimally invasive alternative to treatment of symptomatic BPH. Since TUMT can be performed in a 1- to 2-hour office visit without intravenous sedation, this is a good alternative for patients who are at high surgical and anesthetic risk. Nevertheless, the procedure is not effective for patients with a large median lobe or a very large prostate and results in less urinary flow patterns than transurethral resection of the prostate.

***Dr. Francisco J.B. Sampaio***  
Editor-in-Chief

## RENAL PELVIC STONES: CHOOSING SHOCK WAVE LITHOTRIPSY OR PERCUTANEOUS NEPHROLITHOTOMY

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### ABSTRACT

Introduction of minimally invasive techniques has revolutionized the surgical management of renal calculi. Extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy are now both well-established procedures. Each modality has advantages and disadvantages, and the application of each should be based on well-defined factors. These variables include stone factors such as number, size, and composition; factors related to the stone's environment, including the stone's location, spatial anatomy of the renal collecting system, presence of hydronephrosis, and other anatomic variables, such as the presence of calyceal diverticula and renal anomalies; and clinical or patient factors like morbid obesity, the presence of a solitary kidney, and renal insufficiency. The morbidity of each procedure in relation to its efficacy should be taken in to account. This article will review current knowledge and suggest an algorithm for the rational management of renal calculi with shock wave lithotripsy and percutaneous nephrolithotomy.

**Key words:** kidney; kidney calculi; lithotripsy; nephrolithotomy; percutaneous; shock wave lithotripsy  
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### INTRODUCTION

Perhaps in no other field of surgery has the treatment of a condition changed so dramatically, and in such a short period of time, as in the surgical treatment for nephrolithiasis. The last 25 years have seen a remarkable shift from open procedures, such as nephrolithotomy and ureterolithotomy, to endourological approaches, including shock wave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PNL). Recent data from the Center for Medicare and Medicaid Services (CMS), a United States government agency which oversees payment to physicians and health care organizations for patients age 65 and older, bears out the dramatic shift. In the past decade, Medicare claims for open stone procedures have dropped 74%, while those for PNL have gone up 53% in just the last half of the decade (1). Shockwave lithotripsy is currently

the single, most-commonly performed urological procedure in the US, and over the past decade the total number of SWL claims in the CMS database has increased by 37% (1).

While it is clear that endourology now constitutes the contemporary paradigm for surgical stone therapy, there still exist areas of controversy with regard to choice of specific endourological modality. There has especially been an ongoing debate between proponents of shock wave lithotripsy and percutaneous nephrolithotomy. A number of clinical studies performed over the last 15 years have attempted to define the optimal therapeutic approach for a given stone, although most of these studies have been retrospective in nature. What is most important to consider, however, is that there is a rational approach to the selection of SWL or PNL. Each modality has its specific role in the treatment of nephrolithiasis. It is the purpose of this article,



therefore, to synthesize current knowledge, and to provide guidelines which represent state-of-the-art recommendations for treatment of stones of the renal pelvis using these 2 modalities.

## HOW DO WE DEFINE SUCCESS?

The optimal therapy for a particular stone is the one most likely to achieve success with the least morbidity to the patient. A lack of consensus exists among urologists regarding what constitutes successful stone therapy. Two parameters have been used in the literature: stone-free rate (SFR) and success rate. The stone-free rate is the percentage of kidneys from which all stone material has been cleared based on postoperative radiographic imaging, while success rate encompasses both patients who become stone-free as well as patients who have only clinically insignificant residual fragments (CIRF) at 3 months following SWL (2). Despite the latter definition, which was introduced because of the observation that not all fragments clear completely after SWL, there is substantial evidence that fragments which are considered clinically insignificant (i.e. < 4 mm in greatest dimension) may in fact bear considerable risk of becoming significant. For example, Streem et al. showed that at a mean follow-up of 23 months after SWL, up to 43% of patients with "CIRF" experienced a significant symptomatic episode or required another intervention (3). Furthermore, residual fragments can act as a nidus for further stone growth. In a study of 83 patients with CIRF of < 4 mm followed for a median 40 months, Candau et al. showed that fragments increased in size in 37% of patients, and 22% required further intervention (4).

The fundamental difference between PNL and SWL is that PNL gives the surgeon control not only of fragmentation, but also of extraction, while SWL does not permit the surgeon any control over stone extraction. Theoretically, any stone is amenable to successful treatment with PNL. With SWL, the only way for the urologist to positively influence the stone-free rate is by careful patient selection. Therefore, much of this review will focus on selection factors for, and outcomes of, shock wave lithotripsy.

## VARIABLES IN TREATMENT SELECTION

There are 3 categories of variables to consider when choosing a rational treatment approach to renal stones: factors related to the stone, factors related to the stone's environment, and clinical factors. Stone factors include the number of stones and their size and composition; environmental factors include the stone's location, the spatial anatomy of the renal collecting system, the presence of hydronephrosis, and other anatomic factors such as calyceal diverticula and renal anomalies. Clinical factors such as the presence of morbid obesity or a solitary kidney should also be taken into consideration. Finally, the tools available to do the job must be taken into account, especially when considering the wide variety of extracorporeal lithotriptors in use and the endourological equipment at various institutions.

### Stone Factors

#### *Composition*

Stone composition should be a major consideration in choosing the treatment approach. Zhong & Preminger studied the interactions which occurred between shockwaves and renal calculi of differing compositions, including cystine, calcium oxalate monohydrate (COM), brushite, uric acid, apatite, and struvite (Table-1) (5). They found cystine stones to have the highest fracture toughness of all of the different calculi. Cystine stones were also classified as ductile rather than brittle, indicating that when struck with a pressure wave, they tended to deform rather than crack, explaining the clinical observation that cystine stones are difficult to fragment with SWL. Cranidis et al. used SWL monotherapy on 11 renal units with cystine calculi averaging 9 mm in size and reported only a 54% success rate with a mean number of 2.2 SWL sessions per kidney using a Dornier HM-4 lithotripter (6). In Zhong & Preminger's study, COM stones were found to be harder than cystine stones, but had a lower fracture toughness because COM stones were of a brittle, rather than ductile, composition. Stones composed of brushite (calcium hydrogen phosphate

**Table 1** - Fracture hardness of various types of urinary calculi.

Stone Type	Fracture Hardness (KPa/m <sup>2</sup> )	Material Type
Cystine	> 200	Ductile
COM	136	Brittle
Brushite	119	Brittle
Uric Acid	90	Brittle
Apatite	57	Brittle
Struvite	56	Brittle

Adapted from Zhong P and Preminger GM: *J Endourol* (1994) 8:263-268. kPa/m<sup>2</sup>, kilopascals per meter squared; COM, calcium oxalate monohydrate.

dihydrate) have also been shown to fragment poorly with SWL (7).

For those patients who are recurrent stone formers and have undergone a prior stone analysis, stone composition is known and, therefore, can be used as part of the decision making process. For those patients who present without a previous stone analysis, determining the “a priori” composition of their current stone offers a greater challenge. In addition to simple examination of the urine for crystals, radiographic analysis of the stone may help in determining composition. Dretler & Polykoff documented the relationship between composition and morphology for calcium oxalate stones (8), and Bon et al. took this one step further by attempting to correlate stone-free rates after SWL with radiographic appearance of the stone (9). Using multivariable regression analysis, the latter group found that stone-free rates were higher when stones were less dense than the bone of the 12<sup>th</sup> rib or transverse process of a vertebra, and when they were determined to be subjectively rough in appearance rather than smooth. The authors also found a significant correlation between stone composition and radiographic appearance, with COM stones being smooth in 73% of cases and denser than bone in 70%, while calcium oxalate dihydrate stones were rough 94% of the time and less dense than bone in 74% of cases. They reported a 79% SWL stone-free rate with rough, less dense stones versus a 34% SWL stone-free rate for smooth, more dense stones.

The increasing use of unenhanced helical computerized tomography (CT) for the diagnosis of

upper tract urolithiasis may provide a more sensitive assessment of stone fragility than plain radiography. Helical CT has been used to accurately determine the composition of struvite, uric acid, and calcium oxalate stones “ex vivo”, but there has been overlap between calcium oxalate and brushite, as well as between cystine and struvite (10). Recently, Williams et al. found that using a 1-mm slice width and bone windows improves “ex vivo” visualization of renal stone structure on CT (11). Use of these specific CT parameters in the clinical setting has not yet been reported. However, Joseph et al. published a report in which the Hounsfield attenuation of the stone at the cross-section of its greatest dimension was assessed and compared to stone clearance rates in 30 patients undergoing SWL for stones between 5 and 20 mm diameter. The stone clearance rate for stones of less than 500 Hounsfield units (HU) was 100%, whereas clearance rates for HU of 500 - 1000 and > 1000 were 85.7% and 54.5%, respectively (12). It seems likely that continued advances in preoperative imaging will allow for more accurate pre-treatment determination of stone composition.

### Size

Stone size is much easier to determine preoperatively than stone composition, and has therefore been the primary criterion used to date for treatment selection. When more than one stone is present, the stone burden can be approximated by summing the sizes of all of the calculi.

Although predominantly formed of struvite, the material with the lowest fracture toughness (5),

staghorn calculi are the largest of stones and should be considered a contraindication to the use of SWL monotherapy. In a comparison of complete and partial staghorns treated with PNL or SWL monotherapy (Dornier HM-3), 40% of patients with partial staghorns and 33% of patients with full staghorns treated with SWL required postoperative placement of a nephrostomy tube for obstruction, as well as multiple repeat procedures (13).

Streem et al. have advocated combination PNL and SWL “sandwich” therapy for treatment of “extensive” calculi. They reported results of 100 renal units treated with this approach, using 1 to 3 percutaneous tracts and 1 to 3 SWL procedures per patient. The stone-free rate in this cohort at 1 month was 63%, and 34% of patients experienced a complication, mainly fever or the need for a blood transfusion. Meretyk et al. performed a prospective, randomized trial comparing SWL monotherapy on a Dornier HM-3 to combination PNL/SWL in 50 kidneys with complete staghorn stones. The SFR was 74% for the combination group versus only 22% for the SWL group, and the residual stone load in patients who were not rendered stone free was much greater in the SWL group compared to the combination group. The complication rate in the SWL monotherapy group was also significantly higher (15).

Lingeman et al. compared the SFR and retreatment rates for stones < 20 mm and > 20 mm treated with PNL versus those treated with SWL on a Dornier HM-3. The SFR for stones less than 20 mm in size treated with SWL was 76%, with a 19% retreatment rate. In comparison, the SFR for comparable stones < 20 mm treated with PNL was approximately 90%, with 8% requiring additional treatment. For stones > 20 mm treated with SWL, the SFR was only 41% compared to 82% for PNL. Of these larger stones treated with SWL, 62% required additional procedures compared 32% who initially had PNL. Although the complication rate of PNL in this study was 24% compared to only 2.6% for SWL, the majority of PNL complications were fever > 39° C (responsible for 11% of the PNL complications), the need for blood transfusion, and perforation of the renal pelvis (each responsible for 5.5% of the PNL complications) (16).

## Environmental Factors

### *Location*

The renal pelvis is the most favorable location for the application of shock wave lithotripsy. In an analysis of 9 published series on the treatment of 8000 stones with SWL, stone-free rates for renal pelvic stones ranged from 80% (size < 10 mm) to 56% (size > 20 mm). For stones less than 20 mm in diameter, upper pole stones were completely cleared in 59% to 72% of cases and middle calyceal calculi were cleared in 57% to 77% of cases. Although small (less than 10 mm) lower pole calculi had comparable clearance rates to small stones located elsewhere, the stone-free rates for larger stones in the lower pole were considerably less – 55% for 11 - 20 mm and only 34% for > 20 mm (7).

### *Renal Collecting System Anatomy*

Due to lower clearance rates, the management of lower pole nephrolithiasis has received considerable attention over the years. Sampaio & Aragão proposed that lower pole calyceal anatomy might impact stone clearance after SWL (17). Despite multiple subsequent studies to date, there are still no clear guidelines because of conflicting results and differing anatomic definitions. Sampaio et al. defined the lower pole infundibulopelvic angle (LIA) as the angle between the central axis of the stone-bearing minor calyx and a line running from the central axis of the proximal ureter and the central axis of the ureteropelvic junction (UPJ) (18). They showed a significantly higher stone-free rate at 3 months in patients with LIA > 90° (18). Sabnis et al. defined LIA as the angle formed between the central axis of the stone-bearing minor calyx and the axis of the renal pelvis at the junction of the lower pole infundibulum, and also looked at the role of the lower pole infundibular width (LIW). This group also found that LIA > 90° was associated with improved stone clearance and added that LIW > 4 mm had an 84% SFR compared to LIW < 4 mm (SFR of 30%) (19). Elbahnasy et al. added lower pole infundibulopelvic length (LIL) as a variable. They found that the stone-free group had

significantly more obtuse LIA ( $75^\circ$  vs.  $51^\circ$ ), wider LIW (9 mm vs 6 mm), and shorter LIL (3.2 cm vs. 3.8 cm); and that patients in which all 3 parameters were unfavorable (LIA  $< 90^\circ$ , LIL  $> 3$  cm, and LIW  $< 5$  cm) had a stone-free rate of only 17%. Again, a different definition of LIA was used in this study than in the previous ones (20).

A significant step towards resolving the issue of optimal treatment for lower pole stones was recently taken with the publication of the results of Lower Pole I, a multi-institutional, prospective, randomized trial of SWL and PNL for lower pole renal calculi (21). In this study 128 patients with lower calyceal stones less than 3 cm in greatest dimension were randomized to either SWL or PNL. Overall, SFR were 95% for PNL and 37% for SWL, and PNL was found to yield a significantly higher SFR in all groups stratified by size (Table-2). Interestingly, lower pole infundibulopelvic anatomy had no significant influence on stone free rates after SWL, although this may have been because anatomic data were available for only 38 patients, and the stone-free rate in this group was only 45%. Retreatment rate and use of auxiliary procedures occurred in 31% of patients undergoing SWL, while only 10% of PNL patients required further treatment or an auxiliary procedure. As expected, SWL had a lower complication rate than PNL (12% vs. 23%), but this was not statistically significant. There was a significant improvement in quality-of-life (QOL) scores after treatment in both groups, but no difference was found in QOL scores between the two groups. This study would seem to indicate that PNL is superior to SWL for lower pole calculi. Nevertheless, we would still be hard pressed to advocate PNL over SWL for stones less than 10 mm,

and the present review has not considered the substantial role of ureteroscopy for addressing stones less than 20 mm in diameter, regardless of location.

### **Hydronephrosis**

Hydronephrosis is another important factor to consider when choosing SWL or PNL. Hydronephrosis may be an indicator of an underlying abnormality such as UPJ obstruction. In the setting of a renal pelvic calculus with apparent UPJ obstruction, it is difficult to determine whether the UPJ obstruction preceded the stone or whether the stone has caused edema at the UPJ which will resolve subsequent to removal of the stone. Nevertheless, there is ample evidence to suggest that PNL provides superior stone-free rates in cases associated with hydronephrosis. Winfield et al. noted a stone-free rate of 53% following SWL for staghorns in hydronephrotic systems compared to 70% for staghorns in normal systems (13). Meretyk et al. noted a 26% SFR in patients undergoing SWL monotherapy for staghorns in hydronephrotic systems, compared to 80% for similar patients who had PNL instead (15). In patients with renal stones associated with hydronephrosis secondary to obstruction of a ureteroenteric diversion, SWL renders the kidney stone free in only 25% to 75% of cases, in comparison to PNL, which results in clearance 60% to 100% of the time (22). SWL is contraindicated in cases in which there is obstruction distal to the stone.

### **Calyceal Diverticulum**

A calyceal diverticulum is an outgrowth of a calyx which communicates with the rest of the

**Table 2 - Comparison of stone-free rates for lower pole calculi, shock wave lithotripsy versus percutaneous nephrolithotomy.**

Stone Size	% Stone-Free		p-value
	Shock Wave	PNL	
1-10 mm	63%	100%	0.003
11-20 mm	23%	93%	$< 0.001$
21-30 mm	14%	86%	0.029

*Adapted from Albala et al: J Urol (2001) 166:2072-2080. PNL, percutaneous nephrolithotomy.*



collecting system through a narrow channel. Stones may form in these structures as result of urinary stasis in the diverticulum. Stones in calyceal diverticula may be approached with SWL, PNL, ureteroscopy, or laparoscopy. Stone-free rates for SWL of calyceal diverticular stones are quite low, on average less than 25%, and shock wave has the disadvantage of not being able to get rid of the diverticulum itself. Nevertheless, symptomatic relief, at least in the short term, occurs in upwards of 70% of patients undergoing SWL for calyceal diverticular stones. SWL therapy for calyceal diverticular stones may be considered in select patients with stones less than 1.5 cm and a diverticular neck which is shown to be short and patent on radiography. Yet, even in this group of patients, stone-free rates barely approach 60% (23). The authors of the present review question whether diverticula with short, patent necks and good drainage really exist.

Although more invasive, a percutaneous approach allows direct access to the inside of the diverticulum, facilitates stone removal, and allows the urologist to dilate or incise the neck and fulgurate the wall of the diverticulum. Stone-free rates following PNL of calyceal diverticular stones range from 77% to 100% and resolution of the diverticulum occurs in an average of 78% of cases.

### ***Renal Anomalies***

Renal calculi may occur in horseshoe kidneys as well as pelvic kidneys, owing to the relatively high ureteral insertion in the former and the malrotation often seen in the latter, both of which may result in urinary stasis. SWL can be used to treat stones in both horseshoe and ectopic kidneys, but stone localization may be more difficult.

In order to perform PNL in pelvic kidneys, a laparoscopic-assisted transperitoneal approach, with various modifications, has been described (24-26). However, due to the relative difficulty of accessing the collecting system of a pelvic kidney percutaneously, SWL should be the initial approach to stones in this situation, despite the relatively poor results. Kupeli et al. reported a 54% stone-free rate following SWL therapy to stones in pelvic kidneys

(27). Patient positioning is a key factor in SWL in pelvic kidneys. The patient may be positioned supine if the bony pelvis does not hinder delivery of shock waves to the target; otherwise, the prone position should be used. A similar prone approach may be taken with a patient who has a stone in a transplant kidney.

In horseshoe kidneys, the position of the collecting system may not allow for adequate visualization of the stone, nor for satisfactory stone clearance after SWL, especially from the lower calyces. Stone-free rates following SWL in horseshoe kidneys range from 54% for lower pole calculi to 100% for middle and upper calyceal stones (28). Kirkali et al. found that stones > 10 mm fare poorly (SFR of 28%) (29). Furthermore, there tends to be a very high recurrence rate in patients with horseshoe kidneys who are not rendered stone-free (30).

As an alternative, PNL can be readily performed in horseshoe kidneys, because their position, with the upper pole more posterior and lateral, facilitates percutaneous puncture. However, if the approach is to a lower calyx the risk of bowel injury is higher. Stone-free rates range for PNL in horseshoe kidneys range from 75% to 100% (31,32). In summary, SWL should be the first line therapy for most stones in pelvic kidneys. In horseshoe kidneys, SWL may be used for stones less than or equal to 10 mm in the middle or upper pole, and the kidney should have good drainage documented radiographically. Otherwise, PNL or ureteroscopy are the treatments of choice.

### ***Renal Cysts***

Renal cystic disease may cause distortion of the collecting system which can adversely affect stone clearance after SWL. Deliveliotis et al. performed SWL in 15 patients with large (mean size 5 cm), distorting renal cysts but normal renal function. The mean stone size was 1 cm, and despite a 100% fragmentation rate, only 60% of patients were stone free at one month follow-up. The SFR in patients with polycystic kidney disease was 25% compared to 73% in patients who only had simple cysts (33).

## SPECIAL CIRCUMSTANCES

### *Solitary Kidney and Renal Insufficiency*

Both SWL and PNL are known to produce short-term renal injury. The question therefore arises whether either of these modalities has significant deleterious effects in patients with only one kidney.

In 1990, Brito et al. reported 5 year follow up of 8 patients with solitary kidneys treated with SWL (34). The mean serum creatinine in these patients rose significantly, from 1.53 mg/dl pre-SWL to 2.31 mg/dl at 5 years post-treatment. The small number of patients in this study, as well as the fact that some degree of renal insufficiency was present prior to SWL in some of the patients (as indicated by the elevated mean creatinine level for the cohort prior to treatment), may have biased this study. Chandhoke et al. compared long-term renal function in 31 patients with solitary kidneys with or without renal insufficiency following SWL or PNL (35). In patients with a solitary, normally-functioning kidney, deterioration in renal function (defined as at least a 20% decrease in glomerular filtration rate, GFR) was seen in 22% of SWL patients and in 29% of PNL patients. In patients with 1 or 2 kidneys and moderate renal insufficiency (serum creatinine 2 mg/dl to 3 mg/dl) prior to treatment, no long-term deterioration in GFR was seen after either SWL or PNL. In patients with 2 kidneys but serum creatinine over 3 mg/dl, long-term deterioration in GFR was seen in all 4 patients who underwent SWL, while the only patient in this group who underwent PNL showed no decrease in GFR. This study concluded that SWL and PNL were equally safe in patients with solitary kidneys and normal renal function and in patients with 2 kidneys and mild renal insufficiency, and that the choice of procedure in these patients should be determined by stone factors (size, composition, location, etc.) rather than on renal function or the presence of a solitary kidney. More recently, Liou & Streem compared the long-term effects of SWL, PNL, and combination therapy in patients with solitary kidneys and found no evidence of renal deterioration in any of the treatment arms, even in patients with a pre-treatment serum creatinine higher than 2 mg/dl (36). Thus, it appears that both SWL

and PNL may be safely performed without untoward long-term effects on renal function either in patients with a solitary kidney or in patients with two normal kidneys.

### *Obesity*

The morbidly obese patient with stone disease presents a therapeutic challenge. SWL may not be feasible if the patient is too heavy for the gantry or table. The distance from the patient's skin to the stone may be longer than the focal length of the lithotripter. Therefore, the machine used for SWL in obese patients should have a long focal length and should be able to generate a high peak pressure. Body mass index has been found to be an independent predictor of successful SWL, with a decreased chance of success in larger patients (37). In patients in whom stone factors do not mandate PNL, ureteroscopy may be a better choice than SWL.

Obesity may also pose a problem for patients in whom PNL is contemplated. A longer sheath and instruments may be necessary to traverse the distance to the kidney. If necessary, stay sutures may be placed on the end of the working sheath in order to allow it to be advanced deeper into the abdominal wall, thereby bridging the gap to the kidney. The most significant consideration in obese patients is the potential morbidity of prolonged general anesthesia in the prone position. Morbidly obese patients often have other significant comorbidities, such as hypertension, diabetes mellitus, cardiovascular disease, and pulmonary restrictive disease, all of which increase the risk of general anesthesia. Despite this, most studies have failed to show any significant increase in complications or rates of transfusion in obese patients compared to their leaner counterparts (38,39).

## EXTRACORPOREAL LITHOTRIPTORS

The technologies used to fragment stones during PNL, namely ultrasonic and electrohydraulic lithotripsy, have changed little since their inception. Extracorporeal lithotriptors, on the other hand, have undergone significant modifications since the introduction in the early 1980s of the Dornier HM-3,

especially with regard to down-sizing of the focal area in order to minimize collateral tissue damage. The proliferation of SWL machines over the past decade has made it difficult to compare outcomes because of the variety of machines in use; but in the opinion of many experts, the post-HM-3 modifications have only served to decrease the efficacy of stone fragmentation.

There appears to be no difference in fragmentation ability among the 3 basic types of lithotriptors currently available (electrohydraulic, electromagnetic, and piezoelectric). A recent comparison of electrohydraulic (EH) and electromagnetic (EM) SWL machines at a single institution found a higher stone-free rate in patients treated with the EH unit than in those treated with the EM unit (77% vs. 67%), despite a statistically larger stone burden in the former group. However, the patients treated with the EH device required a greater number of auxiliary procedures, so that the efficiency quotients of the two machines were comparable in the end (40). Bierkens et al., in a multi-institutional trial of five different 2<sup>nd</sup>-generation lithotriptors, found a stone-free rate of only 45%, with 20% of cases requiring re-treatment. There was no significant difference in stone-free rates among the lithotriptors included in the study (41).

Teichman et al. recently tested 7 different lithotriptors *in vitro* against pure stones composed of COM, cystine, brushite, and struvite ranging in size from 1 to 3 cm (42). Mean fragment size and the mass of fragments larger than 2 mm were lowest for the Dornier HM-3, Storz Modulith SLX, and the Siemens Lithostar C, controlling for the total number of shocks. The Dornier Doli and Medispec Econolith produced the largest fragments. There was no correlation between mean fragment size and peak power at focal point F2 or with focal zone volume, although the latter parameters were not actually measured in the study but rather provided by the device manufacturers. As mentioned previously, the newer generation of lithotriptors has been designed with a narrow focus and large aperture in order to increase the energy delivered to the stone while minimizing exposure to surrounding structures (43). Overall, however, it appears that the radical reduction in focal area of

lithotriptors subsequent to the HM-3 has not resulted in any significant improvement in fragmentation ability in these newer devices (42). The model of lithotriptor available to the urologist should therefore also be a consideration when determining treatment modality.

## MORBIDITY AND COMPLICATIONS

Although the morbidity of SWL and PNL is much less than that seen with open stone surgery, significant complications may be associated with both. Proper patient selection and appropriate technique are essential in order to minimize complications from either approach.

### *Percutaneous Nephrolithotomy*

The morbidity of PNL is highly dependent on size of the stone. Although injuries associated with obtaining percutaneous access may occur regardless of the size of the stone, stone burden still plays a role in the rate of access-related injuries because larger stones often require multiple punctures. The morbidity of treating a moderate-sized calculus through a single subcostal puncture is actually quite low. The reader should keep in mind that much of the data on PNL complications presented in large series reflects the relatively numerous staghorn and other complicated stones which are treated at tertiary referral centers.

In a review by Lee et al. of 500 patients undergoing PNL, the most common complications were bleeding necessitating transfusion (12%) and pulmonary problems (7%) (44). The majority of bleeding incidents (88%) in this series occurred at the time of, or immediately following, the procedure, and the remainder were delayed and due to pseudoaneurysm formation. Arteriovenous malformations can also cause delayed bleeding after PNL. Transfusion rates after PNL range between 3% and 23% overall (45,46). The transfusion rate tends to increase with larger stone burdens and use of multiple access tracts. Persistent bleeding refractory to placement of a nephrostomy tube can be managed with angiography and selective embolization. Contemporary methods of super-selective angioinfarction makes significant renal parenchymal loss in these situations highly unlikely (47).

The pleura is the most common adjacent structure to be injured. Pleural complications (effusions, pneumothorax, hydrothorax) are much more likely when supracostal access is used. The rate of pleural complications ranges from 0 to 37%. Of these, however, only a minority (0 to 8%) require treatment with placement of a chest tube (48-51). Nevertheless, supracostal puncture undoubtedly presents increased morbidity for the patient compared to an infracostal approach, and the authors recommend supracostal access only when absolutely necessary. Upper pole access can also be safely achieved through an infracostal approach by advancing the needle cephalad under the 12<sup>th</sup> rib,

although this technique is more challenging as it requires directing the needle in three axes rather than two (52).

Although any organ adjacent to the kidney may be injured during PNL, most such complications are quite rare and can be managed conservatively. Perforation of the colon occurs in less than 1% of cases (53) and can usually be managed by withdrawing the tip of the nephrostomy tube into the colon and placing a double-pigtail stent into the ureter. Injuries to the spleen and liver are extremely rare if these organs are of normal size.

Perforation of the renal pelvis is not uncommon, but usually is readily managed with

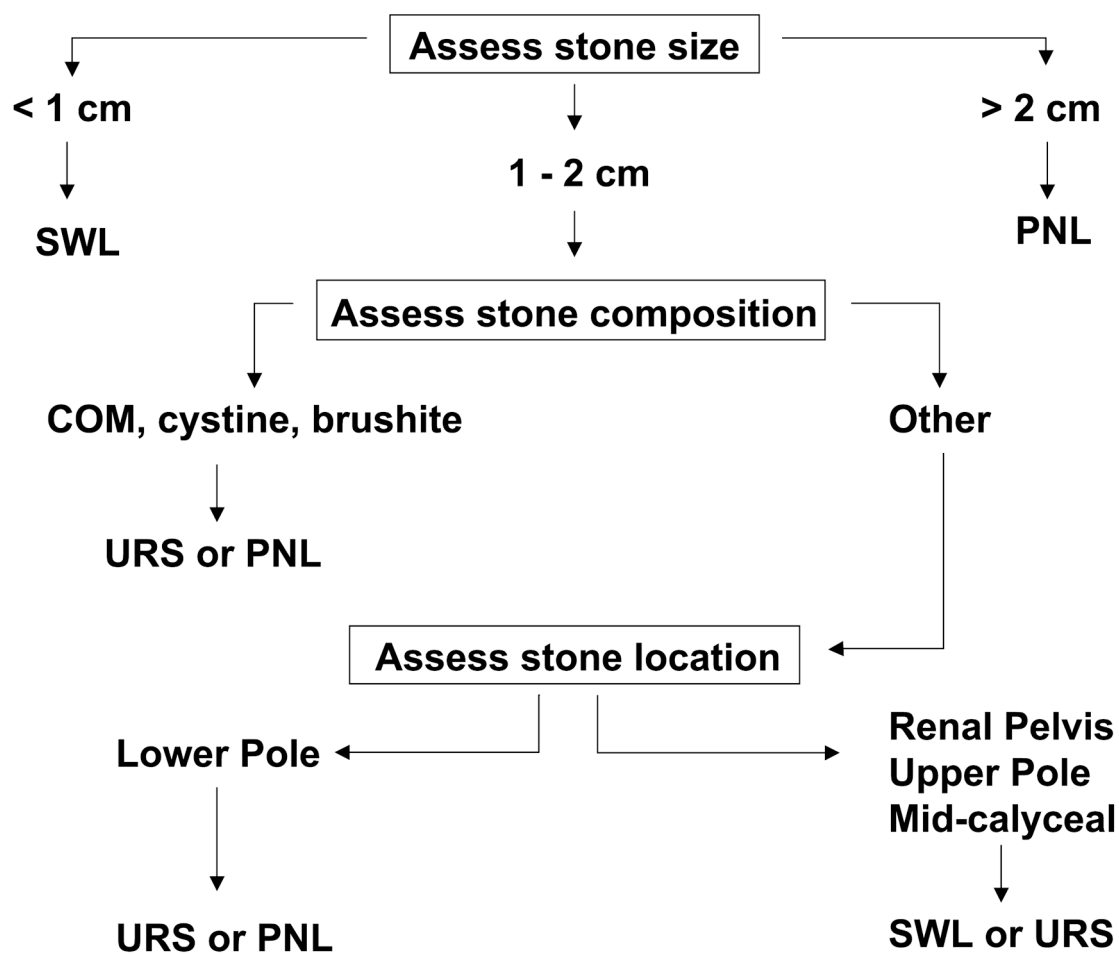


Figure 1 - Algorithm for a rational approach to contemporary management of renal calculi.



nephrostomy tube drainage. A nephrostogram to rule out extravasation is mandatory prior to tube removal in order to avoid a urine leak.

Finally, despite the routine use of perioperative antibiotics, sepsis has been reported to occur in 0.25% to 1.5% of patients undergoing PNL (45,54).

### ***Shockwave Lithotripsy***

The most common serious complication following SWL is steinstrasse, which generally occurs in less than 10% of patients. The risk increases with larger stone burdens – in one study of 885 patients, steinstrasse occurred in 0.3% of stones less than 10 mm, 7% of stones between 10 - 20 mm, and 11.5% of stones between 20 - 30 mm (55). In a recent series of 4,634 patients, multivariable analysis showed stone

size > 20 mm to be an independent predictor of steinstrasse, with a 3.7-fold increase in risk compared to smaller stones (56). Bilateral SWL performed at a single session is also a risk factor for steinstrasse (57). The incidence of steinstrasse after SWL of staghorn calculi approaches 50% and such stones should be considered a contraindication to the use of SWL (58). Placement of a ureteral stent prior to performing SWL has been advocated to prevent steinstrasse, but the discomfort and morbidity associated with stents preclude their use in routine cases. Pre-SWL placement of a ureteral stent is reasonable in patients with a solitary kidney.

Other possible complications of SWL include perirenal hematoma (0.5%), fever > 39° C (0.4%), and machine malfunction (0.7%) (16). Renal colic is quite common (59) and pyelonephritis may also occur. Significant long-term effects of renal injury from SWL have not yet been shown to occur with any frequency; nevertheless, research into potential delayed effects of SWL, such as development or acceleration of hypertension, continues. Overall, SWL currently remains the least invasive, and probably the safest, modality of treating renal calculi.

### **CONCLUSION**

This review has attempted to provide a rational guide to the selection of shock wave lithotripsy and percutaneous nephrolithotomy in contemporary management of renal calculi. Obviously, each approach has its own advantages and disadvantages, and these need to be weighed carefully when choosing therapy. It should be emphasized that with the wide array of options (SWL, URS, PNL) available to treat stones today, routinely approaching stones with an “SWL challenge”, without taking into account factors such as size, composition, location, etc., does not constitute standard of care.

Figure-1 provides an algorithm for a rational approach to surgical therapy of renal stones. Table-3 details options for management when faced with some of the special situations mentioned previously. It is hoped that by applying these principles, urologists

**Table 3 - Approaches to renal calculi in special situations.**

#### Hydronephrosis

Stone < 1.5 cm: URS  
> 1.5 cm: PNL

#### Calyceal Diverticulum

Stone < 1.5 cm, upper pole: URS or PNL  
< 1.5 cm, lower pole: PNL  
> 1.5 cm: PNL

#### Renal Anomalies

1. Pelvic Kidney  
Stone < 2 cm: SWL or URS  
> 2 cm: URS or laparoscopic assisted PNL
2. Horseshoe Kidney  
Stone < 1 cm: SWL  
1 - 2 cm, in upper or mid calyx: SWL or URS  
1 - 2 cm, in lower pole: PNL or URS  
> 2 cm: PNL

#### Solitary Kidney

Select therapy based on stone factors.

#### Morbid Obesity

Stone < 1 cm: lithotripter with adequate focal length?: SWL  
1-2 cm: URS  
> 2 cm: PNL

will be able to optimize therapy for their patients, achieving the highest stone-free rates with the least degree of morbidity in the most efficient and cost-effective manner possible.

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*Dr. Robert Marcovich is American Foundation  
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## **UROLOGICAL SURVEY**

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## STONE DISEASE

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### **A prospective randomized controlled trial on ureteral stenting after ureteroscopic holmium laser lithotripsy**

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*J Urol.* 2003; 169: 1257-60

**Purpose:** A prospective randomized controlled trial was conducted to evaluate whether postoperative ureteral stenting is necessary after ureteroscopic laser lithotripsy. **Materials and Methods:** A total of 58 patients with unilateral ureteral stones were randomized into either stented or unstented groups. Ureteroscopic laser lithotripsy was performed using a semirigid ureteroscope (6.5 / 7Fr) and holmium laser without ureteral orifice dilation. There were no selection criteria regarding stone size, location, preoperative ureteral obstruction and hydronephrosis. Endoscopic evidence of stone impaction or mucosal edema/damage did not exclude a patient from the study. Ureteral perforation on completion retrograde pyelogram was the only intraoperative criterion for study exclusion. Postoperative pain scores and symptoms were recorded. Excretory urography was performed to document stone-free status and stricture formation. Radionuclide scan was performed selectively to exclude functional obstruction when ureteral narrowing was found on excretory urogram.

**Results:** Mean stone size  $\pm$  SD was 9.7  $\pm$  4.0 mm. (range 4 to 27). Proximal ureteral stones accounted for 43% of all stones. Stented and unstented groups were comparable with respect to demographic data, stone parameters, preoperative obstruction and hydronephrosis. There was no significant difference in operating time, laser energy used, stone impaction and mucosal edema/damage between the 2 groups. Postoperative pain and symptoms were more severe and frequent ( $p < 0.05$ ) in the stented group. However, there was no difference in the incidence of postoperative sepsis and unplanned medical visits. The stone-free and stricture formation rates showed no statistical difference between the 2 groups.

**Conclusions:** Ureteral stenting is not necessary after uncomplicated ureteroscopic laser lithotripsy for ureteral stones. Ureteral stent increases the incidence of pain and urinary symptoms but does not prevent postoperative urinary sepsis and unplanned medical visits. Severity of preoperative obstruction and intraoperative ureteral trauma were not shown to be determining factors for stenting.

### **Editorial Comment**

Historically, placement of a ureteral stent after ureteroscopy for stone removal or fragmentation has been routine practice. However, recent retrospective studies and prospective, randomized trials have suggested that placement of a ureteral stent after uncomplicated ureteroscopy may be unnecessary and is associated with greater patient discomfort. The problem lies in what constitutes "uncomplicated". Some investigators restricted their series to distal ureteral calculi only. Others excluded patients requiring balloon dilation of the intramural ureter. Still others excluded patients in whom fragments were extracted after fragmentation, while others excluded patients in whom fragments were left behind! In all cases, it was left to the discretion of the surgeon to exclude patients in whom evidence of mucosal trauma or severe impaction were present. Thus, guidelines for selection of patients who may be safely left unstented are not clear-cut.

The authors of the present randomized trial excluded patients intraoperatively only if the stone was unable to be accessed, a concomitant ureteral stricture was present or a ureteral perforation occurred. Degree of pre-operative obstruction, stone impaction and ureteral trauma or edema did not constitute grounds for exclusion. Furthermore, middle and proximal ureteral stones comprised 59% and 28% of stones in the unstented and stented groups, respectively. Similar to other studies, the authors found no significant difference in stone free



rates, post-operative fever or urinary tract infection, or need for unplanned medical visits in the 2 groups. However, also in common with other studies, urinary symptoms were greater in the stented group compared with the unstented group. This study confirms the safety of stentless ureteroscopy after treatment of stones in all locations in the ureter, but also suggests that the appearance of the ureter after stone removal, provided a perforation has not occurred, is not a reliable indicator of ureteral obstruction post-operatively. Hopefully, with additional confirmation and further study, specific criteria for post-operative stenting can be provided. However, it should be kept in mind that in cases of questionable ureteral injury, placement of a ureteral stent will never be the wrong thing to do.

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### **Characterization of intrapelvic pressure during ureteropyeloscopy with ureteral access sheaths**

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*Urology 2003; 61: 713-8*

**Objectives:** To evaluate the impact of the ureteral access sheath on intrarenal pressures during flexible ureteroscopy in light of the recent resurgence in their use. As such, using human cadaveric kidneys, we studied changes in intrarenal pressure in response to continuous irrigation at different pressures with and without access sheaths of various sizes and lengths.

**Methods:** This study was performed using seven cadaveric kidneys. In three kidneys the study was done in situ with a 7.5F flexible ureteroscope (URS) passed by itself and then passed through a 10/12F sheath (35 and 55 cm in length), whereas, in four kidneys, due to narrowing of the intramural ureter, the study was done ex vivo using the unsheathed URS and then passing the 7.5F flexible URS via the 10/12F, 12/14F, and 14/16F sheaths (all 35 cm in length). A 10F Cope loop pyelostomy was placed to measure intrapelvic renal pressure. Three sets of 3-minute readings (i.e., flow and intrarenal pressure) were taken with the tip of the URS at the distal ureter, middle ureter, and renal pelvis (just above the ureteropelvic junction); the entire process was done at three different irrigant pressure settings: 50, 100, and 200 cm H<sub>2</sub>O. Irrigant flow and intrarenal pressures were measured at all three settings using the URS passed without a sheath and then with the URS passed through the various sheaths positioned at the distal ureter, middle ureter, and renal pelvis.

**Results:** With all of the sheaths, intrapelvic pressure remained low (less than 30 cm H<sub>2</sub>O), and there was a 35% to 80% increase in irrigant flow versus the control unsheathed URS. With the sheath in place, the majority of the irrigant drained alongside the URS and out the sheath. Flow and pressure with the 12/14F sheath were equivalent to the 14/16F sheath.

**Conclusions:** The 12/14F access sheath provides for maximum flow of irrigant while maintaining a low intrarenal pelvic pressure. Even with an irrigation pressure of 200 cm H<sub>2</sub>O, renal pelvic pressure remained below 20 cm H<sub>2</sub>O.

### **Editorial Comment**

Ureteral access sheaths have long been available to facilitate access to the ureter and collecting system. However, a cumbersome design and the potential for ureteral perforation prevented the sheath from achieving

widespread use. Resurgence in interest in the access sheath occurred with advances in design that improved ease and safety of placement and reduced the tendency of the sheath to buckle. Although the ureteral access sheath has been used primarily to facilitate multiple entries and exits from the ureter and it has been proven advantageous in this regard from the standpoint of operative time and cost, Rehman and colleagues have shown that use of the access sheath is advantageous for physiologic reasons as well. Using a variety of sizes of access sheaths and irrigation pressures in a cadaveric model, these investigators demonstrated that renal pelvic pressure could be kept below 30 cm H<sub>2</sub>O and irrigation flow could be improved by 35-80% compared to ureteroscopy without a sheath.

With an increase in the complexity of ureteroscopic procedures has come an increase in operative time. Furthermore, the treatment of larger stones and potentially infected stones has led to an increase in the potential for urinary extravasation and sepsis. The findings of this study suggest that use of a ureteral access sheath, particularly during lengthy ureteroscopic procedures for large renal or ureteral calculi may reduce intrarenal pressure, thereby reducing the likelihood of pyelovenous or pyelolymphatic backflow, as well as the chance of forniceal rupture, extravasation and sepsis, and also improve endoscopic visibility through increased irrigation flow. Particularly when treating a potentially infected stone, maintenance of as low an intrarenal pressure as possible is imperative in order to prevent sepsis. Consequently, use of an access sheath, even when there is no intention of frequent entries and exits from the ureter, may increase the safety of long ureteroscopic procedures.

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## ENDOUROLOGY & LAPAROSCOPY

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### **Aspiration and sclerotherapy versus hydrocelectomy for treatment of hydroceles**

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*Urology 2003; 61: 708-12*

**Objectives:** To compare aspiration and sclerotherapy using sodium tetradecylsulfate (STDS) with open hydrocelectomy in the treatment of hydroceles with regard to safety, efficacy, and cost-effectiveness.

**Methods:** Patients with symptomatic hydroceles were prospectively enrolled in an aspiration and sclerotherapy protocol between October 1998 and June 2000. Patients in this group underwent percutaneous aspiration followed by sclerotherapy with an STDS-based solution. This group was compared with a group of patients chosen consecutively who underwent hydrocelectomy between December 1996 and August 1999. Primary outcome measures included patient satisfaction and procedural success. Secondary outcome measures included complications and comparative costs.

**Results:** A total of 27 patients with 28 hydroceles were enrolled in the aspiration and sclerotherapy protocol and compared with 24 patients with 25 hydroceles in the hydrocelectomy group. Mean follow-up for the aspiration and sclerotherapy group and hydrocelectomy group was 8.9 and 16.4 months, respectively. Patient satisfaction was 75% for aspiration and sclerotherapy and 88% for hydrocelectomy. The overall success rate for aspiration and sclerotherapy was 76% compared with 84% for hydrocelectomy. The complication rate was only 8% in the aspiration and sclerotherapy group, but 40% in the hydrocelectomy group. Comparative costs



per procedure demonstrated that hydrocelectomy was almost ninefold more expensive than aspiration and sclerotherapy.

**Conclusions:** In the treatment of hydroceles, aspiration and sclerotherapy with STDS represents a minimally invasive approach that is simple, inexpensive, and safe but less effective than hydrocelectomy. Aspiration and sclerotherapy is a viable first-line therapeutic option in the management of hydroceles.

### **Editorial Comment**

My experience with regards to surgical hydrocelectomy is similar to that reported by the authors. The complication rate is high and the limitation of patient activity for the first few weeks after the procedure can be significant. The same comments are echoed by my colleagues at the frequent presentation of hydrocele complications during our monthly Mortality and Morbidity Conference. Sclerosis would seem to be an attractive option. Beiko and associates used 4 ml of 3% STDS, 6 ml 2% lidocaine, and 140 ml of 5% dextrose in 0.45% normal saline (final concentration of 0.08% STDS), replacing 25% of the aspirated hydrocele volume. This is similar to the regimen used in another recent study (1). After draining the hydrocele completely, the sclerosing solution is left in place. Antibiotics but no analgesics are provided. In the discussion section of their article, Beiko and associates stated that they now advocate use of a smaller volume of a more concentrated STDS solution. Unfortunately, specifications for their new regimen were not provided. Even with the reported regimen, however, the authors achieved complete or more than 50% reduction of hydrocele volume in 13 of 25 patients (52%), and overall success (includes patient satisfied with outcome but with less than 50% volume reduction) in 19 of 25 (79%). Of these 19, only 4 required a second sclerosis session to achieve the desired outcome. I have used dehydrated alcohol mixed with lidocaine, replacing 10% of the hydrocele volume, with good success in a few patients but that regimen requires a local anesthetic infiltration of the spermatic cord and the patient has pain for about 48 hours. The STDS regimen appears to be easier on the patient. This option should be considered an excellent alternative to the surprisingly morbid “minor surgery” called hydrocelectomy.

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### **Technique for laparoscopic running urethrovesical anastomosis: the single knot method**

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*Urology 2003; 61: 699-702*

**Objectives:** To describe a technique for facilitating the urethrovesical anastomosis at the time of laparoscopic radical prostatectomy.

**Methods:** Two 6-in. polyglycolic acid sutures (one dyed, one white) are tied together at their tail ends and delivered into the operative field by way of a 12-mm port. A running suture is completed from the 6:30 to the 12:00-o'clock position and from the 5:30 to the 12:00-o'clock position, at the end of which a single

intracorporeal tie is completed. The catheter is placed before completing the anterior row of sutures; the catheter is left in place for 5 to 7 days.

**Results:** This anastomotic technique has been used in 122 laparoscopic radical prostatectomies and 8 robot-assisted laparoscopic radical prostatectomies. The average time for the anastomosis was 35 minutes (range 14 to 80). All anastomoses were watertight. No symptomatic postoperative urinary leaks have occurred, and no clinically evident clinical bladder neck contractures resulted.

**Conclusions:** We describe a simple, watertight, running laparoscopic suture technique for accomplishing the urethrovesical anastomosis during laparoscopic radical prostatectomy.

### Editorial Comment

This really is a wonderful suturing technique, which I was fortunate enough to learn about directly from the authors while visiting the University of California Irvine. Although I have not found it useful for laparoscopic pyeloplasties (I use the Endostich device with a non-robotic laparoscopic technique), the 2 of us at our institution performing robotic-assisted laparoscopic radical prostatectomies have used it with great satisfaction for the urethrovesical anastomosis. The authors' current modification of the technique described in this article (accepted in December 2002) includes using a monofilament suture for one arm and a braided suture for the other. The braided suture is first placed for 2 throws (outside-in on bladder neck, then inside-out on the urethra) and then the monofilament suture is placed for 5 throws (first 2 as for the braided suture, then 3 more throws). At this point 20- 25% of the anastomosis is complete and the bladder is pulled down to the urethra with gentle traction. The monofilament slides easily. Traction on the monofilament suture by the assistant keeps the anastomosis opposed as a few more throws are placed with the braided suture. Friction from the braided suture now keeps the anastomosis together without additional assistance and the remainder can be completed rapidly. This technique markedly simplifies the laparoscopic urethrovesical anastomosis. Our experience to date (albeit with short follow-up) is similar to that of the authors with no "clinically evident post-operative urinary leak or symptomatic bladder neck contractures."

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## **PATHOLOGY**

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### **Basal cell cocktail (34βE12 + p63) improves the detection of prostate basal cells**

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*Mod Pathol.* 2003; 16: 177A

**Background:** High molecular weight cytokeratin (34βE12) and p63 are frequently used as basal cell markers in aid of diagnosis of prostate cancer (PCa). Absence of a basal cell marker in an atypical lesion histologically suspicious for PCa supports a malignant diagnosis. Yet, absence of basal cells by immunohistochemistry (IHC) is not always conclusive. Improving the sensitivity of basal cell IHC is critical to help make diagnostic decisions in conjunction with standard histology. We test the hypothesis that inclusion of both 34βE12 and p63 in a cocktail reaction is advantageous over either marker used alone.

**Design:** 1350 benign glands from 9 TURP specimens were used to study the immunostaining intensity and pattern for 34 $\beta$ E12, p63 and the basal cell cocktail. Basal cell marker expression was scored as strong, moderate, weak and negative. Basal cell staining was considered complete if 75% of the gland circumference was positive for the basal cell marker, and partial if 25% of the circumference was stained.

**Results:** By IHC, benign glands lack basal cell lining in 2, 6 and 2% of glands with cocktail, 34 $\beta$ E12 and p63 staining, respectively. The staining variance for cocktail is significantly smaller than that for 34 $\beta$ E12 (0.0100 vs. 0.1559,  $p=0.0008$ ). No significant difference was seen between cocktail and p63 (0.0100 vs. 0.0345,  $p=0.099$ ). The cocktail stains the basal cell layers more intensely than either 34 $\beta$ E12 or p63 alone, with complete and partial strong basal cell staining in 93 and 1 % of benign glands, compared to 55 and 4% with 34 $\beta$ E12, and 81 and 1% with p63. Complete and partial weak staining is seen in 0 and 0% of benign glands with the cocktail, compared to 8 and 7% with 34 $\beta$ E12 and 4 and 1% with p63 ( $p=0.007$  and 0.014 for cocktail vs. 34 $\beta$ E12 and cocktail vs. p63, respectively). 2.8% of clinically localized PCa had positive 34 $\beta$ E12 staining and 0.3 % had positive p63 staining.

**Conclusions:** IHC of the prostatic glands from transition zone is subject to staining variability. 34 $\beta$ E12 is most susceptible, and basal cell cocktail is least susceptible to such variability. Basal cell cocktail not only increases the sensitivity of the basal cell detection, but also reduces the staining variability and therefore renders the basal cell IHC more consistent.

#### **Editorial Comment**

Basal cells are of utmost importance for the diagnosis of adenocarcinoma of prostate. Their presence excludes this diagnosis. Their absence, however, does not mean necessarily that the acinus's is neoplastic. Most of the times their presence is recognized on hematoxylin and eosin stains. They are located close to the basement membrane, are round, oval or pyramidal and sometimes the nucleus is involved by a clear halo. They are precursors to the secretory cells and not myoepithelial cells.

In cases of "atypical small acinar proliferation" (ASAP) the presence of basal cells may help a final diagnosis of adenocarcinoma. ASAP is used in cases of "suspicious but not diagnostic of adenocarcinoma". I prefer this last expression because ASAP may give the impression of an entity or a particular lesion. It only expresses lack of some criteria for the definitive diagnosis of adenocarcinoma.

In this circumstance the immunostaining for basal cells is critical for the diagnosis. The pathologist uses high molecular cytoqueratins (34 $\beta$ E12) to disclose these cells. Not always this stain is uniform and uncertainty remains as to the correct diagnosis. The cocktail, that is, adding to 34 $\beta$ E12 the p63 seems to improve the efficacy of this immunostaining. We hope that other studies confirm the findings of this paper considering that using 2 antibodies makes the immunostaining more expensive.

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#### **The addition of a negative 34 $\beta$ E12 stain to a small focus of atypical glands on prostatic core biopsies does not predict a higher incidence of prostatic adenocarcinoma on follow up biopsies**

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*Mod Pathol. 2003; 16: 152A*

**Background:** Atypical glands on prostate needle biopsy with a negative 34 $\beta$ E12 immunostaining, indicating a lack of a basal cell layer, are typically diagnostic criteria of prostate cancer. However, there are certain cases in which a negative 34 $\beta$ E12 immunostaining in a small focus of atypical glands is still not convincing enough to make the diagnosis of cancer. This study is the first report to evaluate the incidence of prostate cancer on follow-up biopsy in individuals with this diagnosis.

**Design:** 543 men who had prostate core biopsies diagnosed as a small focus of atypical appearing glands with a negative 34 $\beta$ E12 immunostaining between 1/1/97 and 12/31/00 were selected for study.

**Results:** 61% of the 543 individuals had at least one follow up biopsy (n=332). Of these, 43% of repeat biopsies were diagnostic of prostate cancer (n=142). 46 men had at least 2 follow up biopsies, with 48% of these (n=22) being diagnosed as cancer. The percent of carcinomas having Gleason grades 3+2=5, 3+3=6, 3+4=7, 4+3=7 and 4+4=8 were 6%, 86%, 1%, 4% and 3% respectively. The median amount of time to the first follow up biopsy was 79 days, with 52% of follow up biopsies being performed within 90 days.

**Conclusions:** A negative 34 $\beta$ E12 immunohistochemical stain in a small focus of atypical glands is not associated with an increased prediction of prostate cancer on follow up biopsy (43%), compared with previously published data for “small focus of atypical glands” alone (approximately 45%). As 48% of men with an initial negative biopsy and multiple follow up biopsies were found to have cancer, more than one repeat biopsy or more extensive sampling on first repeat biopsy may be necessary to maximize the identification of cancer. This is the same as has been shown for men with atypical diagnoses in general, without a negative 34 $\beta$ E12 immunohistochemical stain. Only half of all individuals with a diagnosis of 34 $\beta$ E12 negative focus of atypical glands were rebiopsied within 3 months. Urologists need to be educated as to the significance of an atypical diagnosis and the need for rebiopsy.

### Editorial Comment

The presence of basal cells excludes the diagnosis of adenocarcinoma but their absence does not mean necessarily that the acinus is neoplastic. This article emphasizes the need of morphologic criteria for the diagnosis of adenocarcinoma. The pathologist should not rely on his diagnosis exclusively on the result of immunostaining.

In cases of “atypical small acinar proliferation” (ASAP), immunostaining is indicated to help making the diagnosis of adenocarcinoma. This study, however, showed that a negative 34 $\beta$ E12 immunohistochemical stain in a small focus of ASAP is not associated with an increased prediction of prostate cancer on follow up biopsy (43%), compared with previously published data (approximately 45%).

In cases of ASAP the pathologist, besides immunostaining, performs new sections in other levels of the biopsy hoping the lesion appears more extensive. In cases the immunostaining does not show basal cells but the morphologic criteria are still not sufficient for the diagnosis of adenocarcinoma, the diagnosis is ASAP and not adenocarcinoma.

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## IMAGING

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### **High-resolution multidetector CT in the preoperative evaluation of patients with renal cell carcinoma**

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*AJR Am J Roent.* 2003; 180: 1271-7

**Purpose:** The purpose of our study was to evaluate the accuracy of multidetector CT (MDCT) using a high-resolution protocol in the preoperative assessment of patients with renal cell carcinoma who are possible candidates for nephron-sparing surgery.

**Materials and Methods:** Forty patients with suspected renal cell carcinoma underwent MDCT. Contrast-enhanced acquisitions were obtained during arterial, nephrographic, and urographic phases using a thin-slice protocol. One-millimeter-thick source images were evaluated by two observers on a dedicated workstation for the identification and characterization of the tumor, presence of a pseudocapsule or invasion of perirenal fat, involvement of adrenal glands or surrounding tissues, presence of satellite lesions within Gerota's fascia, infiltration of renal vein and inferior vena cava, involvement of lymph nodes, and presence of distant metastases. Imaging findings were compared with surgical specimens using criteria from the Robson and TNM classification systems.

**Results:** The presence and size of all lesions were correctly shown in all patients. In evaluating Robson stage I of renal cell carcinoma, we were able to diagnose fat infiltration on 1-mm scans with 96% sensitivity, 93% specificity, and 95% accuracy; the positive and negative predictive values were, respectively, 100% and 93%. One hundred percent accuracy was achieved in staging high-grade lesions.

**Conclusion:** High-resolution MDCT is accurate in the preoperative evaluation of patients with renal cell carcinoma.

### **Editorial Comment**

Robson's Stage I (T1-T2) tumors are defined on spiral CT as a tumor confined within the kidney with an intact renal capsule. This is usually characterized when the perinephric fat and renal fascia adjacent to the lesion are preserved. Until now, the most specific sign of extension of the tumor to these structures has been the presence of a discrete mass measuring at least 1 cm in diameter projecting into the perinephric space. Although this finding is 98% specific for Robson's stage II (T3a) tumors, its sensitivity is too low (only 46%) as this finding is absent in the majority of patients with perinephric extension (1). As the perinephric fat and Gerota's fascia are resected during a radical nephrectomy, the radiological distinction between T1 and T3a has not been very important. More recently, however, renal conservative surgery has been performed with more frequency including the laparoscopic approach; thus, an accurate preoperative radiological staging is essential.

The point of this report is that the use of 1-mm-thick-multidetector CT images (MDCT) allowed the differentiation between Robson stage I (T1-T2) and T3a renal cell carcinoma, with 96% sensitivity, 93% specificity, 95% accuracy, 100% of positive predictive value and with 93% of negative predictive value. These results are very enthusiastic but studies with a larger series of patients are desirable. As we know CT-false positives diagnoses has been described in up to 50% of patients with Robson's Stage I disease. This can be explained because perinephric stranding and fascial thickening can occur due to perinephric edema (very nicely illustrated in one case of this report), fat necrosis and fibrosis from remote inflammation (2). Obviously, these data are related to studies performed with single slice spiral CT that has lower spatial resolution than the new generation of MDCT. Multidetector CT provides substantial improvement in volume coverage over single-

slice spiral CT. More rapid image acquisition allows better definition of renal capsule and greater separation of arterial and venous phases, thus facilitating multiphasic acquisition. This improvement was very well shown by the superb high resolution multiplanar reconstruction of the kidneys and renal vessels showed in this interesting manuscript.

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#### **Imaging-guided radiofrequency ablation of solid renal tumors**

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*AJR Am J Roent.* 2003; 180: 1509-13

**Purpose:** We performed a retrospective review of imaging-guided radiofrequency ablation of solid renal tumors.

**Materials and Methods:** Since May 2000, 35 tumors in 20 patients have been treated with radiofrequency ablation. The size range of treated tumors was 0.9 - 3.6 cm (mean, 1.7 cm). Reasons for patient referrals were a prior partial or total nephrectomy (nine patients), a comorbidity excluding nephrectomy or partial nephrectomy (10 patients), or a treatment alternative to nephron-sparing surgery (one patient who refused surgery). Tumors were classified as exophytic, intraparenchymal, or central. Sixteen patients had 31 lesions that showed serial growth on CT or MR imaging. Of these 16 patients, four patients with 10 lesions had a history of renal cell carcinoma, and two patients with 11 lesions had a history of von Hippel-Lindau disease. Four patients had incidental solid masses, two of which were biopsied and shown to represent renal cell carcinoma, and the remaining two masses were presumed malignant on the basis of imaging features. Successful ablation was regarded as any lesion showing less than 10 H of contrast enhancement on CT or no qualitative evidence of enhancement after IV gadolinium contrast-enhanced MR imaging.

**Results:** Of the 35 tumors, 22 were exophytic and 13 were intraparenchymal. Twenty-seven of the 35 were treated percutaneously using either sonography (n = 22) or CT (n = 5). Two patients had eight tumors treated intraoperatively using sonography. Patients were followed up with contrast-enhanced CT (n = 18), MR imaging (n = 5), or both (n = 5) with a follow-up range of 1 - 23 months (mean, 9 months). No residual or recurrent tumor and no major side effects were seen.

**Conclusion:** Preliminary results with radiofrequency ablation of exophytic and intraparenchymal renal tumors are promising. Radiofrequency ablation is not associated with significant side effects. Further follow-up is necessary to determine the long-term efficacy of radiofrequency ablation.



### Editorial Comment

Cryotherapy has been the most frequently thermal ablative technique used for alternative treatment of localized renal cell carcinoma. There are only few reports describing the utilization of radiofrequency ablation (RF) to renal tumors including only small series of patients. Radiofrequency renal tumor ablations can be performed under sonography or computed-tomography-guided percutaneous approach. After treatment, patients are usually followed up with CT scans at 6 weeks and 3, 6, and 12 months, and every 6 months thereafter. Successful ablation has been considered by many authors as a lesion along with a margin of normal parenchyma that no longer enhanced (less than 10 Hounsfield units) on follow-up contrast studies. The point of this report is that 35 tumors, ranging in size from 0.9 to 3.6 cm (mean = 1.7 cm), were treated by RF with no residual or recurrent lesions. The criterion of successful ablation was the same used by other authors and based strictly on radiologic findings (absence of lesion's enhancement). Radiographic follow-up of radiofrequency ablated small renal tumors, however, may demonstrate little or no residual contrast enhancement depending on tumor size, location within the kidney, and mode of delivering radiofrequency energy. As already pointed out by the authors the absence of postprocedural biopsy can be considered a relative limitation of this study since pathologic examination after RF ablation may show a residual viable tumor in few patients. Another point to be considered is that when performed, adequate histopathologic evaluation of the tumors specimens treated by RF-ablations should include hematoxylin-eosin and a nicotinamide adenine dinucleotide staining in order to determine the presence or absence of tissue viability. This manuscript is recommended because shows very clearly that RF ablation can successfully destroy small peripheral renal tumors with no significant damage to the normal renal parenchyma and more important without significant side effects.

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## INVESTIGATIVE UROLOGY

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### **Radiation increases fibrogenic cytokine expression by Peyronie's disease fibroblasts**

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*J Urol. 2003; 170: 281-4*

**Purpose:** Peyronie's disease is a crippling penile deformity that results from fibrosis in the tunica albuginea. To our knowledge its cause is unknown and empirical therapies are used extensively. A factor involved in the development of Peyronie's disease is fibrogenic cytokine over expression. Radiation therapy is an empirical therapy for this condition and, while some data suggest a role for it, no literature exists on the effects of radiation on tunical tissue or cells derived from this tissue. We evaluated the effect of radiation on fibrogenic cytokine production in cells cultured from Peyronie's disease plaque tissue.

**Methods and Materials:** Using a well established cell culture model cells derived from Peyronie's disease plaque tissue and neonatal foreskins were irradiated with 5 Gy (treatment group) or left nonirradiated (control group). At 24 hours cells were harvested and the supernatant was analyzed using enzyme-linked immunosorbent assay to determine the levels of the 2 fibrogenic cytokines basic fibroblast growth factor and platelet-derived growth factor-AB.

**Results:** Four Peyronie's disease plaque derived cultures and 2 neonatal foreskin derived cultures were analyzed. All plaque derived fibroblasts demonstrated significant elevations in basic fibroblast growth factor and platelet-derived growth factor-AB compared with foreskin derived fibroblasts.

**Conclusions:** These data suggest that radiation may in fact increase the production of fibrogenic cytokines, which may promote the fibrotic process involved in Peyronie's disease. Further study is aimed at defining the effect of irradiation on plaque tissue.

### Editorial Comment

Repeated tunical mechanical stress and microvascular trauma is one the most accepted causes of Peyronie's disease. Microvascular trauma or subtunical bleeding consequent to sexual intercourse can result in fluid and fibrinogen in the subtunical layers. The resulting fibrin deposits may initiate a wound healing response, which in addition to pain and hematoma; determine a subsequent inflammatory response with recruitment of macrophages and neutrophils. These cells release a variety of cytokines and vasoactive factors that may lead to a fibrotic reaction (1-4).

Among nonsurgical options for management of Peyronie's disease, extracorporeal shock wave therapy and radiation are proposed. Nevertheless, there is no clear information on the effects of radiation on tissue of Peyronie's disease. In this elegant study, the authors used their established cell culture model to define the effects of radiation on the biology of Peyronie's disease plaque tissue derived fibroblasts. Interestingly and surprisingly, the authors found that radiation at a dose of 5 Gy induced the Peyronie's disease fibroblasts to dramatically increase the production of basic fibroblast growth factor and platelet-derived growth factor-AB, when compared to controls. These findings suggest that radiation therapy would determine the fibrotic process of the disease, and, therefore, worsen the Peyronie's plaque.

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**Dimethyl sulfoxide: does it change the functional properties of the bladder wall?**

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*J Urol.* 2003; 170: 253-8

**Purpose:** Dimethyl sulfoxide (DMSO) is used in a 50% solution to treat interstitial cystitis. Symptomatic relief occurs in about two-thirds of cases. The mechanism of action and effects of DMSO on bladder tissue function are poorly understood. Therefore, the effect of DMSO on bladder muscle compliance and contractility was evaluated.

**Materials and Methods:** Contractility and compliance were evaluated in rat bladder strips exposed to various concentrations of DMSO for 7 minutes, followed by 7 to 60-minute washout periods. The effect of DMSO at concentrations of 25%, 30%, 35%, 40% and 50% on electrical field stimulation induced contractions was assessed. Acetylcholine and high KCl (Sigma Chemical Co.) induced contractions were measured after exposure to 30% DMSO. Compliance was evaluated after exposure to 30% and 50% DMSO.

**Results:** Exposure to 40% DMSO completely abolished electrical field stimulation contractions, while 30% DMSO decreased the electrical field stimulation contraction to  $40\% \pm 6\%$  of the initial force but there was almost complete recovery within 30 minutes. Contractile force was unaltered by 25% DMSO. Acetylcholine and KCl stimulation after exposure to 30% DMSO produced contractile forces of  $78\% \pm 6\%$  and  $39\% \pm 6\%$  of pre-DMSO control contractions, respectively. Compliance decreased by 2.4 and 4.6-fold following 30% and 50% DMSO exposure, respectively.

**Conclusions:** DMSO completely and irreversibly abolishes contractions at a 40% concentration. Compliance is altered at even lower concentrations (30%). These findings bring into question the current practice of treating patients who have IC with 50% DMSO. Lower concentrations (25%) of DMSO may serve as a safe, effective analgesic and anti-inflammatory treatment for IC and other bladder pathologies.

**Editorial Comment**

Interstitial cystitis (IC) has been described more 100 years ago; nevertheless, its pathogenesis and etiology remain unknown. For that reason, the treatments available for IC are empirical and symptomatic.

Dimethyl sulfoxide (DMSO) is the treatment of choice for intravesical therapy in IC. DMSO is a scavenger of the intracellular OH radical believed to be an important trigger of inflammatory process (1). Although its mechanism of action in IC is not fully elucidated, this substance has multiple effects and DMSO treatment is associated with a low frequency of serious adverse effects. In general, DMSO is administered twice weekly as 50 ml sterile filtered 50% solution (2).

The same group of the present work investigated previously the effect of DMSO on the proliferation of bladder smooth muscle cells in culture and noted that DMSO at high concentration (greater than 10%) can result in apoptotic cell death, while in low concentrations (less than 5%) it can act as an antiproliferative agent and inhibit cell growth in a dose dependent manner without direct cellular toxicity (3).

In the present work, the authors demonstrated that application of DMSO at concentrations of 30% might lead to irreversible changes in bladder smooth muscle contractility and bladder tissue compliance. Although the current investigation has been performed in rats and in a nonphysiological environment (bladder strips), these results present cause for apprehension, because if these consequences also exist in vivo and in humans, the DMSO concentration of 50% may need to be reassessed for clinical use.

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## RECONSTRUCTIVE UROLOGY

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### **Topography of the pelvic autonomic nervous system and its potential impact on surgical intervention in the pelvis**

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*Clin Anat.* 2003; 16: 119-30

Bladder, bowel, and sexual dysfunction caused by iatrogenic lesions of the inferior hypogastric plexus (IHP) are well known and commonly tolerated in pelvic surgery. Because the pelvic autonomic nerves are difficult to define and dissect in surgery, and their importance often ignored, we conducted a gross anatomic study of 90 adult and four fetal hemipelves. Using various non-surgical approaches, the anatomic relations and pathways of the IHP were dissected. The IHP extended from the sacrum to the genital organs at the level of the lower sacral vertebrae. It originated from three different sources: the hypogastric nerve, the sacral splanchnic nerves from the sacral sympathetic trunk (mostly the S2 ganglion), and the pelvic splanchnic nerves, which branched primarily from the third and fourth sacral ventral rami. These fibers converge to form a uniform nerve plate medial to the vascular layer and deep to the peritoneum. The posterior portion of the IHP supplied the rectum and the anterior portion of the urogenital organs; nerve fibers traveled directly from the IHP to the anterolateral wall of the rectum and to the inferolateral and posterolateral aspects of the urogenital organs. The autonomic supply from the IHP was supplemented by nerves accompanying the ureter and the arteries. An understanding of the location of the autonomic pelvic network, including important landmarks, should help prevent iatrogenic injury through the adoption of surgical techniques that reduce or prevent postoperative autonomic dysfunction.

### **Editorial Comment**

A description of the pelvic autonomic nerves system is nothing totally new. However, even after more than a century of pelvic surgery and interventions we still have not clearly straightened out the exact role of autonomic nerve fibres for some of the pelvic organs nor do we know everything about their variability in relation to pelvic organs. Recent papers have shown that autonomic nerve fibres may be responsible for sensory stimuli in the membranous urethra of male patients after prostatectomy or cystoprostatectomy. Furthermore these nerves regulate contractility and muscle tone in the remnant urethra in female cystectomy patients undergoing an orthotopic neobladder. Urinary retention in patients undergoing rectal surgery may at least in part be caused by irritation or destruction of parasympathetic or sympathetic fibres contributing to the plexus.

In this paper the authors have demonstrated among other things that the sacral contributions to the pudendal nerve were the same as for the autonomic inferior hypogastric plexus. This brings an old discussion back whereby at least some autonomic nerve functions may be transmitted via the pudendal nerve. Another important message in this paper is that surgeons should be much more aware of nerve sparing techniques during rectal surgery because of its implications to urinary and sexual function of their patients. Clinical anatomy using both new staining techniques and fetal specimens can still yield interesting and sometimes even new aspects regarding pelvic surgery and preservation of life quality without oncological compromise.

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**Identification of communicating branches among the dorsal perineal and cavernous nerves of the penis**

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*J Urol. 2003; 170:153-8*

**Purpose:** The mechanism of human erection requires the coordination of an intact neuronal system that includes the cavernous, perineal, and dorsal nerves of the penis. We defined the communication of these 3 nerves that travel under the pubic arch using specific neuronal immunohistochemical staining and 3-dimensional reconstruction imaging technique.

**Materials and Methods:** A total of 18 normal human fetal penile specimens at 17.5 to 32 weeks of gestation were studied by immunohistochemical techniques. Serial sections were stained with antibodies raised against the neuronal markers S-100, and neuronal nitric oxide synthase (nNOS), vesicular acetylcholine transporter (VAcHT), calcitonin gene-related peptide and substance P.

**Results:** The continuation of the dorsal neurovascular bundle of the prostate was documented under the pubic arch. Two distinct nerve bundles were identified superior to the urethra and medial to the origin of the crural bodies. Nerve bundles were observed to join the corporeal bodies at the penile hilum. Proximal to the penile hilum the dorsal nerves stained only for S-100 and VAcHT. From the junction of the crural bodies at the hilum to the glans penis dorsal nerve fibers stained positive for S-100, VAcHT and nNOS. Calcitonin gene-related peptide and substance P demonstrated positive staining at the distal nerves, particularly at the glans. In contrast, the whole course of the cavernous nerve stained for S-100 and nNOS. Under the pubic arch at the penile hilum the cavernous nerves were found to convey nNOS positive branches to the dorsal nerve to transform its immunoreactivity to nNOS positive. Proximal nNOS negative perineal nerves were shown to stain positive for nNOS distal on the penis. Interaction between nNOS positive dorsal nerve branches and perineal nerves was at the cavernous-spongiosal junction, where the bulbospongiosus muscle terminates.

**Conclusions:** At penile hilum, where the corporeal bodies start to separate, the cavernous nerve sends nNOS positive fibers to join the dorsal nerve of the penis, thereby, changing the functional characteristics of the distal penile dorsal nerve. Similarly the nNOS negative, ventrally located perineal nerve originating from the pudendal nerve becomes nNOS reactive at the cavernous-spongiosal junction. These 2 examples of redundant neuronal wiring in the penis may impact erectile function, especially during reconstructive surgery.

### Editorial Comment

This is another paper that shows again our imperfect knowledge of urogenital innervation. Yucel and Baskin in an elaborate work demonstrate the interaction of both pudendal and dorsal penile nerves with branches of the hypogastric nerves at the level of the base of the penis. All of a sudden we cannot be sure anymore that e.g. the pudendal nerve has only somatic purposes or that branches of the hypogastric plexus are purely autonomic.

If there exists such an interacting network in an area where we are very close during pelvic floor surgery than the differences of nerve-sparing surgical procedures in the individual patient may become more understandable. Could it be that in some patients where no nerve-sparing procedure is performed collateral nerve supply from other nerves result in good functional outcome with regards to the potency, which is otherwise not explainable?

We constantly have to refine and sometimes revise old dogmas especially in areas such as pelvic surgery and their anatomy if what we find does not 100% correspond with published schemes. Above all preservation of autonomic nerves does not result in perfect penile functions even in the hands of the best surgeons. And on the other hand deliberate dissection of autonomic nerves may still not lead to erectile dysfunction in all cases. Maybe studies like this one explain one of several possibilities.

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## UROLOGICAL ONCOLOGY

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### Port site metastases in urological laparoscopic surgery

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*J Urol.* 2003; 169: 1213-8

**Purpose:** Laparoscopic surgery is rapidly gaining widespread acceptance among urologists, including extensive application in malignant conditions. However, untoward occurrences of port site metastases have not eluded to urological applications. This up-to-date review on port site metastases in urology delineates possible contributing factors and describes techniques to prevent it.

**Materials and Methods:** We comprehensively reviewed published experimental and clinical studies with special emphasis on the incidence, pathophysiology and prevention of port site metastases.

**Results:** Nine cases of port site metastases after urological laparoscopy have been described in clinical and experimental studies. Etiological factors include natural malignant disease behavior, host immune status, local wound factors, laparoscopy related factors such as aerosolization of tumor cells (the use of gas, type of gas, insufflation and desufflation, and pneumoperitoneum) and sufficient technical experience of the surgeons and operating team (adequate laparoscopic equipment, skill, minimal handling of the tumor, surgical manipulation and wound contamination during instruments change, organ morcellation and specimen removal).

**Conclusions:** Port site metastases is a multifactorial phenomenon with an as yet undetermined incidence. The problem is influenced to some extent by surgeon and operating team experience and, therefore, it could be partially prevented. The suggested preventive steps are avoiding laparoscopic surgery when there are ascites, trocar fixation to prevent dislodgment, avoiding gas leakage along and around the trocar, sufficient technical readiness of the operating team (adequate laparoscopic equipment and technique, minimal handling and avoiding tumor boundary violation of the tumor), using a bag for specimen removal, placing drainage when needed before desufflation, povidone-iodine irrigation of instruments, trocars and port site wounds, and suturing 10 mm. and larger trocar wounds.

### Editorial Comment

This thorough review describes a rare but existent event in laparoscopy of urological tumors, metastases in the port tract. The authors analyzed the published literature on incidences of port site metastases and (only) found 9 cases. They conclude, that the real incidence of a port site metastases is yet undetermined (that is, many might be falsely referred to as local recurrences of the tumor).

Factors to prevent port site metastases are analyzed and specified in detail. Further to the data given in my one analysis of the data, 1 important point became obvious: 5 of the 9 cases described were transitional cell carcinomas. With the background of the known implantation rate in transurethral resection of superficial bladder tumors, this tumor entity might not be the ideal indication for a laparoscopic approach. Certainly further research on this phenomenon is necessary.

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## FEMALE UROLOGY

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### **Management of vaginal erosion of polypropylene mesh slings**

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*J Urol. 2003; 169: 2242-3*

**Purpose:** The SPARC (American Medical Systems, Minneapolis, Minnesota) polypropylene sling has recently been introduced as an alternative delivery system to TVT (Ethicon, New Brunswick, New Jersey) tension-free vaginal tape for placement of a tension-free mid urethral sling. Erosion must always be considered a risk of synthetic materials. We present 4 cases of vaginal erosion of polypropylene mesh placed with this system and the successful conservative management done.

**Materials and Methods:** A total of 90 patients received a SPARC polypropylene pubovaginal sling at our institution between October 1, 2001 and October 1, 2002. During followup 3 of our patients and 1 patient with tension-free vaginal tape who was referred from elsewhere presented with vaginal exposure of the mesh.

**Results:** Two patients described persistent vaginal discharge 6 weeks postoperatively, including 1 who complained primarily of partner discomfort during sexual intercourse. Two patients were completely asymptomatic and mesh erosion was discovered at routine physical examination 6 weeks postoperatively. Pelvic examination demonstrated vaginal exposure of the mesh in all cases. Each patient was observed conservatively and 3 months postoperatively all 4 had complete spontaneous epithelialization over the mesh. None had stress incontinence, urgency or urge incontinence, all emptied the bladder to completion and all patients were completely satisfied with the procedure.

**Conclusions:** The recent literature suggests that polypropylene mesh erosion should be treated with complete removal of the sling material. We present 4 cases of vaginal erosion of polypropylene slings that were managed conservatively with observation and resulted in complete spontaneous healing. Sling preservation with continued patient continence and satisfaction is a feasible option in those with vaginal exposure of polypropylene mesh.

### Editorial Comment

The authors describe their experience with four patients with vaginal erosion of their polypropylene mesh sling into the vagina. None of the patients had an erosion of the urinary tract (i.e. into the urethra or into the bladder). Two of the patients were completely asymptomatic while the other two had persistent vaginal discharge including one whose partner complained of pain with sexual relations. All four patients were treated conservatively and at 3 months post-operatively all the erosions had complete epithelialization with a normal exam noted. None of the patients had any voiding dysfunction such as recurrent stress urinary incontinence or urge incontinence during their course of treatment.

This is an important paper with regards to management of those patients who have vaginal erosion of their artificial material slings. It is succinct and well written. Many times in practice a patient will be identified who has deemed herself an operative success but has an erosion of artificial material noted in the vagina. The next clinical question is usually: should this patient be subjected to complete removal of the sling if they are indeed asymptomatic with good urinary control? This paper addresses this very point. They illustrate that with a minimalist approach there was complete epithelialization and no voiding dysfunction.

In addition to the reported clinical results, the article is valuable for the discussion on sling removal versus oversewing of the vaginal mucosa over the sling. Excellent points are made regarding the potential impact of the loosely woven polypropylene mesh with regards to its large pores and allowing tissue in-growth. They make a direct contrast between the construction and properties of the polypropylene as opposed to other synthetic materials such as polyester and silicone (1). In addition, the authors do point out that none of the patients in their report had a urinary tract erosion such as into the urethra and bladder which would be a different malady to both diagnose and treat (2). This paper gives clinicians food for thought with regard to management of those patients who have a simple vaginal erosion after a polypropylene mesh sling. Perhaps the rate of vaginal erosion is higher and the clinician does not appreciate its presence secondary to the lack of symptoms and its eventual auto-resolution. The authors should be lauded for delineating a plan of action that allows us to be more heartened with the counsel of simple sexual abstinence and tincture of time for this post operative complication.

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## PEDIATRIC UROLOGY

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### **Vulvovaginitis in prepubertal girls**

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*Arch Dis Child.* 2003; 88: 324-6

This retrospective study evaluated the clinical features and findings in bacterial cultures and in microscopic examination of vaginal secretions in 80 prepubertal girls, aged 2-12 years, with vulvovaginitis. Vaginal secretions were obtained directly from the vagina with a sterile catheter carefully inserted into the vagina. Pathogenic bacteria were isolated in 36% of cases. In 59% of these cases the isolated pathogen was group A beta-haemolytic streptococcus. Candida was not found in any of the patients. The finding of leucocytes in vaginal secretions as an indicator for growth of pathogenic bacteria had a sensitivity of 83% and a specificity of 59%. Antimicrobial treatment should therefore be based on bacteriological findings of vaginal secretions and not on the presence of leucocytes alone.

### **Editorial Comment**

This study evaluates retrospectively the clinical features and culture results in 80 prepubertal girls referred to a pediatric gynecology clinic. Nearly all had vaginal discharge and many had itching and redness as well. Cultures revealed pathogenic bacteria in 29 of the 80, Group A, beta-hemolytic streptococcus being the most common (41% of these patients had a recent history of sore throat). With blood cells (WBCs) were present in the secretions in 24/29 patients with pathogenic organisms and 21/51 of those without.

This study provides guidance in the management of vulvovaginitis in girls. In particular, in the absence of WBCs, it is unlikely that pathogenic bacteria are present. Furthermore, Group A streptococcus is the most common organism. However the study has several important flaws. First and foremost there are no controls. What percentage of normal girls have WBCs or streptococcus in their vaginal secretions? Also, no cultures were done for Chlamydia, gonorrhea or Trichomonas. Despite the fact that none of these children had a history of sexual abuse, this is an unfortunate error.

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**Relationship between age at initiation of toilet training and duration of training: a prospective study**

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*Pediatrics* 2003; 111: 810-4

**Objective:** To study the relationship between age at initiation of toilet training, age at completion of toilet training, and the duration of toilet training.

**Methods:** A total of 406 children seen at a suburban private pediatric practice were enrolled in a study of toilet training between 17 and 19 months of age, and 378 (93%) were followed by telephone interviews with the parents every 2 to 3 months until the child completed daytime toilet training. Information obtained at follow-up interviews included how often parents were asking their child to sit on the toilet or potty and where the child urinated and defecated. Parents were considered to have initiated toilet training when they first took out a potty chair and discussed some aspect of training with the child. Intensive toilet training was defined as asking the child to use the toilet or potty more than 3 times per day.

**Results:** Age of initiation of toilet training correlated with age of completion of training ( $r = 0.275$ ). The correlation between age at initiation of intensive training and age at completion was even stronger ( $r = 0.459$ ). Younger age at initiation of intensive toilet training was not associated with constipation, stool withholding, or stool toileting refusal. However, age at initiation of intensive toilet training was negatively correlated with duration of toilet training ( $r = -0.481$ ), indicating that initiation of training at younger ages was associated with a longer duration of training. In addition, the correlation between age at initiation of intensive toilet training and age at completion of training was not significant for those who began intensive training before 27 months of age ( $r = 0.107$ ).

**Conclusions:** Early initiation of intensive toilet training correlates with an earlier age at completion of toilet training but also a longer duration of toilet training. Although earlier toilet training is not associated with constipation, stool withholding, or stool toileting refusal, initiation of intensive training before 27 months does not correlate with earlier completion of toilet training, suggesting little benefit in beginning intensive training before 27 months of age in most children.

**Editorial Comment**

This study evaluates prospectively the consequences of early toilet training in a suburban private pediatric practice setting. Early toilet training did not correlate with constipation or stool withholding. Earlier toilet training did correlate with prolonged duration of training. The authors conclude that the initiation of intensive toilet training before 27 months of age is rarely indicated.

This study is important in that there have been concerns that attempts at toilet training started too early might be counterproductive, with more voiding dysfunction and constipation resulting. That did not appear to be the case in this study, although younger children did take longer to train. This study was limited to suburban private practice patients and may not be generalized to other groups. Another problem relates to the fact that the patients were evaluated by regular phone interviews every 2-3 months. Telephone interviews may be unreliable as a method of evaluating voiding dysfunction and constipation. Furthermore, one wonders whether the regular telephone interviews might also have had a therapeutic effect in and of itself. Nonetheless, the study does provide some useful data that suggests that early and aggressive toilet training is not dangerous.

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## RADIOLOGICAL CLASSIFICATION OF RENAL ANGIOMYOLIPOMAS BASED ON 127 TUMORS

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### ABSTRACT

**Purpose:** Demonstrate radiological findings of 127 angiomyolipomas (AMLs) and propose a classification based on the radiological evidence of fat.

**Materials and Methods:** The imaging findings of 85 consecutive patients with AMLs: isolated (n = 73), multiple without tuberous sclerosis (TS) (n = 4) and multiple with TS (n = 8), were retrospectively reviewed. Eighteen AMLs (14%) presented with hemorrhage. All patients were submitted to a dedicated helical CT or magnetic resonance studies. All hemorrhagic and non-hemorrhagic lesions were grouped together since our objective was to analyze the presence of detectable fat. Out of 85 patients, 53 were monitored and 32 were treated surgically due to large perirenal component (n = 13), hemorrhage (n = 11) and impossibility of an adequate preoperative characterization (n = 8). There was not a case of renal cell carcinoma (RCC) with fat component in this group of patients.

**Results:** Based on the presence and amount of detectable fat within the lesion, AMLs were classified in 4 distinct radiological patterns: Pattern-I, predominantly fatty (usually less than 2 cm in diameter and intrarenal): 54%; Pattern-II, partially fatty (intrarenal or exophytic): 29%; Pattern-III, minimally fatty (most exophytic and perirenal): 11%; and Pattern-IV, without fat (most exophytic and perirenal): 6%.

**Conclusions:** This proposed classification might be useful to understand the imaging manifestations of AMLs, their differential diagnosis and determine when further radiological evaluation would be necessary. Small (< 1.5 cm), pattern-I AMLs tend to be intra-renal, homogeneous and predominantly fatty. As they grow they tend to be partially or completely exophytic and heterogeneous (patterns II and III). The rare pattern-IV AMLs, however, can be small or large, intra-renal or exophytic but are always homogeneous and hyperdense mass. Since no renal cell carcinoma was found in our series, from an evidence-based practice, all renal mass with detectable fat should be considered an AML.

**Key words:** kidney neoplasms; angiomyolipomas; diagnostic imaging; tomography, X-ray computed; hemorrhage

**Int Braz J Urol. 2003; 29: 208-216**

### INTRODUCTION

Renal angiomyolipomas (AMLs) are benign neoplasms composed of mature adipose tissue, thick-walled blood vessels, and smooth muscle in varying proportions (1). Definite diagnosis of AML on computed tomography (CT) studies is made when macroscopic fat (low-density areas of -30 to -100 HU) is identified within the lesion (2,3). Our purpose is to

demonstrate the imaging findings of 127 AMLs and to propose a radiological classification based on the presence and amounts of detectable fat.

### MATERIALS AND METHODS

Between March 1995 and December 2001, renal AML was diagnosed in 85 consecutive patients

at our institution. We retrospectively reviewed the imaging findings of these patients with AMLs (isolated,  $n = 73$ ), multiple with tuberous sclerosis - TS ( $n = 8$ ) and multiple without TS ( $n = 4$ ). The patients were aged from 17 to 68 years (mean = 32 years). All patients had previous ultrasound (US) and were submitted to a dedicated helical CT. Non-contrast scans using 10-mm sections was initially done. If fat was not seen, 3- to 5-mm wide sections were scanned. In lesions smaller than 2 cm, 1 or 3-mm CT sections were performed and measurement of the attenuation values of individual pixels, were obtained (4). If fat was identified (more than 3 contiguous pixel with values below -30 HU), no further work-up was done. If no fat was seen, the patient received intravenous contrast injection for adequate preoperative staging since the mass was considered a renal cell carcinoma (RCC). Magnetic resonance was done as an additional method of evaluation in 16 patients. Of the 85 patients, 53 were followed by US or CT for 1 to 3 years to confirm stability, 32 were treated surgically due to a large perirenal component ( $n = 15$ ), hemorrhage ( $n = 13$ ) and impossibility of an adequate preoperative characterization ( $n = 4$ ).

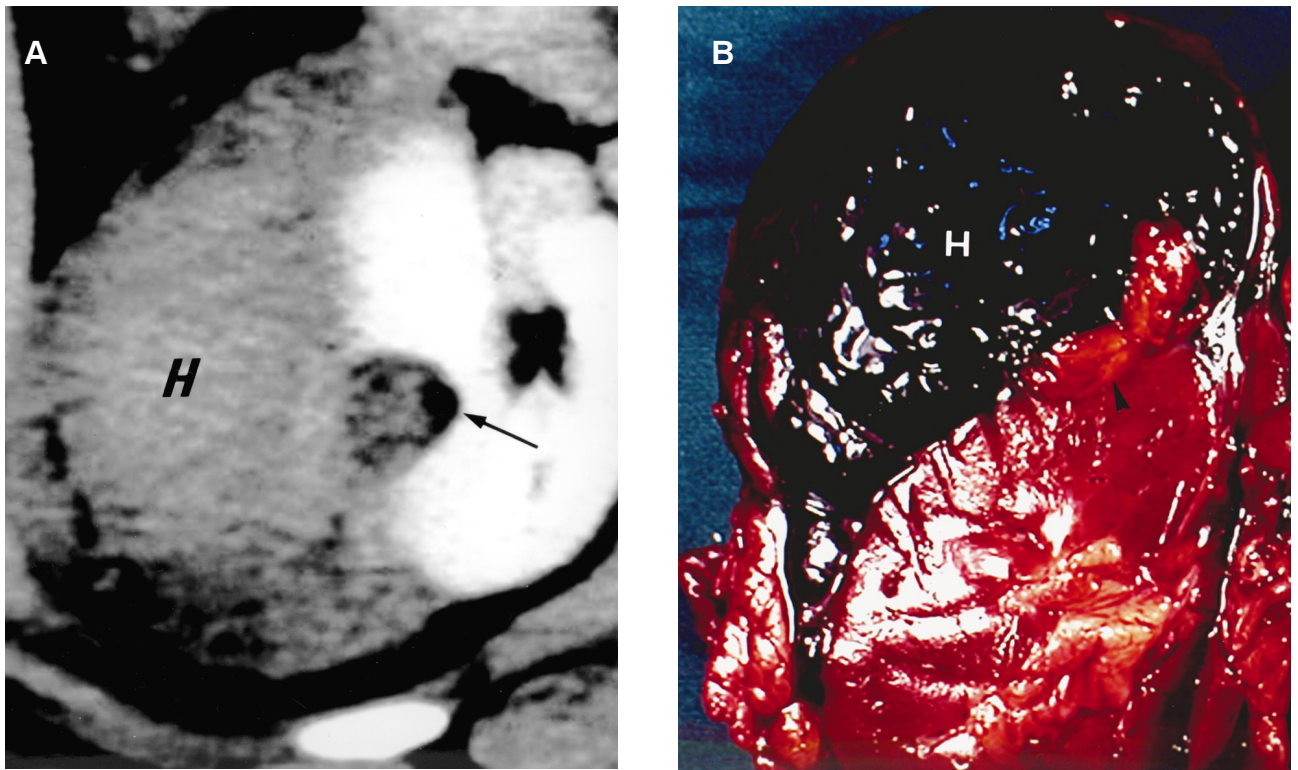
## RESULTS

Tumor size ranged from 0.5 to 36.5 cm in diameter. Follow-up studies demonstrated growing of the AMLs in 2 patients with multiple lesions. Eighteen AMLs (14%) were hemorrhagic, including 11 associated with spontaneous renal bleeding. Three of these lesions measured 2 to 4 cm in diameter (Figure-1). The presence of an intrarenal or perinephric hematoma almost obscured the fatty component of the tumor in the majority of patients. All hemorrhagic and non-hemorrhagic lesions were grouped together since our objective was to analyze the presence and the amounts of detectable fat. Based on this criterion, AMLs were classified into 4 distinct radiological patterns: a) Pattern-I AML, predominantly fatty, included 68 lesions (54%): in this group, the AMLs measured 0.5 to 3 cm in diameter and were oval or round in shape, predominantly intrarenal or with discrete protrusion outside the kidney (Figure-2). All oval, or less frequently round, highly echogenic lesions smaller

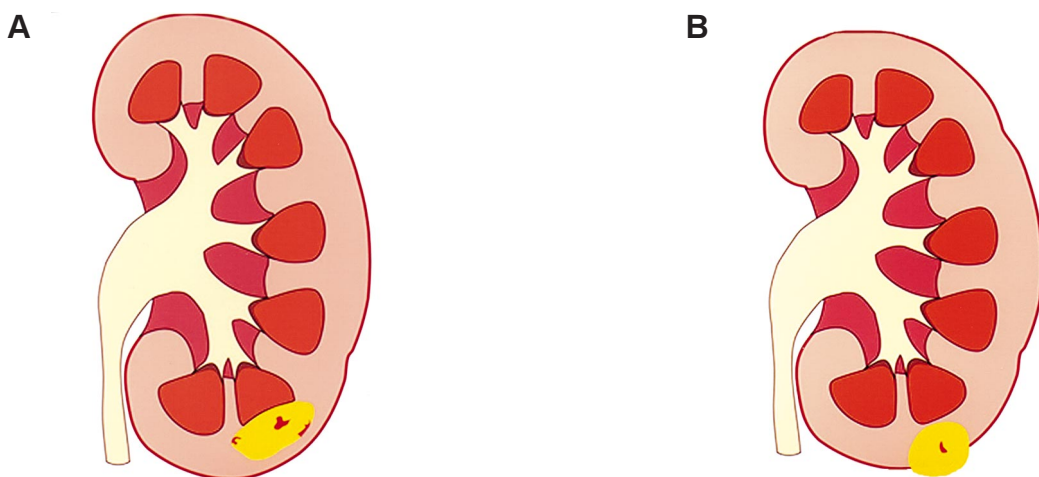
than 1.5 cm on ultrasound were proved to be an AML by helical-CT (Figure-3). Three of 16 lesions larger than 2 cm occurred in the renal sinus; b) Pattern-II AML, partially fatty, included 36 lesions (29%): this group consisted of 22 small (3 to 5 cm) and 14 large (>5 to 36.5 cm) partially or predominantly exophytic masses extending outside the kidney into the retroperitoneal space (Figure-4). These lesions presented with variable amounts of non-fatty soft tissue mass, intratumoral vessels or internal or perinephric hematoma (Figure-5). Only 2 AMLs were completely intrarenal and other 2 manifested as a renal sinus tumor; c) Pattern-III AML, minimally fatty, included 8 lesions (11%): most AMLs with minimal fat content manifested as a tumor with a predominantly extrarenal growth extending into the perirenal space (Figure-6). The report pixels method was essential for the detection of tiny amounts of fat within these lesions (Figure-7); d) Pattern-IV AML, without detectable fat, included 4 lesions (6%): all 4 masses were predominantly exophytic and occurred only in non-TS patients (Figure-8). All lesions showed high homogeneous attenuation on nonenhanced CT scans and homogeneous enhancement on contrast-enhanced CT images (11). In large lesions the presence of a small parenchyma defect was important to determine its renal origin. All tumors were surgically removed due to the preoperative diagnosis of a RCC (Figure-9).

## DISCUSSION

Renal AML is a fairly common lesion, often discovered incidentally during ultrasound examination in women (30 - 60 years of age) and appears as hyperechoic mass with echogenicity similar or less intense than the renal sinus fat. They are usually single and small lesions, measuring 0.5 to 3 cm. About 20% of patients with AMLs have tuberous sclerosis (TS). In this condition, these tumors tend to be multiple and bilateral and have no gender predilection. Flank pain, hematuria or palpable mass, may result from its bleeding or large size. Small AMLs are usually further investigated with CT in order to differentiate from small hyperechoic renal cell carcinomas while larger AML may mimic perirenal liposarcomas. For these reasons and the fact that there are still controversies



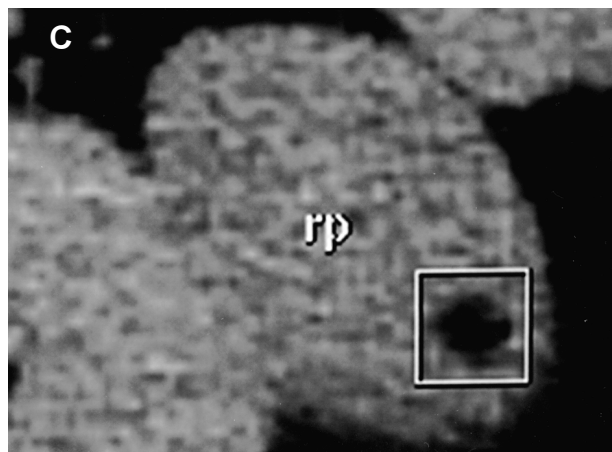
**Figure 1** - Small ruptured angiomyolipoma associated with spontaneous renal hemorrhage. A) - Enhanced helical CT scan shows a large perirenal hematoma (H). A heterogeneous exophytic mass can be seen at the lateral portion of the right kidney (arrow). A small amount of fatty tissue can be seen at the periphery of the lesion (arrowhead). B) - Gross specimen shows a small angiomyolipoma (arrow-head) causing a large hematoma (H).



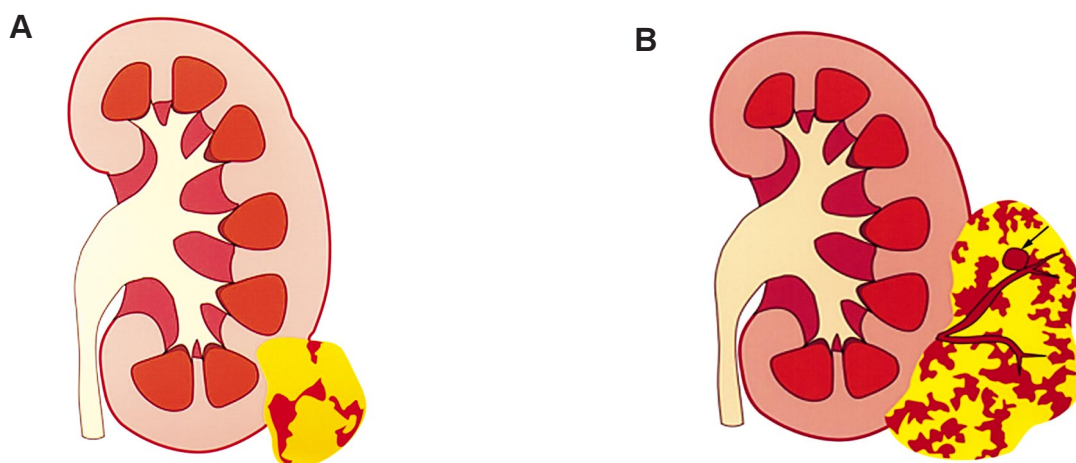
**Figure 2** - Diagrams illustrating the 2 variants of pattern-I angiomyolipoma. A) - A small, oval predominantly fatty intrarenal lesion. B) - A small rounded predominantly fatty lesion with minimal protrusion from the periphery of the kidney.



-82	-103	-72	-68	-78
-69	-94	-89	-88	-68
-63	-65	-42	-42	-67
-52	-52	-62	-64	-63
-60	-66	-66	-95	-103
-66	-67	-66	-66	-68

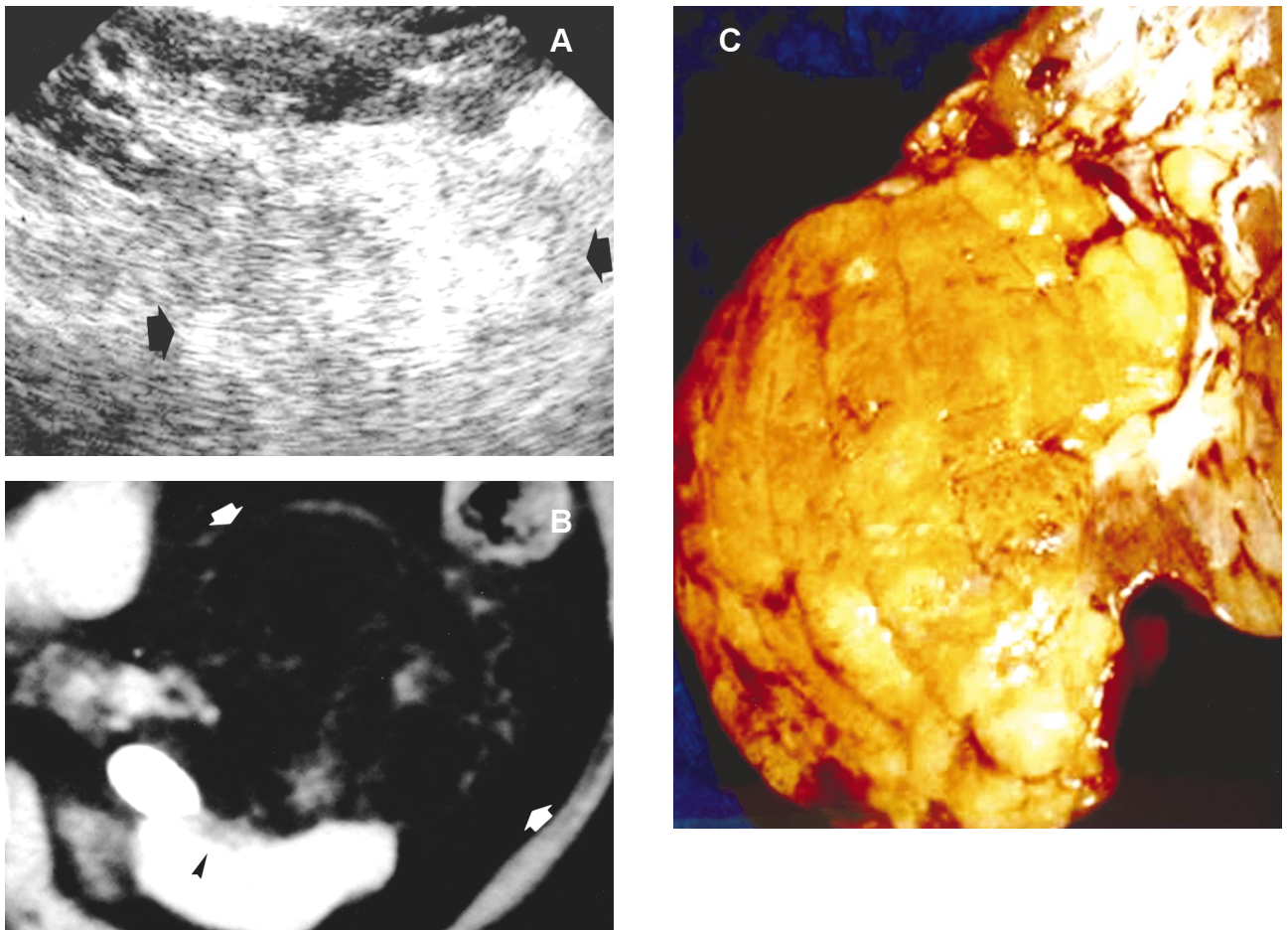


**Figure 3** - Pattern-I angiomyolipoma. A) - Ultrasound scan shows an oval, highly echogenic lesion (1.3 x 0.9 cm) in the periphery of the lower pole of the left kidney (arrow). B) - Corresponding CT scan with report pixel voxel applied. C) - Note that the hypoattenuating lesion shows only negative numbers representing fat densities (-42 to -103).



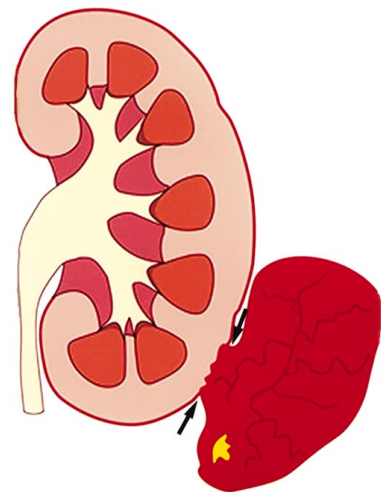
**Figure 4** - Diagrams illustrating the 2 variants of pattern-II (partially fatty) angiomyolipoma. A) - Small partially exophytic fatty mass. B) - A larger predominantly exophytic mass containing tortuous and bridging vessels with a pseudoaneurysm (arrow). Both tumors present variable amounts of non-fatty tissues.



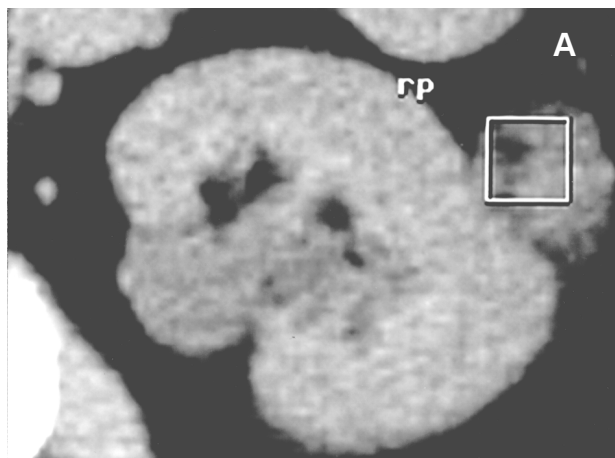


**Figure 5** - Pattern-II angiomyolipoma. A) - Prone longitudinal ultrasound shows a large echogenic mass at the anterior aspect of lower pole of the left kidney (arrows). B) - Correspondent enhanced CT scan demonstrates the fatty component of the exophytic mass (arrows) with internal linear and branching vessels. Note a focal parenchyma defect (arrowhead). C) - Gross specimen confirmed the fatty nature of the mass

regarding the incidence of AMLs without fat, we propose an original radiological classification of these tumors. The purpose of this classification, which is based on the presence and amounts of detectable fat, is to demonstrate that variable radiological manifestations of AMLs are related to their growing mechanism. This knowledge may facilitate their differential diagnosis and their radiological work-up. In our series of 127 lesions, all tumors with detectable fat by dedicated helical-CT study, even those were fat

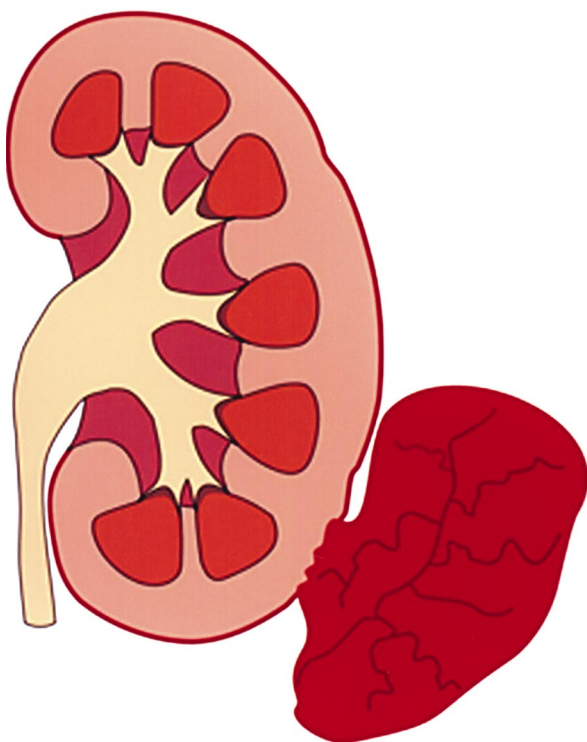


**Figure 6** - Diagram illustrates pattern-III angiomyolipoma. A predominantly myomatous / angiomatous mass with only minimal amounts of fat that originates from the renal cortex (arrows = site of focal parenchymal defect).



-39	-29	-15	13	21	-10
-51	-57	-50	-26	-6	-5
-59	-48	-19	-9	10	22
-42	-32	-13	16	29	13
-12	4	-7	6	20	22
-21	-14	-19	14	19	33
-27	4	9	18	23	34
-1	30	38	28	34	23

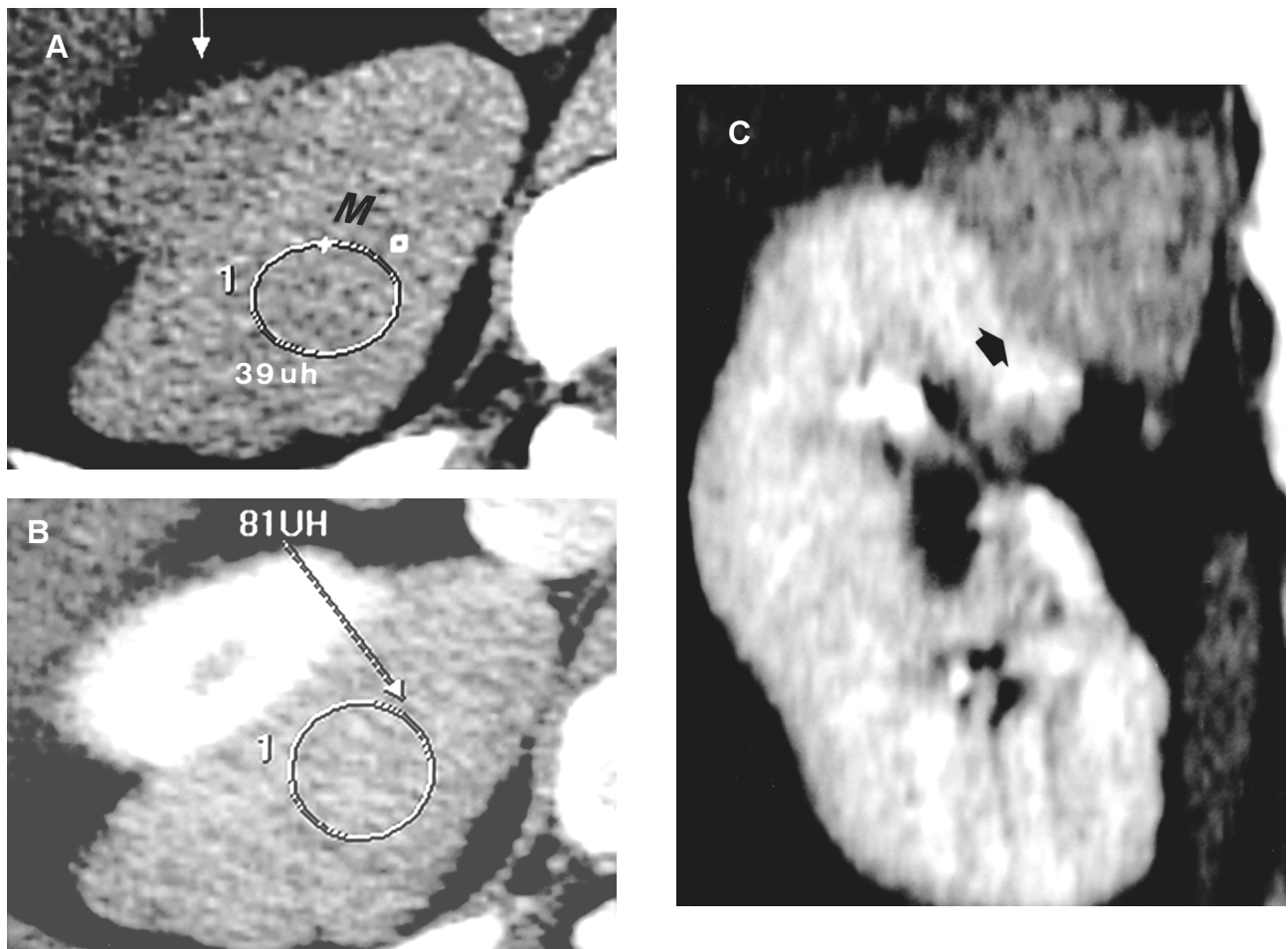
**Figure 7** - Pattern-III angiomyolipoma. A) - Nonenhanced CT scan (3-mm section) shows a predominantly soft-tissue exophytic mass, at the lateral aspect of the left kidney. A tiny hypoattenuating area is identified at the periphery of the lesion. The report pixel voxel (rp) has been applied to this area. B) Note that clusters of pixels with negative numbers are coincident with the tiny hypoattenuating area and represented fat (the lowest attenuation value was -59 HU).



**Figure 8** - Diagram illustrates pattern-IV angiomyolipoma. An exophytic homogeneously myomatous / angiomatous mass, without a radiologically detectable fat.

was obscured by hematoma, proved to be an AML (n = 123, 94%). Pattern-I, the most common manifestation of AML, can be differentiated from hyperechoic small RCC when a hypoechoic rim (pseudocapsule) or intratumoral tiny cysts are identified (5-7). When small pattern-I lesions (< 1.5 cm), are detected by ultrasound, no further investigation with CT is necessary since in our series all of these lesions proved to be AMLs. Spontaneous renal bleeding secondary to an AML usually occurs when the tumor is larger than 4 cm (8), but in 3 of 11 lesions (27%), the tumor measured 2.5 to 4 cm in diameter. Spontaneously hemorrhagic pattern-II renal AMLs must be differentiated from a RCC or other vascular entities (9). For this reason a careful search must be done during CT evaluation in order to detect fat (3), which in our series was invariable found at the periphery of the lesion (Figure-2). As this tumor grows they tend to be exophytic (pattern II or III). These lesions should be distinguished from well-differentiated, low grade retroperitoneal or capsular liposarcoma and the very rare RCC engulfing perirenal fat (10,11). AML can be distinguished from a perirenal liposarcoma on CT scans by the presence of typical internal tortuous angiomatous vessels and a renal parenchyma defect (Figure-5); both





**Figure 9** - Pattern-IV angiomyolipoma mimicking RCC. A) - Nonenhanced CT scan shows a homogeneously hyperattenuating (39 HU), exophytic mass (M), at the posterior aspect of the upper pole of the right kidney. B) - The attenuation of the mass on the enhanced CT image is lower (81 HU) than the renal parenchyma (the lesion attenuation increased 42 HU). C) - Coronal reconstruction better shows the focal parenchyma defect (arrow) demonstrating that the lesion originates from the kidney. Fatty elements were demonstrated only by histology.

findings usually not seen in liposarcomas (10). Pattern-IV AML has a distinct radiological behavior; as they grow the lesions maintain its high attenuation, homogeneous enhancement and its exophytic appearance (12). Similarly to pattern-III AML, the demonstration of a renal parenchyma defect in pattern IV AML is essential in order to establish its origin. Although isolated cases of calcified and non-calcified RCC containing fat has been described (13,14), for an evidence-based practice, all renal mass with detectable fat should be considered an AML.

## CONCLUSIONS

This proposed classification might be useful to understand the imaging manifestations of AMLs, their differential diagnosis and the necessity for eventual further radiological work-up. Small (< 1.5 cm), pattern-I AMLs tend to be homogeneous predominantly intra-renal, fatty lesion. In our series, all hyperechoic lesions measuring 1.5 cm or less represented an AML; therefore, further evaluation with helical CT is probably not necessary in this group of patients. As these lesions grow they tend to present

variable amounts of non-fatty tissue and vascular components and to appear as partially or completely exophytic and heterogeneous (patterns II and III). Pattern-IV AMLs, however, although extremely rare (only 6%) can be small or large, but are always exophytic homogeneous and hyperdense renal mass. Although pattern-IV AML present some suggestive radiological signs, differentiation from malignant renal tumor is almost impossible. Since no renal cell carcinoma was found in our series, from an evidence-based practice, all renal mass with detectable fat should be considered an AML.

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## EDITORIAL COMMENT

The authors add important new information to the literature by demonstrating the variable radiologic features of angiomyolipomas (AMLs). Four specific categories are defined. The use of this categorization permits the application of new information concerning these lesions in a more effective manner. Such a framework has been needed to for appropriate patient care, particularly since a variety of therapeutic approaches are available.

Pattern I lesions, which are predominantly fatty, intrarenal and small, represent an important group. The current paper found no renal cell carcinomas in patients whose lesions were less than 1.5 cm in size and highly reflective on ultrasonographic studies. Forman et. al. (1) reviewed 90 pathologically proven RCCs. In their series, all 5 renal cell carcinomas, which were less than 1.5 cm in size, were highly echogenic. Thus, one would conclude from these 2 articles that echogenic masses under 1.5 cm in size are typically angiomyolipomas, but that when renal cell carcinoma is seen when it is under 1.5 cm in size it is echogenic and indistinguishable from an AML. The current article concludes that echogenic masses under 1.5 cm can be considered AMLs and need no further work-up. A more conservative approach of verifying this diagnosis with CT or magnetic resonance imaging to identify the rare, small RCC is standard at many institutions. The cost effectiveness of this conservative approach remains to be defined.

Pattern II and III lesions which contain some macroscopic fat can clearly be considered AMLs. Many physicians would use follow-up studies of these lesions to define the growth rate of these masses both for prophylactic treatment of rapidly growing AMLs and to identify the very rare renal cell carcinoma that contains macroscopic fat.

Pattern IV lesions which contain no fat and are typically exophytic and perirenal remain the most challenging category. All of these masses were considered RCCs and treated surgically which is the standard approach. Biopsy of renal masses, once considered to be risky because of the possibility of spread of tumor, has been found to be safe using fine

needle technique (2). Such biopsies are used for such indications including transitional vs. renal cell carcinoma, lymphoma vs. carcinoma, infection vs. tumor and to diagnose RCC when a tumor is unresectable. Two angiomyolipomas were biopsied successfully by Caroli et. al., establishing the diagnosis (2). The use of biopsy for echogenic masses without fat when seen in an appropriate setting, such as a middle-aged female or a premenopausal female with lymphangiomyomatosis (3), remains limited to a few institutions, but it has great potential.

Finally, 32 of the 53 patients were treated surgically in the current series. In cases in which hemorrhage or large size are the indications for surgery, an alternative technique is catheter embolization. (4). This is generally the initial approach used at our institution in these situations.

The categorization of AMLs in this article, based on a large series of cases that were carefully studied, has significant management implications and will be of use in evaluating therapeutic alternatives.

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## METABOLIC INVESTIGATION OF PATIENTS WITH UROLITHIASIS IN A SPECIFIC REGION

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### ABSTRACT

**Objective:** To assess the prevalence of the main metabolic alterations found in patients with recent diagnosis of urolithiasis in the West region of Paraná state, Brazil.

**Materials and Methods:** We made a retrospective study on 425 patients with evidence of recent formation of renal stones. Laboratory assessment consisted in 3 samples of 24-hour urine with dosing of calcium, uric acid, citrate, oxalate, sodium and creatinine. A urine culture was also made and qualitative cystinuria and urinary pH following 12-hour fasting and water restriction were evaluated.

**Results:** In 96.5% of patients a cause was detected for the urolithiasis. Metabolic alterations most frequently found were: hypercalciuria (38.3%), hypocitraturia (29.6%) and hyperexcretion of uric acid (21.6%). Low urinary volume (17.9%), urinary tract infection (12.9%), hyperparathyroidism (3.3%), renal tubular acidosis (1.2%), cystinuria (0.9%) and anatomical alterations (12.7%) were also observed.

**Conclusions:** Hypercalciuria, hypocitraturia and hyperuricuria are the most frequent metabolic disorders in the population under study and these data are in accordance to the literature.

**Key words:** urolithiasis; metabolism; metabolic disease; risk factors; calcium oxalate; calcium  
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## INTRODUCTION

Renal lithiasis affects 12% of the United States of America population and its recurrence can reach 50%. Significant advancements in surgical approach have occurred, but they did not change the natural history of urolithiasis (1,2). In Brazil there is a report that 5% of the population has urolithiasis, which corresponds to more than 7 million of patients with lithiasis. It is a pathology that affects young people, with its peak incidence during the third decade of life and a very high recurrence, reducing productivity of such individuals (3). The dissemination of preventive metabolic investigation programs and nephrologic approach is necessary, however the high costs of laboratory tests and the poor adhesion of pa-

tients to treatment and to dietary orientation limit the success of the medical approach.

The objective of the present work is to show the prevalence of major metabolic alterations found in patients with renal lithiasis coming from urban and rural zones of West region of Paraná state, Brazil.

## MATERIALS AND METHODS

It was performed a retrospective study on 425 patients from general nephrology outpatient service coming from rural and urban zones who presented evidences of recent urolithiasis, in the period from 1995 to 2002. Inclusion criteria for patients in this retrospective study were spontaneous, endoscopic or surgical elimination of stones and/or radiological con-

firmation of presence of stones in urinary tract in the past 6 months.

Laboratory investigation consisted in 3 blood and 24-hour urine samples, with a 30-day interval between them. Calcium, uric acid, citrate, sodium, creatinine and oxalate were evaluated in 24-hour urine, and calcium, uric acid, creatinine and parathormone in blood. Qualitative cystinuria, urinary pH following a 12-hour fasting and water restriction and urine culture were also performed.

General nutritional orientations were offered to all patients following the second samples collection, consisting in: 6 grams of salt/day, 1 gram/Kg of weight of proteins, restriction of purines to 150 mg, adjustment of calcium intake to 1000 mg and increase in fluid intake to maintain a urinary volume above 20 mL/kg/day.

Laboratory methods employed and reference values adopted for 24-hour urine samples were: calcium – atomic absorption spectrophotometry method (< 4.0 mg/kg), uric acid – uricase enzymatic method (up to 750 mg for females and 800 mg for males), citrate – citrate-lyase enzymatic method (> 320 mg), sodium – selective ion method (< 150 mEq), creatinine – alkaline picrate method (> 1000 mg) and urinary volume – volumetric measurement in Becker by visual analysis. For plasma dosing the methods employed were: calcium – colorimetric method (8.5 – 10.5 mg/dL), uric acid – uricase colorimetric method (2.0 to 7.0 mg/dL), creatinine – alkaline picrate method (0.7 a 1.4 mg/dL) e parathormone – intact molecule assay. For assays in single urine sample the methods were: qualitative cystinuria – sodium nitroprusside test, and urinary pH – measurement by reactive strips with methyl red and bromthymol blue indicator system. Urinary volume was considered to be decreased, when at least one of the samples presented a 24-hour urinary volume lower than 15 mL/kg.

## RESULTS

1,023 patients with lithiasis were assessed out of a total of 5,207 attended patients, among whom only 425 concluded the metabolic study. Patients mean age was 32.2 years (ranging from 2 months to 67

years), 61.2% were male and 38.8% were female. As for race, 85% were Caucasian.

Among the 425 patients with lithiasis under study, at least one alteration was found in 410 (96.5%). 604 diagnoses were made, showing that some patients present more than one alteration. Metabolic alterations found were: hypercalciuria in 38.3%, hypocitraturia in 29.6%, hyperexcretion of uric acid in 21.6%, low urinary volume in 17.9%, urinary tract infection in 12.9%, hyperparathyroidism in 3.3%, renal tubular acidosis in 1.2% and cystinuria in 0.9% (Table-1). Anatomical alterations were found in 12.7%. In 3.5% of patients no alterations were found.

Among the anatomical alterations found (Table-2), we observed 22 renal cysts (40.7%), pyelocaliceal duplications (20.4%), 5 atrophic kidneys (9.3%), 5 stenoses of ureteropelvic junction - UPJ (9.3%), 5 single kidneys (9.3%), 3 neurogenic bladders (5.5%), 1 pelvic kidney (1.8%), 1 horse-shoe kidney (1.8%) and 1 medullary sponge kidney (1.8%).

## DISCUSSION

Nephrolithiasis is a disease with high prevalence and recurrence, being one of the most common diseases of the urinary tract (4). We do not have available data about prevalence of renal lithiasis in the general population in the West region of Paraná state, Brazil. In this study we observed that approximately

*Table 1 – Metabolic alterations found.*

Metabolic Alteration	N	%
Hypercalciuria	163	29.6
Hypocitraturia	126	22.9
Hyperuricuria	92	16.7
Low urinary volume	76	13.8
Urinary tract infection	55	10.0
Hyperparathyroidism	14	2.5
Renal tubular acidosis	5	0.9
Cystinuria	4	0.7
No alteration detected	15	2.7
Total	550	100



**Table 2** – Anatomical alterations found in 12.7% of patients with urolithiasis.

Anatomical Alteration	N	%
Renal cyst	22	40.7
Pyelocaliceal duplication	11	20.4
Atrophic kidney	5	9.3
Ureteropelvic junction stenosis	5	9.3
Single kidney	5	9.3
Neurogenic bladder	3	5.5
Pelvic kidney	1	1.8
Horseshoe kidney	1	1.8
Medullary sponge kidney	1	1.8
Total	54	100

20% of attended patients in a general nephrologic outpatient service, which receives patients coming from urban and rural zones, have the diagnosis of urolithiasis. The risk of terminal chronic renal insufficiency (CRI) is small in these patients, but some conditions, if left untreated, present a high risk of evolving to renal failure (cystinuria, hyperparathyroidism, oxaluria, etc.). The prompt recognition of such conditions is important to prevent CRI (5).

Urolithiasis affects preferably young males (6). In our study there was a predominance of male gender (61.2%) and patients mean age was 32.2 years, what is in accordance to the literature (7). There was a predominance of Caucasian race (85%), reflecting the racial distribution in our region, and it does not enable us to say that incidence is higher in this race.

We detected a causal alteration in 96.5% of patients. Metabolic alterations most frequently found were hypercalciuria (29.6%), hypocitraturia (22.9%) and hyperexcretion of uric acid (16.7%), data that is consonant with the majority of works, and it shows that there is a lack of balance between the promoters of stone formation and its inhibitors (7,8).

Decrease in urinary volume is considered a cause of lithiasis (9). In hot climate countries extrarenal losses and low fluids intake can contribute to stone formation. In this study we observed a decreased urinary volume in 13.8% of alterations, a much lower

index than the 77% index reported in the interior of São Paulo state, where climate is warmer (7).

Hypercalciuria is responsible for more than 50% of metabolic disorders in adults and 53 to 75% in children (10). It is thought to have a strong genetic component, probably with dominant autosomic inheritance (11). A sodium-rich diet is one factor to be considered in pathogenesis of hypercalciuria (12). In this study hypercalciuria was the prevalent metabolic disorder. In West region of Paraná state the ingestion of milk and dairy products is small, but salt and protein intake is high, probably contributing to occurrence of hypercalciuria. Oral calcium overload test was not routinely performed due to technical implications of the method and its cost, therefore patients were not classified according to type of hypercalciuria (renal or intestinal), because we understood that this classification does not change significantly the treatment of a patient who has hypercalciuria.

Hypocitraturia is found in about 30% of patients with lithiasis (13). In this study we observed this alteration in 22.9% of metabolic disorders. Hyperuricuria is due to a high intake of purines or an elevated endogenous production. Low intake of water and urinary pH < 5.5 favor the precipitation of uric acid (14). Hyperuricuria was evidenced in 16.7% of metabolic disorders in our patients, and we believe that the high regional protein intake is a risk factor. National literature observes this disorder, from 18% to 76% (7).

Hyperoxaluria is a rare disorder, and is found in approximately 1% of individuals under study (2), and it was not routinely investigated in our study. We understand that the lack of oxalate dosing in 24-hour urine did not compromise the diagnosis of the metabolic disorders reported here.

We believe that the right approach to these disorders with a multidisciplinary team can reduce both incidence and recurrence of urolithiasis in our population.

This work served as a base for knowing the metabolic profile of lithiasis patients from West region of Paraná state, Brazil. The most frequent metabolic alterations were hypercalciuria, hypocitraturia and hyperuricuria.



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## RUPTURE OF VESICourethRAL ANASTOMOSIS FOLLOWING RADICAL RETROPUBIC PROSTATECTOMY

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### ABSTRACT

**Objective:** Rupture of vesicourethral anastomosis following radical retropubic prostatectomy is a complication that requires immediate management. We evaluated the morbidity of this rare complication.

**Materials and Methods:** We analyzed retrospectively 5 cases of disruption of vesicourethral anastomosis during post-operative period in a consecutive series of 1,600 radical retropubic prostatectomies, performed by a single surgeon.

**Results:** It occurred in a ratio of 1:320 prostatectomies (0,3%). Management was conservative in all the cases with an average catheter permanence time of 28 days, being its removal preceded by cystography. Two cases were secondary to bleeding, 1 followed the change of vesical catheter and 2 by unknown causes after removing the Foley catheter. Only one patient evolved with urethral stenosis, in the period ranging from 6 to 120 months.

**Conclusion:** Rupture of vesicourethral anastomosis is not related to the surgeon's experience, and conservative treatment has shown to be effective.

**Key words:** prostatic neoplasms; retropubic prostatectomy; anastomosis, surgical; rupture  
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### INTRODUCTION

Prostate adenocarcinoma is a worldly public health problem, and about 2 hundred thousand men had a prostate cancer diagnosed in the USA in 2001 (1), with a forecast of forty thousand deaths (2). Routine use of prostate-specific antigen (PSA) has favored early diagnosis of prostate cancer (3,4) and, thus, has improved the results of surgical treatment in controlling the neoplasm (1,2,5). After significant advances in the surgical technique established by Walsh et al. (6), including preservation of neurovascular bundle and a better control of the penile dorsal vein complex, radical prostatectomy has become safe and feasible for most urologists. Two decades after the publishing of Walsh's technique (6), several surgeons have already achieved a large experience, obtaining expressive series of treated patients (7-9), with ma-

jor immediate and late complications related to radical prostatectomy being well documented (5,10-13).

Disruption of vesicourethral anastomosis following radical retropubic prostatectomy (RRP) is a rare complication and, undoubtedly, a dramatic situation for the surgeon to decide between surgical intervention and conservative management (7). Management is controversial, since the superiority of a particular treatment method has not been established.

The objective of this study is to demonstrate our experience when facing a rupture of vesicourethral anastomosis following radical prostatectomy.

### MATERIALS AND METHODS

One thousand and six hundred consecutive patients submitted to RRP associated to bilateral iliac lymphadenectomy due to prostate carcinoma, per-

formed by a single surgeon (MS) at our Institution, in the period from January 1988 to November 2002 were retrospectively assessed. Our study included 5 patients with ages ranging from 55 to 72 years (mean = 64.8 years) and who presented disruption of vesicourethral anastomosis during RRP post-operative. In 2 patients, the disruption occurred due to bleeding in surgical resection bed, one due to inadvertent change of Foley catheter and 2 ruptures of anastomosis occurred in the first and in the tenth day after Foley catheter removal, 13 and 23 days post-operatively respectively.

Immediate management consisted in urethrocystoscopy associated with introducing of a guide-wire and positioning of Foley catheter by fluoroscopy in 4 cases. Only 1 patient was immediately catheterized. Follow-up was performed through weekly cystographic examination, with removal of Foley catheter after absence of extravasation of contrast media confirmed in urethrocystography. Follow-

up ranged from 6 to 120 months (mean = 25.2 months). Patients were assessed through anamnesis, with emphasis on voiding patterns and monthly urethrocystography during the first semester, bi-annual PSA, abdomen tomography and bone scintigraphy yearly.

## RESULTS

Table-1 presents the etiology of the rupture of anastomosis and early clinical manifestations. Table-2 demonstrates the repercussions of long-term permanence of the Foley catheter.

Of the 5 cases of rupture of vesicourethral anastomosis following radical retropubic prostatectomy analyzed, 4 evolved satisfactorily and 1 presented sclerosis of the anastomosis, requiring the introduction of an urethral stent. Next, we present the report on each case in details.

**Table 1** - Characteristics of rupture of vesicourethral anastomosis.

Patient	Cause of Rupture	Manifestation	POD
1	Change of Foley catheter	Low urinary output	5
2	?	Urinary retention	13*
3	Bleeding	Anemia	4
4	?	Urinary retention	23*
5	Bleeding	Anemia	2

\* Following removal of Foley catheter; POD: Post-operative day.

**Table 2** - Period with vesical catheter and complications.

Patient	Days with Foley Catheter	Sclerosis of Bladder Neck	Urinary Continence	Prolonged Urinary Incontinence
1	31	No	Yes	No
2	22	No	Yes	No
3	14	No	Yes	No
4	31	Yes *	No	Yes ♣
5	42	No	Yes	Yes

\* Placement of stent (Urolume); ♣ placement of AMS 800 artificial sphincter

**Case 1: RM, 64 years, stage pT2b, Gleason 2+3**

On the third post-operative day (POD) the Foley catheter was changed by nursing. Subsequently there was inversion of urinary output, being larger through suprapubic Penrose drain and lower through the Foley catheter. On 5th POD, the confirmation of disruption of vesicourethral anastomosis was established during cystoscopy (Storz flexible cystoscope). During this procedure, a vesical catheter was placed with the aid of a guide-wire and cystographic control insufflating Foley's balloon with 60 mL of a solution containing iodated contrast media. Release from hospital was granted on 8th POD and the patient remained with Foley catheter for 31 days. Urinary continence was established in a definitive way from the third month on, when hygienic diapers were dispensed, however the patient evolved with erectile dysfunction.

**Case 2: SM, 65 years, stage pT3a, Gleason 4+3**

Following removal of Foley catheter on 13th POD the patient evolved with acute urinary retention. An urethrocystoscopy was performed, showing a disruption of anastomosis, which remained united only by one point. Management was conducted on an out-patient basis, by introducing a Foley catheter under fluoroscopy with the aid of a guide-wire previously inserted in the bladder. On 35th POD, the vesical catheter was removed after a normal urethrocystography. The patient evolved without interurrences remaining continent and with sexual potency preserved.

**Case 3: FB, 55 years, stage pT3a, Gleason 3+2**

On 4th POD, patient evolved with pallor, tachycardia, sweating and interruption of urinary output through Foley catheter associated to a drop in serum hemoglobin levels. Five units of erythrocyte concentrate were transfused for correction of anemia. A fluoroscopy was performed and a new vesical catheter was introduced with the aid of a guide-wire through urethrocystoscopy, which evidenced the disruption of vesicourethral anastomosis associated with the presence of hematoma between the anastomosis margins, extending hospital permanence to 8 days until clinical stability. The Foley catheter was removed on the 14th POD, after a normal urethrocystography,

and during follow-up, the patient did not present any voiding difficulty remaining continent and with sexual potency preserved.

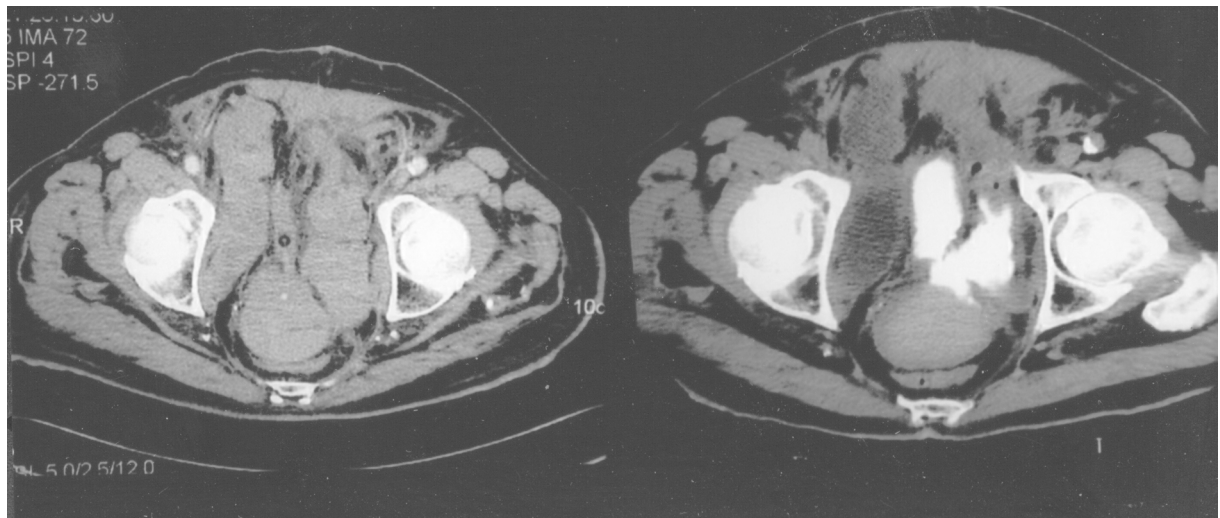
**Case 4: JCB, 68 years, stage pT2b, Gleason 3+3**

On 23rd POD, 10 days after removal of Foley catheter, the patient who was maintaining spontaneous diuresis entered in acute urinary retention. Introduction of a vesical catheter was performed without the need of aids from cystoscopy with drainage of 500 mL of clear urine. Disruption of vesicourethral anastomosis was confirmed by cystography, which demonstrated extravasation of contrast media. Removal of Foley catheter took place on the 54th POD, after performing an urethrocystography, which showed vesical filling and absence of extravasation of contrast media.

Patient evolved with sclerosis of the vesical neck (vesico-urethral anastomosis site), which was corrected by urethral stenting (Urolume®). After the procedure, the patient manifested urinary incontinence, which was subsequently resolved by placing an AMS 800 artificial sphincter. Sexual function is satisfactory with the aid of intracavernous injections of prostaglandin.

**Case 5: J G, 72 years, stage pT2c, Gleason 4+3**

On 2nd POD patient presented an acute myocardial infarction and was subjected to coronary angioplasty with placement of a vascular stent associated to administration of anti-platelet aggregating factor. He evolved with massive pelvic hemorrhage and hemodynamic instability, requiring the transfusion of 6 units of erythrocyte concentrate to correct anemia. Computerized tomography demonstrated disruption of the vesicourethral anastomosis separated by a large hematoma that pushes the bladder cranially (Figure-1). This hematoma was drained through puncture guided by computerized tomography (Figure-2). After 3 weeks with Foley catheter, it was removed; however, patient evolved with acute urinary retention. Foley catheter was reinserted with the aid of urethrocystoscopy with introduction of a guide-wire and positioning with fluoroscopic assistance. Control cystography performed after 42 days, demonstrated persistence of extravasation of contrast



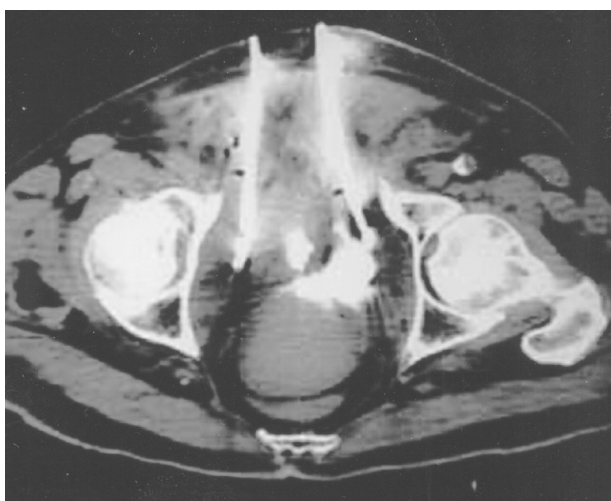
**Figure 1** - Perivesical hematoma causing rupture of vesicourethral anastomosis evidencing by extravasation of contrast medium.

media, with the aggravation that Foley catheter was positioned outside the bladder (Figure-3). Foley catheter was repositioned with the aid of cystoscopy and dynamic cystography with insufflation of 80 mL of contrast medium in the catheter balloon. During the passage of the cystoscope there was drainage of hematic secretion around the device. Weekly urethrocytographies were performed, until complete urethrovesical healing (Figure-4). Vesical catheter was

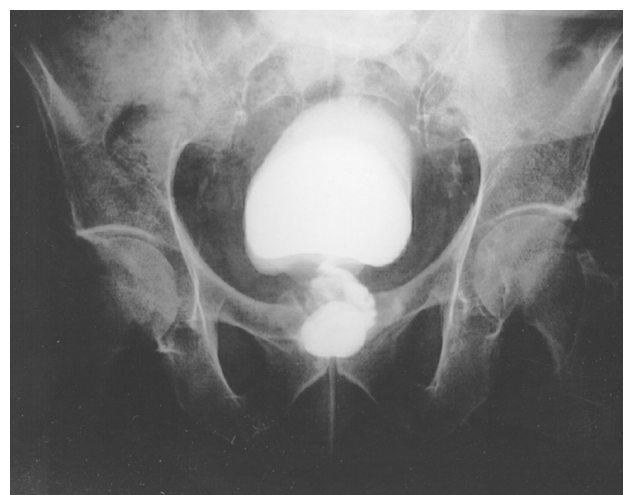
removed after 30 days (83rd POD), with patient obtaining spontaneous diuresis. Currently, after a 6 months follow-up, the patient is continent.

## DISCUSSION

This work demonstrated that conservative management for treating post-RRP rupture of vesicourethral anastomosis through permanence of



**Figure 2** - Percutaneous drainage of hematoma, guided by computerized tomography.



**Figure 3** - Complete dehiscence of bladder neck with escape of Foley catheter associated to cranial displacement of the bladder.





**Figure 4** - Cystographic control showing minimum extravasation of contrast medium and descending of bladder to its anatomical position.

Foley catheter was effective. The incidence of disruption of vesicourethral anastomosis is 0.2% to 0.5% (7-9) and the best management is still a subject for discussion.

The most common transoperative complication of radical prostatectomy is bleeding (8), which decreases with surgeon's expertise (10), however, with a blood transfusion rate of 9% to 29% (5,8), what can reflect in prognosis (11). Acute myocardial infarction is the most common unrelated post-operative complication (10) oscillating between 0.1-0.5% (8,9,12), on the other hand, the need of using an anti-coagulant increases intraoperative bleeding and post-operative lymphatic drainage (10). We had a patient who presented an acute myocardial infarction on 2nd POD in whom the use of anti-platelet aggregating factor had precipitated the hemorrhage.

On the other hand, the incidence of significant bleeding in the dissection bed during post-operative period ranges from 0.3% to 3.2% (7,9,12,14)

and the need of blood transfusion is very rare (10). Formation of small hematomas suggests an expectant management (10), however bulky hematomas can compress and displace the bladder causing disruption of vesicourethral anastomosis, if they are not drained (7). In our series, 2 patients had bleeding with rupture of anastomosis whose conservative treatment was effective. In one case there was the need of draining the perivesical hematoma through puncture guided by computerized tomography in order to avoid infection and to control severe perineal pain.

Hedican & Walsh (7) studied 7 patients with rupture of vesicourethral anastomosis secondary to bleeding in surgical bed, dividing the patients in 2 groups. In the first group, comprised by 3 patients, a conservative treatment was instituted, with indwelling vesical catheterization, whose outcome revealed sclerosis of vesical neck in all 3 patients, with 2 of them evolving with prolonged urinary incontinence. The second group, submitted to surgical exploration for hematoma drainage with revision of anastomosis had a better outcome, presenting sclerosis of vesical neck in 1 patient and prolonged urinary incontinence in another one. When indicating a new surgery in cases of post-radical prostatectomy pelvic hematomas, Lepor et al. (9), advised the repair of vesicourethral anastomosis.

Conservative treatment can be associated to sclerosis of vesical neck and also to prolonged urinary incontinence (7,15), on the other hand, early intervention with suturing of urethral margins increases the risk of complications such as urinary incontinence, erectile dysfunction and bleeding (16). In our cases, out of 5 treated patients, we had one case of sclerosis of vesical neck refractory to endoscopic treatment, whose definitive treatment consisted in the placement of a stent (Urolume), however the patient evolved with urinary incontinence requiring the implantation of an artificial sphincter (AMS-800) in order to solve definitely the problem.

When facing disruption of vesicourethral anastomosis, in order to reposition Foley catheter, cystoscopy with introduction of a guide-wire is fundamental (10,15), and while introducing the catheter, its position must be confirmed by fluoroscopy with contrast injection. Differently from Fisher & Koch



(15), we did not fix the catheter on the vesical dome; we simply used the artifice of insufflating the Foley catheter's balloon with a volume around 60 mL. Despite this precaution, in one case occurred a displacement of the Foley catheter outwards the bladder, due to complete dehiscence of vesical cervix with cranial displacement of bladder. In radical retropubic prostatectomy, while confectioning the new vesical neck, we usually use a 2-zero chromium catgut suture, making separate stitches in total plane and vesicourethral anastomosis is done with 8 separate stitches with poliglactin 3-zero incorporating the striated sphincter together with the urethra. Normally, we remove the Foley catheter on 13th POD, however there are series indicating the catheter's removal in an earlier period without impairment in healing (14). We had 2 cases of urinary retention following removal of the Foley catheter, on the first and on the 10th days following catheter's removal, without evidencing the reason for such rupture. In only one case premature change of catheter promoted the disruption of the anastomosis.

We believe that rupture of anastomosis is not related to the surgeon's experience, considering the occurrence of such complication in teams with expressive casuistry (7-9), neither is it changed by the number of stitches used for vesicourethral anastomosis (5,8,9,13,15,17,18). Antibiotic therapy was used in all patients, and no cases of sepsis were recorded. Upon confirmation of stability in the clinical picture and adequate positioning of the Foley catheter, patient is released from hospital with oral antibiotics and is re-evaluated every week on an outpatient basis through cystography, thus avoiding an excessive increase on treatment costs.

Analogously to trauma of posterior urethra, where there is disruption of prostate-membranous urethra with cranial displacement of the bladder, introducing of a Foley catheter through the urethral route allows the alignment of margins with a lower incidence of stenosis in the region, and subsequent descending of bladder to its anatomical position (15), because of this, we do not advise performing a cystostomy. Prolonged drainage constitutes an adequate management and avoids potential failure in a new surgery.

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## EDITORIAL COMMENT

Fortunately it is an uncommon situation, but a rather concerning one. The authors were very fortunate when choosing conservative management, with excellent results in the 5 cases presented. We entirely agree that this complication is not related to the learning curve.

However, being controversial, immediate surgical approach must be restricted to surgeons with a larger casuistry, thus avoiding major complications, such as sphincter compromise, leading to urinary incontinence, as well as lesions of neurovascular bundle.

In our casuistry, using continuous suture in 471 cases of radical retropubic prostatectomy, there were no cases of rupture of vesicourethral anastomosis. It is interesting to emphasize that in 6 patients with short urethras that were too much embedded into the urogenital diaphragm, in addition to such adverse

pelvic anatomy, it was impossible to perform the vesicourethral continuous suture (1.2%; 6 in 477 consecutive RRP). Of these patients, 2 presented rupture of anastomosis during immediate post-operative, as a consequence of replacement of Foley catheter by nursing. These 2 patients were immediately reoperated, and it was verified that the Foley catheters balloons had been insufflated in the anastomosis area, tearing it completely. We performed a new vesicourethral anastomosis with 6 separate stitches. The Foley catheter was maintained for 4 weeks and the patients were continent after 6 months.

We believe that continuous suture of vesicourethral anastomosis enables the safe removal of the Foley catheter on 3rd or 4th post-operative day, and additionally can prevent the rupture of vesicourethral anastomosis.

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## CLODRONATE FOR TREATMENT OF BONE METASTASES IN HORMONE REFRACTORY PROSTATE CANCER

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### ABSTRACT

**Introduction:** Approximately 85% of patients who die from prostate cancer have bone metastases. Even though the radiological aspect of such metastases is osteoblastic, we currently know that these lesions are mixed, with coexisting blastic and lytic lesions, always beginning with bone lysis by osteoclast proliferation. Treatment options are palliative and have poor response, and when there is an improvement it is usually short-lived. This work intends to study the effect of clodronate in the treatment of skeletal complications of prostate cancer.

**Materials and Methods:** In an open prospective study 32 patients with hormone refractory prostate cancer with metastases to bones were assessed, in the period between November 2000 and September 2002. Mean age was 69 years (51 to 83 years). Patients were previously assessed by a pain scale and Karnofsky index. They underwent bone scintigraphy, X-ray, dosage of prostate specific antigen (PSA) and biochemical tests before and following treatment (administration of intravenous clodronate every 28 days). The Student's t-test was used for statistical analysis.

**Results:** Twenty-nine patients (90.6%) showed improvement after the first and the 2nd cycles, which persisted for at least 4 months. Average on the pain scale improved from 7.7 to 2.1 and Karnofsky index raised from 42 to 71. Radiological aspect of the metastases improved in 15 patients (46.8%) and side effects were low (only 2 patients - 6.2%).

**Conclusion:** Bisphosphonate was effective in the treatment of skeletal complications of prostate cancer, presenting an objective response in 90.6% of treated patients, with a marked improvement in the pain scale, Karnofsky index and consequently in the quality of life of patients, and with low side effects.

**Key words:** prostatic neoplasms; neoplasm metastasis; bone; bisphosphonates; palliative treatment  
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### INTRODUCTION

The incidence of prostate adenocarcinoma has increased greatly in the last decade and, currently it is the most common type of non-cutaneous cancer found in men over 50 years old. During the year of 2002, approximately 210,000 new cases were diagnosed in the USA. Currently, at the time of diagnosis, even with all efforts for an early detection, 20%

of patients present bone metastases already. Considering that about 30% of patients who receive treatment for localized prostate cancer presented a relapse, the number of patients with advanced disease is high. Most of such patients who are under hormone treatment become resistant to the hormone between 18 and 36 months after the therapy initiation and 85% to 95% of these patients will present bone metastases and their complications (such as pain, fractures and

plegias) (1-3). The patient who presents already bone metastases has an average survival of 2 years, which is a very long time, considering that he will suffer with skeletal complications (2-4).

The majority of bone metastases of prostate cancer are visualized on plain radiography as osteoblastic lesions, however they always begin as lytic lesions with osteolysis caused by the tumorous prostatic cells that interrupt normal bone remodeling through irregular stimulation of osteoclasts and osteoblasts. Following the lytic lesion, there is an excessive deposit of lamellar bone in the lacunae, forming the osteoblastic aspect. This mechanism results in osteosclerosis, increasing bone volume and destroying the normal bone (5-7).

Bisphosphonates have been widely employed in bone metastases caused by breast cancer and multiple myeloma with excellent results. It is a potent inhibitor of bone reabsorption, both normal and pathologic, exerting a depressant effect on mature osteoclasts and inhibiting the stimulation of osteoblasts, thus decreasing skeletal complications (6).

The objective of the present study is to evaluate clinically the effect of bisphosphonate clodronate in patients with bone metastases due to hormone refractory prostate adenocarcinoma.

## MATERIALS AND METHODS

Between November 2000 and September 2002, 32 patients with bone pain due to metastasis from hormone refractory prostate adenocarcinoma were evaluated, and treated with clodronate in an open prospective study.

Mean age was 69 years (51 to 83). Among those, 9 had undergone orchiectomy, 11 were using cyproterone acetate, 6 used LH-RH analogs, 2 used bicalutamide, and 4 patients were using estrogens. Patients were considered hormone-refractory after 3 consecutive increases of PSA during hormone therapy. In 8 patients mitoxantrone and corticoids were administered, 5 patients received estramustine phosphate, 4 patients used ketoconazole with corticoids and 3 patients used PC-SPES. These medications were suspended when clinical or biochemical response ceased.

Before administration of first clodronate dose, patients underwent a skeletal mapping for recording the quantity and location of metastases, and every point with hypercaptation highly suggestive of metastases was radiographed.

All patients answered to a visual pain scale from 0 to 10 (no pain, to very strong pain), and general conditions were assessed by Karnofsky index. Analgesics were taken as necessary, and these patients were contacted every 14 days (office visits or telephone calls). Those who showed no improvement after the second cycle received adjuvant treatments (radiotherapy, chemotherapy or samarium).

After 4 months of treatment the patients underwent a new bone scintigraphy for comparison with the initial one. Radiographs of metastases locations were also taken. Monthly, determination of PSA, phosphatases, calcium, creatinine, transaminases, and hemogram with erythrocyte sedimentation rate were made.

Clodronate was administered intravenously every 28 days at a dosage of 1,500 mg (5 vials of 300 mg diluted in 500 ml of saline solution, infused in 2 h). The procedure was done at an outpatient basis without requiring admission to hospital. Following the infusion, the patient was released for his normal activities.

For parametric and non-parametric statistical analysis of variations in the pain scale and in the Karnofsky index, the Student's t-test was used for comparing data before and during treatment.

## RESULTS

According to the visual pain scale, 29 patients (90.6%) showed improvement, with 27 (84.3%) having a score equal or superior to 5 (Table-1).

A total of 29 patients (90.6%), responded to treatment with bisphosphonate. Radiologically, an improvement in metastases was observed after the first 6 months in 15 patients (46.8%), Table-2.

The average value on the visual pain scale before treatment was 7.7, and after treatment it decreased to 2.1. Of the 32 treated patients, 29 (90.63%) responded to treatment with bisphosphonate and the Karnofsky index improved from 42 (range 32 to 58) to 71 (range 50 to 82), Table-3.

**Table 1** - Improvement in pain according to visual scale after 2 cycles of bisphosphonate.

Pain Scale Level Following Clodronate	Patients	%
< 5	27	84.38
≥ 5	2	6.25
Without improvement	3	9.37
Total with improvement	29	90.63

**Table 2** - Improvement in radiological image after treatment with bisphosphonate.

Type	Nº	%
Osteoblastic	12	48
Osteolytic	3	42.8
Total	15	46.8

Side effects were minimal, with findings of epigastralgia and excessive salivation in 1 patient, and superficial phlebitis in left upper limb in another (Table-4).

## DISCUSSION

It is known those bone metastases are the most frequent ones in advanced prostate cancer. It is known that approximately 85% of patients who die with prostate adenocarcinoma have skeletal lesions and complications such as pain, pathological fractures or spinal compression (4).

Based on clinical and experimental studies, one can conclude that bone metastasis both in prostate and in breast cancer have a similar behavior, and in the latter bisphosphonates are widely employed as an adjuvant treatment with excellent results (7). Recently a double-blind study was published, involving 1,069 patients with breast cancer where it was concluded that the use of bisphosphonate clodronate had a significant influence on the increase of survival (8).

Recent researches demonstrated that in the physiology of bone metastasis, either in multiple myeloma, or in prostate or breast cancer, the key to the lesion's initiation is an increase in osteoclastic activity promoting a bone lysis. Subsequently an excessive and disordered deposit of sclerotic bone will occur due to the increase in osteoblasts activity (osteoblastosis). In the case of prostate cancer, such deposit is what most often confers the radiological aspect of an osteoblastic lesion (6).

Cancerous prostatic cell detach from prostate, reach blood circulation and are attracted to bone by local and distant chemotactic factors such as metalloproteinases. Among the main local factors are growth factors and cell-cell and cell-matrix interactions, favoring thus the installation and growth of metastasis in the bone (6,9-12). The release of paracrine factors that promote the initial bone absorption is triggered by osteoclasts activation, initiating the lytic lesion. The most important factors are: interleukin 1, 6 and 11;  $\alpha$  and  $\beta$  tumor necrosis factor, epidermal growth factor, parathormone-related peptide, prostaglandins and procatepsin D. Factors that promote the increase of osteoblastic activity are released subsequently, which will allow the excessive bone deposit over the initial lytic lesion. Among the most important are the fibroblastic growth factor,

**Table 3** - Summary of patients who underwent treatment with bisphosphonate.

Parameters	Patients	Before Treatment	After Treatment
Average of pain scale score (0-10)	32	7.7	2.1
No. of patients who had a response	3	-	29
Average of Karnofsky index	32	42 (32% a 58%)	71 (50% a 82%)



**Table 4 - Side effects.**

Type	Patients	%
Slight digestive disorders	1	3.1
Superficial phlebitis	1	3.1
Total	2	6.2

bone morphogenetic protein and insulin-like growth factor (6,9-11,13).

Bisphosphonates cause a decrease in osteoclasts activity, inhibiting bone lysis, and act also on osteoblasts preventing the hyperactivity of these cells (osteoblastosis) that culminates with excessive bone formation. A direct action over the tumor was also described, inhibiting angiogenesis and promoting the apoptosis of cancerous cells, in addition to inhibiting metalloproteases and cytokines (1,7-9,13).

According to their molecular mechanism of action, bisphosphonates are divided in 2 large groups: amino bisphosphonates (NBPs) and non-amino bisphosphonates (non-NBPs). Differently from non-NBPs (clodronate and ethidronate), NBPs (pamidronate, ibandronate, alendronate and zoledronate) do not have a nitrogen atom in their formulation, what confers a different mechanism of action as for the molecular aspect. While NBPs act intracellularly, inhibiting the mevalonate cycle, non-NBPs act by promoting a direct toxicity over osteoclasts and osteoblasts inducing the apoptosis and inhibiting the ATP/ADP translocase enzyme (9,15,16). The differences between the 2 groups' mechanism of action determine differences in their effects, such as for instance, their activity over the inflammatory process. Non-NBPs such as clodronate have anti-inflammatory action and anti-rheumatic activity that occur with NBPs (16).

Pre-clinical studies demonstrate that osteolytic lesions always precede the abnormal bone deposit (osteoblastosis), what confer the osteoblastic aspect to the majority of metastatic skeletal lesions of prostate cancer (6). It was shown through biopsies of metastatic skeletal lesions that excessive bone reabsorption occurs at these sites, similarly to breast cancer (6,7,13). The rational for using

bisphosphonates in prostate cancer comes from studies that demonstrated their beneficial effects in inhibiting the invasion of prostate cancerous cells as well as their adherence and lysis of bone matrix. Another advantage of clodronate over other bisphosphonates is the possibility of using it orally, since its absorption and effects have been already demonstrated in clinical use (13).

As we have seen, bisphosphonates are used in breast cancer and multiple myeloma since the early 80s with excellent results, however only in the beginning of the 90s the first studies with bisphosphonates in prostate cancer have appeared (9,15). The first study with bisphosphonate in prostate cancer was conducted with clodronate by Adami et al. in 1985 (17), who treated 17 patients with osteoblastic metastasis by administering 300 mg of daily intravenous clodronate during 14 days and 3,200 mg orally during the other 4 to 11 weeks. Significant improvement was observed in pain and in Karnofsky index in 16 patients (94.1%) for 4 to 8 weeks.

In another study, Verreuther (13) administered to 41 patients with skeletal lesions due to prostate cancer, intravenous clodronate in a dosage of 300 mg daily for 8 days, along with 1,600 mg orally. Twenty patients (71%) presented a significant improvement in pain as soon as in the first 3 to 5 days and 9 remained asymptomatic.

Heidenreich et al. (2001) treated 85 patients with skeletal complications due to metastatic prostate cancer with 300 mg of daily intravenous clodronate for 8 days, and 1,600 mg daily by oral route for maintenance. They presented a response with an important decrease in pain in 64 patients (75%) and 19 (22%) became asymptomatic, with improvement in Karnofsky index from 45% to 70% (18).

These studies corroborate our results. As well as in the paper by Adami et al. (17) more than 90% of our patients had a significant improvement in pain, with 27 of 32 patients staying below 5 (0 – 10) in the pain visual scale score and improvement in Karnofsky index from 42% (range 32% to 55%) to 71% (range 50% to 82%), following treatment with clodronate. In our study we used intravenous clodronate in bolus, at the posology of 1,500 mg (5 vials containing



300 mg) diluted in 500 ml of saline solution applied during 2 h every 28 days, and performed at an outpatient basis.

Side effects were observed in only 6.2% of cases, and those were diarrhea and epigastralgia in one patient and superficial phlebitis in another, what is close to Verreuther's results (13) and is lower than the complication reported by Heidenreich et al. that is 17% (18). Maybe this fact has occurred due to the association with oral clodronate used by these authors for maintenance of treatment and that can lead to slight digestive disorders.

Following administration, 70 to 80% of the active substance is cleared by urine in up to 24 h. Clodronate's advantage relative to other bisphosphonates is the possibility of using it orally. Smith (19) used oral ethidronate and did not observe patients' improvement in relation to the placebo group, because this medication had a very low absorption by this route, becoming ineffective and failing to produce the desired effect.

Among our patients, 25 (78.12%) had osteoblastic and 7 (21.8%) osteolytic bone metastasis. Both types responded well to treatment with clodronate. Pelvic bones were the most affected by single metastasis, and associated lesions were the predominant (50%). In 15 patients (46.8%) there was improvement and even disappearance of lesions in radiological studies. This effect can be explained by the direct action that clodronate exerts over the metastatic tumorous cell (induction of apoptosis, inhibition of angiogenesis and cytostatic effect) (8,9,14).

In conclusion, one can verify that clodronate is an effective drug for palliative treatment of bone complications caused by hormone refractory prostate cancer, with prompt effects on pain, few side effects and a significant improvement in the quality of life.

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## ESTIMATED COSTS OF TREATMENT OF BENIGN PROSTATE HYPERPLASIA IN BRAZIL

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### ABSTRACT

**Introduction:** The treatment of benign prostate hyperplasia (BPH) presents 2 options: medical or surgical, and there are doubts about what is the best treatment since 80% of patients who undergo surgery become asymptomatic and 10 to 40% of those under medical regimen undergo surgery within a 5 years period. It is difficult to assess the actual costs of treating BPH in Brazil due to several factors, among them regional particularities and the scarcity of current statistical data.

**Patients and Methods:** Recently, in the Ribeirão Preto area, São Paulo, Brazil, the IPSS (International Prostatic Symptoms Score) and quality of life were verified in 934 volunteers. It was determined the percentage of individuals with ages ranging from 40 to 79 years with moderate symptoms (score 8-19) and with severe symptoms (score 20-35), values for which are indicated medical and surgical treatment, respectively, according to the Brazilian Society of Urology consensus on BPH. Data on Brazilian population in that age range were obtained from the Brazilian Institute of Geography and Statistics referent to the year of 2000. It was determined the number of patients, according to the criteria above, subjected to either one of the treatments mentioned. Surgical costs of prostate transurethral resection were researched according to Unified Health System - SUS tables (US\$ 173) and of Brazilian Medical Society - AMB with a mean cost in 3 hospitals of US\$ 933. Drug costs were calculated by the annual mean price (US\$ 355) of 4 alpha-blockers (tamsulosin, alfuzosin, doxazosin and terazosin).

**Results:** The estimated population for medical treatment was 5,397,321 individuals, with a cost corresponding to US\$ 1,916,489,055.00. The estimated population for surgical treatment was 2,040,299 men, what would represent a cost of US\$ 353,291,204.00 based on the SUS table and of US\$ 1,904,279,066.00 based on AMB with hospital expenses included.

**Conclusion:** All these facts induce us to predict that the treatment of BPH in a not-so-far future can become a public health problem for Brazilian society, since the current estimate would be, approximately, costs around 2.26 – 3.83 billion dollars, added by the yearly increase in the risk population (24.99%) for the group under medical treatment and over the non-operated amount of the surgical group.

**Key words:** prostate; prostatic hyperplasia; drug therapy; surgery; treatment costs  
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### INTRODUCTION

Benign prostate hyperplasia (BPH) is very frequent in men and its prevalence increases with age, reaching figures of 85% to 90% in the age range above

80 years (1). The intensity lower urinary tract symptoms fluctuates with time and may no be consequent to BPH (2). This fact makes the identification of defined criteria difficult for indicating treatment, since about 80% of patients subjected to surgery become

asymptomatic (3). Brazilian consensus tried to define some parameters for guidance when indicating any type of treatment for BPH based in IPSS score. Thus, observation was recommended for cases with scores lower than 8. For patients with values between 8 and 19 pharmacological treatment would be indicated, and above these levels (20 to 35) the option would be surgical (4). In the United States of America, transurethral resection of the prostate (TURP) is the second most performed surgical procedure, with an estimated cost between 2 to 3 billion dollars per year. As for costs with pharmacological treatment during a 5-year period, it is expected to range between US\$ 1,800.00 and US\$ 3,150.00 dollars/patient (5). The purpose of the present work was to estimate, with data from the Brazilian population, which would be the cost of BPH treatment.

## MATERIALS AND METHODS

In 1997 it was made a screening for early diagnosis of prostate cancer, where 1,106 volunteers

were examined. The IPSS and quality of life were verified in all patients. To assess the participation of patients only with BPH, patients presenting cancer, intraepithelial neoplasia or those who refused biopsies when indicated were excluded, with 934 volunteers remaining for study. The results from this assessment allowed the creation of a table referent to frequency and distribution of lower urinary tract symptoms and signs in age ranges between 40 years and 79 years (Table-1), as well as score classification according to what was determined by the National consensus on BPH (6) (Table-2). The number of men pertaining to each age range existing in Brazil was obtained from the national census of 2000, conducted by the Brazilian Institute of Geography and Statistics (IBGE) (7) (Table-3). Having the frequency percentages of IPSS in several ranges of population under study, the total of risk population in each range and the criteria for indicating the type of treatment, the estimated number of individuals subjected to pharmacological and surgical treatments was obtained. The mean annual cost (September/2002) of drug treat-

**Table 1** – Frequency of lower urinary tract symptoms according to age range in years.

Age Range	IVE		P		H		U		WFR		VE		N	
	f	%	f	%	f	%	f	%	f	%	f	%	f	%
40 – 49	72	28.1	107	41.8	62	24.2	46	14.1	85	33.2	57	22.3	159	62.1
50 – 59	99	28.9	152	44.3	103	30.0	57	16.6	118	34.4	78	22.7	244	71.1
60 – 69	101	39.1	132	52.2	98	38.7	80	31.6	137	54.2	71	28.1	200	79.1
70 – 79	38	46.3	44	53.7	37	45.1	41	50.0	79	59.8	29	35.4	73	89.0

IVV – feeling of incomplete vesical emptying; P – pollakiuria; H – hesitation; U – voiding urgency; WFR – weak flow rate; VE – voiding effort; N – nycturia; f – frequency.

**Table 2** – Intensity of lower urinary tract symptoms score according to age range in years.

Age Range	Score 0 – 7		Score 8 – 19		Score 20 – 35	
	f	%	f	%	f	%
40 – 49	182	71.0	53	20.7	21	8.3
50 – 59	233	67.9	81	23.6	29	8.5
60 – 69	131	57.1	86	34.0	36	8.9
70 – 79	34	41.4	31	37.8	17	20.8

f – frequency.

## COSTS OF BPH TREATMENT

**Table 3** – Population of Brazilian men, divided by age range in years.

Age Range	Number of Men
40 – 49	9,332,857
50 – 59	6,000,922
60 – 69	3,792,534
70 – 79	2,009,900
<b>Total</b>	<b>21,136,213</b>

ment, based on prices of alpha-blockers (tamsulosin, alfuzosin, doxazosin and terazosin) in minimal dosages prescribed, was calculated in US\$ 355 per patient. The surgical cost of TURP as per SUS table was budgeted in US\$ 173 per patient and as per AMB table in US\$ 933 per patient including hospital expenses.

From this data, the costs of drug and surgical treatments were calculated for each age range, thus obtaining the estimated total value (Table-6).

## RESULTS

Population subjected to medical treatment with IPSS of 8 to 19, according to the age range is presented in Table-4. The value obtained for medical treatment of the estimated risk population, was determined from calculation: 5,397,321 (patients) x US\$ 355.00 = US\$ 1,916,489,055.00.

As for surgical treatment the estimated risk population is presented in Table-5. The value obtained for surgical treatment of estimated risk population, based on the SUS table, was determined from calculation: 2,040,299 (patients) x US\$ 173.00 = US\$ 353,291,204.00. Estimated cost for surgical treatment based on AMB table's values was obtained from calculation: 2,040,299 x US\$ 933.00 = US\$ 1,904,279,066.00.

Total values found for treatment of BPH in Brazil are presented in Table-6 and represent the sum of medical and surgical treatments.

**Table 4** – Estimated risk population subjected to medical treatment, according to age range in years.

Age Range	Detected Population	Risk Percentage	Estimated Population
40 – 49	9,332,857	20.7%	1,931,901
50 – 59	6,000,922	23.6%	1,416,217
60 – 69	3,792,534	34.0%	1,289,461
70 – 79	2,099,900	37.8%	759,742
<b>Total</b>			<b>5,397,321</b>

**Table 5** – Estimated risk population subjected to surgical treatment, according to age range in years.

Age Range	Detected Population	Risk Percentage	Estimated Population
40 – 49	9,332,857	8.3%	774,627
50 – 59	6,000,922	8.5%	510,078
60 – 69	3,792,534	8.9%	337,535
70 – 79	2,099,900	20.8%	418,059
<b>Total</b>			<b>2,040,299</b>

**Table 6** – Total annual estimate costs needed for treatment of BPH in Brazil in 2002.

Medical Treatment	Surgical Treatment (SUS)	Surgical Treatment (AMB)
US\$ 1,916,489,055.00	US\$ 353,291,204.00	US\$ 1,904,279,066.00

SUS – Unified Health System; AMB – Brazilian Medical Association



## DISCUSSION

In 1999 it was presented a work concerning the estimated costs of BPH treatment in Brazil. At the time, the estimated population for calculation was obtained through IBGE data from 1996. We were impressed by the values determined, especially in reference to costs of medical treatment. Four years later we decided to reassess those numbers to get an idea about their evolution. There was a significant increase in risk population both for medical treatment (52.4%) and for surgical treatment (118.7%). Such data show that Brazilian population is growing older, with a significant increase in risk population for BPH treatment. Associated with the population growth is the increase in the procedure costs. Drugs cost has raised about 21.02%. SUS added about 69.19% to TURP package, noting the addition of anesthetist's medical fees, which were separated from the package. AMB table plus hospital expenses suffered an increase of 26.6% for TURP. The sum of these factors has promoted an increased in the costs of annual medical treatment for the risk population total of US\$ 877,292,155.00, that is, 84.5%. On the other hand, annual SUS cost to finance surgical treatment of risk population has increased about US\$ 258,360,324.00, which means an addition of 270.2%. As for TURP costs according to AMB table for medical fees plus hospital costs, it was calculated an addition of US\$ 1,216,702,071.00, which represents an increase of 176.9%.

This work's intention is not discuss if such increases could represent substantial gains to urologists or not, but to analyze the necessary amount to be spent by the community in order to finance BPH treatment. Obviously, these costs can present variations with time due to the annual percentage increase in risk population, which were calculated in 24.99% for both groups. For the medical group this percentage is added yearly. However for the surgical group this percentage falls over the non-operated amount.

Another interesting fact is that the total resources spent with medical treatment are really significant, showing that the urologist must be moderate in his/her indications so that he/she will not burden society too much.

All these facts induce us to foresee that the treatment of BPH in a not-so-far future can become a public health problem for Brazilian society, since the current estimate would be of costs around 2.26 to 3.83 billion dollars, added by the yearly increase in the risk population (24.99%) for the group under medical treatment and over the non-operated amount of the surgical group.

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## SURGICAL TREATMENT OF METACHRONOUS METASTASES IN DIFFERENT ORGANS FOLLOWING RADICAL NEPHRECTOMY

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### ABSTRACT

Renal clear cell carcinoma (RCCC) is a neoplasia resistant to radio and chemotherapy, with surgical treatment being the procedure that is recognized for its curative treatment. This case report demonstrates the success of an aggressive surgical treatment for consecutive and late metachronous metastases following radical nephrectomy.

Case report: Asymptomatic 50-year old man. During a routine examination, an incidental mass was found by renal ultrasonography. He underwent right radical nephrectomy due to RCCC in June 1992. During the follow-up metastases were evidenced in cerebellum on the seventh year, and in left lung and pancreas on the eighth year following the radical nephrectomy, with all of them successfully treated by surgical excision.

Comments: The surgical excision of consecutive and late metachronous metastases in different organs arising from RCCC is feasible, being a good therapeutic alternative in selected cases.

**Key words:** renal cell carcinoma; metastases; cerebellum; lung; pancreas; surgery

**Int Braz J Urol. 2003; 29: 238-240**

### INTRODUCTION

Renal clear cell carcinoma (RCCC) is a neoplasia resistant to radio and chemotherapy, with surgical ablation being the recognized method for its treatment with curative purposes. Radical nephrectomy is the gold standard for localized disease with tumors larger than 4 cm, with a 5-year survival ranging from 70 to 90% in these cases (1). However, in metastatic disease there are few therapeutic alternatives, such as immunotherapy, with low success rates (2). This report presents a rare case with late and consecutive metachronous metastases of RCCC in different organs, successfully treated by surgical excision.

### CASE REPORT

A male, 50-year old, Caucasian, asymptomatic patient, during routine examination was subjected

to abdominal ultrasonography where an heterogeneous renal mass was found in the superior pole of the right kidney, measuring 7 x 5 cm. An abdominal computerized tomography was performed and detected a tumoral thrombus in the renal vein.

In June 1992, a right radical nephrectomy was performed, and the histopathological examination identified a grade II renal cell carcinoma in the superior pole, measuring 7.5 x 5 cm, with tumoral thrombus in the renal vein. Ipsilateral perirenal fat, capsule and suprarenal were free of neoplasia. Patient evolved post-operatively without intercurrents and was followed in an outpatient basis every 6 months with physical examination, chest RX, and abdominal tomography.

On the seventh year of follow-up, the patient suffered 2 episodes of syncope. A computerized tomography of the cranium was performed and detected a 3 cm tumoral mass in the left side of cerebellum. A

craniotomy was indicated for exeresis of the mass with a histopathology compatible with RCCC.

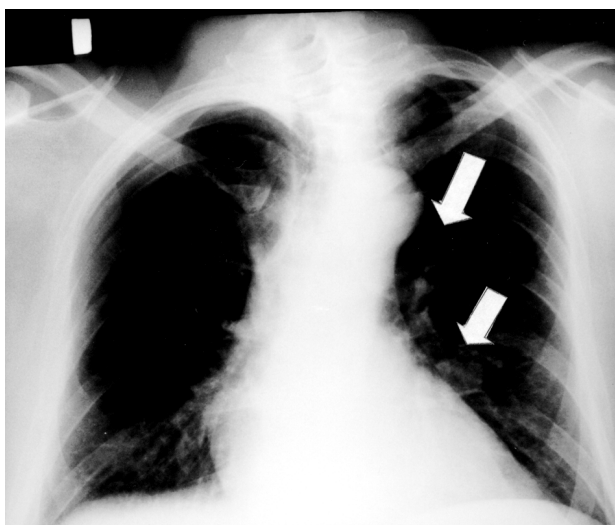
One year after follow-up, 2 nodules of 1 cm were observed in the left lung (Figure-1). Left thoracotomy with wedge resection was indicated, evidencing grade II RCCC, compatible with previous histopathological examinations.

Finally, 6 months following thoracotomy, in an abdominal ultrasound there was the suspicion of a 2 cm hypoechogenic nodule in the body of pancreas. An abdominal computerized tomography was indicated, which confirmed the mass, and during the same procedure a guided puncture was performed that confirmed RCCC (Figure-2). It was then performed a body-tail pancreatectomy and splenectomy.

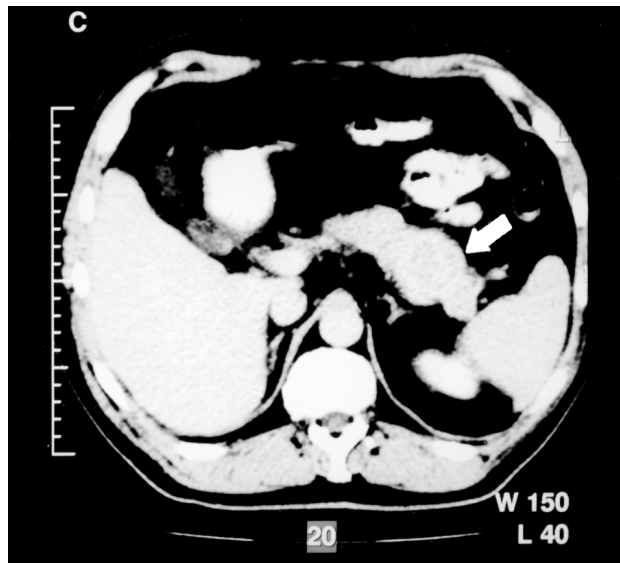
The patient is being followed for 2 years in an outpatient basis without evidences of neoplastic progression, presenting an excellent quality of life.

## COMMENTS

Among the total cases of metastatic diseases due to RCCC, there is a subgroup where the metastatic disease arises as a single lesion in a particular organ following radical nephrectomy, which corresponds to 3 or 4% in large series of patients under



**Figure 1** - Presence of renal clear cell carcinoma metastasis in left lung after the seventh year of follow-up (arrows).



**Figure 2** - Pancreatic metastasis of renal clear cell carcinoma. Note the pancreatic nodule between body and tail of pancreas (arrow).

such conditions. In such cases, the following are considered as good prognostic factors for treatment: 1) otherwise healthy patients, 2) age under 60 years, 3) single metastasis in lung, 4) period between nephrectomy and the occurrence of the lesion longer than 24 months (2,3).

The successful aggressive treatment of consecutive metachronous metastases in different organs is a theme poorly addressed in the literature. Despite the controversial management and the short period of follow-up in this case relative to the exeresis of the last lesion (24 months) the patient presents an excellent outcome. We believe that in young, otherwise healthy patients who present a late recurrence with a single and organ-independent metastasis, the hypothesis of surgical treatment should be considered as a first line option for this selected subgroup.

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## NEPHROBRONCHIAL FISTULA SECONDARY TO XANTOGRANULOMATOUS PYELONEPHRITIS

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### ABSTRACT

**Introduction:** Nephrobronchial fistula is a rare complication of xanthogranulomatous pyelonephritis, a disease that can fistulize to lungs, skin, colon and other organs.

**Case Report:** A 37-year old patient presented a chronic history of lumbar pain and thoracic symptoms such as cough, dyspnea and oral elimination of pus. Patient went to several services and was submitted to 2 thorax surgeries before definitive treatment (nephrectomy) was indicated. After nephrectomy, the patient presented an immediate improvement with weight gain (8 kg / 1 month) and all his symptoms disappeared.

**Conclusion:** This clinical case illustrates the natural history of nephrobronchial fistula, the importance of clinical history for diagnosis and the relevance of early treatment of renal lithiasis.

**Key words:** kidney; xanthogranulomatous pyelonephritis; kidney calculi; urinary fistula; urinary tract infection; bronchial fistula

**Int Braz J Urol. 2003; 29: 241-242**

### INTRODUCTION

Xanthogranulomatous pyelonephritis is caused by chronic presence of stones in the excretory system, which evolves with localized infection, renal destruction and systemic impairment. Fistulization is a rare complication (1-3). There are reports of nephrobronchial (1,2), nephrocutaneous (2), colonic (3), gastric, jejunal fistulas, and also fistulas to psoas muscle, flank and gluteal region.

### CASE REPORT

VSL, 37 years old, Caucasian, without pathological antecedents. Between 1985 and 1993, the patient presented several crises of renal colic and eliminated 20 calculi. From 1994 to January 1999, he presented a continuous pain in right lumbar region and medicated himself with analgesic drugs. Early in

1999, he presented pyuria, 40°C fever, anorexia and renal stones that were treated clinically.

After 3 months, he evolved with dyspnea, being hospitalized several times. In 1999, he sought the General Hospital due to dyspnea, when 1 liter of pus was drained from his right hemithorax and he was subjected to antibiotic therapy.

In July 1999 he presented "pus taste in the mouth", cough and dyspnea. He sought the hospital where thorax was drained and surgically debrided. Fifteen days later, still with a thorax drain, he came back for presenting the initial clinical picture. By the end of July 1999 a right inferior lobectomy was performed, with clinical improvement and release from hospital.

After some months cough returned and there was fistulization with purulent drainage through the right thoracolumbar wall. Output from lumbar fistula decreased progressively as the patient began to expel pus by the mouth until the fistula's closure.



From 2000 to April 2001 patient expelled pus by the mouth in larger amount during periods of cough, physical efforts and mainly when he flexed the abdomen over his thighs. During this period, the patient was assessed by several medical teams. According to him, clinical doctors and urologists thought that the disease was basically renal, but pneumologists disagreed with this hypothesis.

Patient was then seen in General Hospital and, after urologic assessment and right retrograde pyelography (Figure-1), a nephrobronchial fistula was suggested and patient underwent a right nephrectomy with drainage of a subphrenic abscess by mid-2001. He evolved with immediate improvement, ceasing of cough and oral elimination of pus, disappearance of anemia and anorexia, recovering 8 kilograms within 1 month post-operatively. The anatomopathological examination evidenced xanthogranulomatous pyelonephritis.



**Figure 1** – Right retrograde pyelography with an image of subphrenic abscess and nephrobronchial fistula.

## COMMENTS

Nephrobronchial fistula are rare complications of renal lithiasis that usually occur following a long period of disease. Infection by human immunodeficiency virus, association with diabetes and the presence of untreated renal stones are predisposing factors (1-3).

The patient in this report presented untreated renal stone associated with renal colic, renal cavity infection, thoracocutaneous fistulization, cough, dyspnea, and finally purulent expectoration.

Treatment in advanced cases should be nephrectomy with drainage of the abscess and the fistula (3).

This case illustrates the natural history of nephrobronchial fistula, the significance of clinical history for diagnosis and the relevance of early treatment of renal lithiasis.

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**BILATERAL HYDRONEPHROSIS CAUSED BY VAGINAL PROLAPSE**

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*Humanae Vitae Medicine Institute, São Paulo, SP, Brazil***ABSTRACT**

**Introduction:** Even though it is uncommon, uterine prolapse can cause compression of ureters and bilateral hydronephrosis, predisposing to arterial hypertension and renal failure. Hydronephrosis consequent to cystocele and to vaginal prolapse is even rarer.

**Case Report:** This paper reports on a 59 year-old patient, Caucasian, obese and hysterectomized who presented complete vaginal prolapse with bilateral hydronephrosis and slight alteration in serum urea and creatinine. Patient underwent correction of vaginal prolapse by endoscopic suspension technique with improvement of hydronephrosis and normalization of renal function. This work emphasizes the rarity of such case and the requirement of surgical approach.

**Key words:** vagina; vaginal prolapse; hydronephrosis

**Int Braz J Urol. 2003; 29: 243-244**

**INTRODUCTION**

Uterine prolapse can cause dilatation of upper urinary tract due to ureteral obstruction that, if left untreated, can impair renal function leading to anuria and arterial hypertension (1). Bilateral hydronephrosis due to cystocele and, especially, to vaginal prolapse, is very rare.

**CASE REPORT**

E.F.C.B., 59 years old, Caucasian, widowed, was referred to the Urology Service with vaginal prolapse and ultrasonography of urinary tract evidencing bilateral grade II/III hydronephrosis.

As for her antecedents, she reported having 4 pregnancies in the past, with 2 normal deliveries, 1 cesarean and 1 miscarriage. She was hysterectomized by abdominal route 1 year before due to uterine myoma, and on that occasion, a vesical suspension was also performed. She did not present urinary incontinence.

On physical examination, she had a pyknic constitution, was obese and presented a good general

state. Gynecologic examination showed a marked vaginal prolapse throughout its entire extension with excoriations, hyperemia and fissures on the posterior wall of vagina (Figure-1). Laboratory tests showing alteration in urea 67.1 mg % (normal < 40 mg %), creatinine 1.35 mg % (normal < 1.30 mg %) and glycemia 131 mg % (normal < 110 mg %). She did not present urinary infection. The excretory urography confirmed the presence of bilateral hydronephrosis (Figure-2).

Patient underwent an endoscopic colposuspension (3), with good post-operative results within 3 months of follow-up, and improvement of hydronephrosis grade (grade I).

**COMMENTS**

It is estimated that 4 to 7% patients with uterine prolapse have obstructive uropathy. The mechanism most likely is direct compression of ureters (2). In the uterine prolapse, there is herniation of bladder, uterus and ureters through the pelvic floor and the ureters are compressed between the fundus of uterus and the bladder, against the levator ani muscles. In this case,



**Figure 1** – Marked vaginal prolapse throughout its entire extension.

since there was no uterus, we suspect that obstruction had occurred due to ureteral compression against the pelvic musculature, as well as to ureteral stretching itself, what makes peristaltic movements difficult.

Stress urinary incontinence usually is associated to small cystoceles. Large cystoceles, associated or not with uterine prolapse, predispose to obstructive voiding symptoms, chronic residual urine and rarely to bilateral hydronephrosis with potential impairment of renal function. In women presenting dilatation of upper urinary tract one must always rule out, among other causes, uterine or vesical prolapse.

Surgical correction either by suprapubic or vaginal approach, intends to resolve the obstructive urinary picture, even though it is known that it can predispose to stress urinary incontinence. When the uterus is present, hysterectomy and vaginal plastic surgery are performed. When there are contraindications to surgery, the pessary can be indicated in order to reduce the uterine prolapse (1).

In the case found in literature, it was performed the fixation of the vaginal dome in sacral promontory complemented with colpourethropy in Cooper's ligament (2). In the case reported here, despite the patient being pyknic and obese, with 2 previous surgeries in lower abdomen, the use of vaginal suspension with endoscopic control has shown to be a simple and practical procedure.



**Figure 2** – Excretory urography evidencing bilateral hydronephrosis due to vaginal prolapse.

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**INTRAMURAL LEIOMYOMAS OF THE BLADDER IN ASYMPTOMATIC MEN**

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*Women's Beneficent Society, Syrian and Libyan Hospital, São Paulo, SP, Brazil***ABSTRACT**

Bladder leiomyomas are rare benign mesenchymal tumors, which account for less than 0.43% of all bladder tumors with approximately 200 cases described in the literature. These tumors may be classified into 3 different locations: endovesical, intramural and extravesical. Endovesical is the most common form, accounting for 63-86% of the cases, while intramural occurs in 3-7% and extravesical in 11-30%.

The intramural form, especially small tumors, may not produce symptoms hardening detection. We report two cases of intramural bladder leiomyomas in asymptomatic men observed incidentally by transabdominal ultrasonography during the follow-up of benign prostatic hyperplasia.

We discuss the diagnosis and management of these lesions.

**Key words:** leiomyoma; bladder; benign neoplasm

**Int Braz J Urol. 2003; 29: 245-247**

**INTRODUCTION**

Bladder leiomyomas are rare benign mesenchymal tumors that account for less than 0.43% of all bladder tumors (1). Approximately 200 cases have been described in the literature (1).

**CASE REPORTS**

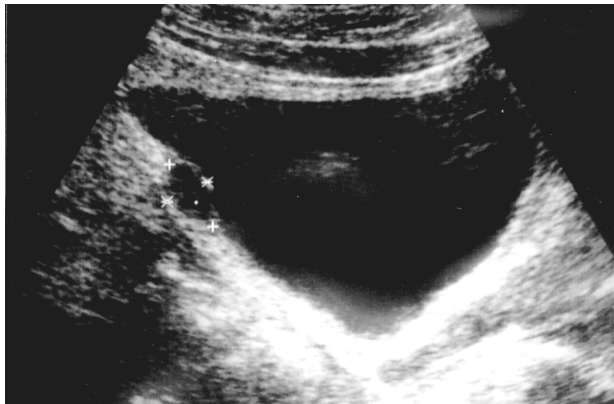
Case 1 - 59 year-old man with a 3-year history of benign prostatic hyperplasia without clinical manifestations. During follow-up, a pelvic ultrasonography demonstrated a well-circumscribed hypoechoic mass at the postero-superior bladder wall measuring 1.74 x 1 cm (Figure-1). Cystoscopy demonstrated a lesion covered with normal bladder mucosa. A transurethral resection was performed and the pathologic examination revealed a leiomyoma. No recurrence was observed after 10 months.

Case 2 - A 59 year-old asymptomatic man had been accompanied for benign prostatic hyperplasia for 9 years. Transabdominal ultrasonography revealed a 2.8 x 2.2 x 1.8 cm well-circumscribed hypoechoic mass at the antero-superior bladder wall thought to be an urachal cyst, due to its midline location. Computed tomography scan showed bilateral renal cysts and a lesion at the bladder apex (Figure-2). Open segmental resection was performed for the latter and pathologic examination revealed leiomyoma. There has been no evidence of recurrence after 10 months.

**COMMENTS**

Bladder leiomyomas have been reported to occur equally in both men and women (2). However, more recently a review demonstrated predominance in women (3), which may be attributed to the in-





**Figure 1** – Ultrasonography (longitudinal scan) demonstrating the bladder tumor (intramural leiomyoma).

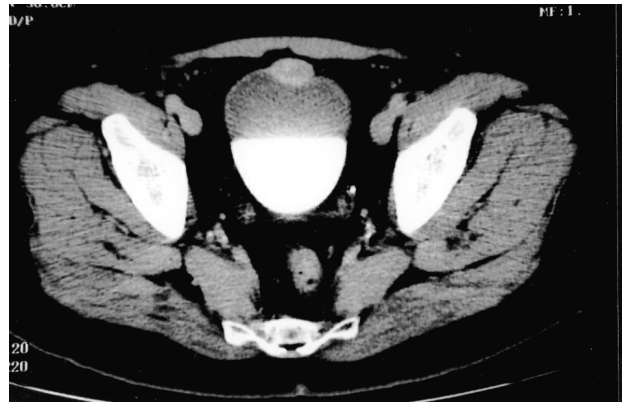
creased use of pelvic ultrasonography in female patients (1). In our 2 cases, pelvic ultrasonography performed during follow-up of benign prostatic hyperplasia led to incidental diagnosis of bladder leiomyomas, suggesting that the reported predominance of these tumors in women is questionable.

These tumors may be classified into 3 different locations: endovesical, intramural and extravesical. Endovesical is the most common form, corresponding to 63-86% of the cases, while intramural occurs in 3-7%, and extravesical in 11-30% (2,3). Based on cystoscopic findings, an intramural leiomyoma can be distinguished from an endovesical tumor. Endovesical tumors are usually pedunculated or polypoid, while intramural myomas are usually well encapsulated and surrounded by bladder wall muscle.

The endovesical form usually causes irritative or obstructive symptoms and gross hematuria (2) that result in detection (1). Intramural form, especially small tumors, may not produce symptoms.

Radiologically, leiomyomas appear as well-circumscribed hypoechoic masses at ultrasonography and as in case 2, these tumors may be misinterpreted as other bladder lesions such as an urachal cyst when observed in a bladder midline position. To rule out other benign lesions and, especially, bladder cancer, the tumor should be biopsed.

Intramural tumors may be managed according to their size and location. Small easily accessible tumors may be treated with transurethral resection, while unfavorable positioning and recognition difficulties may require segmental resection as in case 2.



**Figure 2** – Computed tomography demonstrating a midline intramural leiomyoma at the bladder dome.

Management of unfavorable lesions comprises open segmental resection or laparoscopic partial cystectomy.

Histopathologically, leiomyoma of the bladder is composed of fascicles of smooth muscle fibers separated by connective tissue. The etiology of these tumors remains unknown. It is proposed that bladder leiomyomas may arise from chromosome abnormalities (1), hormonal influences, bladder musculature infection, perivascular inflammation or dysontogenesis (3).

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## EDITORIAL COMMENT

Leiomyomas of the bladder is distinctly unusual as the author's report. They provide a concise case report of 2 men who were discovered to have this unusual lesion of the bladder.

They provide a wide range of incidences for the 3 locations for a leiomyoma of the bladder. It would seem that given the paucity of this tumor, that it would be difficult to indicate other than the most common location, is what they term endovesicle. I am not even certain what they mean by endovesicle and how they differentiate this from intramural with any precision.

It would seem that an important part of this manuscript, which is overlooked, is whether one can make the diagnosis based upon radiographic configuration and avoid any surgery. The authors do not provide this as an option and simply state that there are several ways of removing these tumors. Since this is a benign neoplasm and if there are no signs or symptoms, one would wonder why it would be necessary to remove the lesion. For instance, if a percutaneous biopsy was performed and the diagnosis was a benign leiomyoma, would it be necessary to proceed with any further surgery, such as removal?

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## REPLY BY THE AUTHORS

The term endovesical refers to the submucosal growth of leiomyoma, first described by Campbell & Gislason (1). The endovesical (submucosal) tumors are usually pedunculated or polypoid, while intramural leiomyomas are surrounded by the musculature of the bladder wall (as in these 2 cases reported) and are usually well encapsulated. Distinction between these 2 types is based on cystoscopic findings.

To rule out other benign lesions, and, especially, bladder cancer that may have the same radiologic appearance of an intramural leiomyoma, the tumor should be biopsed. Since bladder leiomyomas are rare tumors, there is no trial comparing tumor observation and surgery for the management of these lesions.

***The Authors***

## MAGNETIC RESONANCE IN DIAGNOSIS OF URETEROCELE

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### ABSTRACT

Ultrasonography is the main non-invasive technique for screening of ureterocele, but presents some difficulties for its diagnosis. Other supplementary diagnostic methods have the disadvantage of being invasive or using ionizing radiation. Magnetic resonance (MR) has a high sensitivity for diagnosing urinary tract malformations in adults and children. We report one case of ureterocele in a 1-year old child with the purpose of presenting its diagnosis through MR

**Key words:** ureter; infant; ureterocele; diagnosis; magnetic resonance  
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### INTRODUCTION

The study of urinary tract anatomy and pathology in pediatric patients can be obtained by a number of imaging methods. Ultrasonography represents the main screening technique, but rarely it enables an accurate analysis of the entire urinary tract. Other diagnostic methods such as voiding urethrocytography, excretory urography, computerized tomography, ascending pyelography, cystoscopy and renal scintigraphy complement the diagnosis, but have the disadvantage of exposing the patient to invasive procedures or to ionizing radiation. Uro-resonance has a high sensibility for the diagnosis of urinary tract malformations in adults and children (1), and can be performed by 2 distinct techniques: one that uses images of the body's static fluids (the technique employed in this case) and the other using a paramagnetic contrast medium associated with a diuretic. The technique that employs paramagnetic contrast and diuretic, do not require the dilatation of the excretory system, presenting a better contrast in image and a higher sensitivity.

### CASE REPORT

We studied a female, 1-year old patient, with a clinical history of recurrent urinary tract infection since birth. Ultrasonography evidenced severe bilateral pyelocaliceal dilatation and left pyelocaliceal duplication, with an image inside the bladder suggesting ureterocele. Voiding urethrocytography demonstrated absence of vesicoureteral reflux, excretory urography showed functional exclusion of the right kidney, and scintigraphy with DMSA showed 9% of function on the right side. The diagnosis of left ureterocele was confirmed by uro-resonance (Figure-1). An endoscopic puncture of the ureterocele was performed without intercurrents and the child evolved with clearing of the ipsilateral renal unit.

### COMMENTS

Ultrasonography is a good examination for viewing pyelocaliceal duplicity; however, it is limited for a complete study of the ureter. In the dilated urinary tract, the ureterovesical junction can be eas-

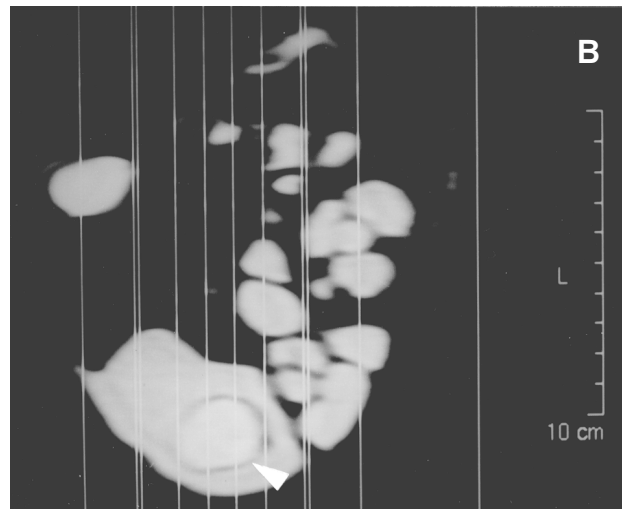


**Figure 1 A** – Weighted image in T2, in frontal plane, showing pyeloureteral duplication and ureterocele (arrow).

ily localized by ultrasound, but it is impaired in ectopic or slightly dilated ureters. Computerized tomography can be employed as an alternative diagnostic technical modality; however, the exposure to high doses of radiation restricts its use in pediatrics (2).

Uro-resonance can be employed in cases of dilated ureters and functional exclusion, because it provides an adequate visualization of the entire urinary tract. It defines the morphology and the thickness of the renal parenchyma, and additionally it provides an indirect analysis of renal function concerning urinary excretion. It is a rapid technique, which contributes substantially to the diagnosis of ureterocele, since its performance does not depend on the patient's respiratory rate and offers images with high definition and quality.

Recently, the utilization of uro-resonance in the prenatal diagnosis of ureterocele has significantly



**Figure 1 B** – Weighted image in T2, in frontal plane. The illustrative arrow shows a rounded image with regular contours, in the interior of bladder, corresponding to ureterocele.

decreased morbidity, potential lesions due to repeated urinary infections, and the need of secondary surgical interventions (3). Magnetic resonance can be an alternative in relation to conventional diagnostic techniques, since it does not expose the patient to ionizing radiation or the use of an iodinated intravenous contrast medium.

Uro-resonance images are acquired in weighted sequences in T2, in frontal (coronal) or sagittal sections, presenting very prolonged echo time and repetition time, promoting an adequate analysis of the urinary tract's morphology. Uro-resonance weighted in T2 can be performed with administration of furosemide before the examination, but the identification of urinary tract can be impaired if those are not dilated. Adding a paramagnetic contrast medium (gadolinium), favors the adequate study of kidneys and urinary tract, even in the absence of dilatation, promoting a more sensitive and more specific diagnosis.

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## TRANSURETHRAL MICROWAVE THERMOTHERAPY FOR BENIGN PROSTATIC HYPERPLASIA

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### ABSTRACT

Transurethral resection of the prostate (TURP) remains the gold standard for treatment of benign prostatic hyperplasia (BPH). In general, while this procedure is safe, patients require a spinal, epidural, or general anesthesia and often several days of hospital stay; the potential morbidity and mortality limits the use of TURP in high-risk patients. Pharmacotherapy has been recommended as a first-line therapy for all patients with mild to moderate symptoms. Patients are oftentimes enthusiastic if they are offered a one-time method to treat lower urinary tract symptoms secondary to BPH, provided that the method offers reduced risk and allows an efficacy equal to that of medical therapy. One such method is transurethral microwave thermotherapy (TUMT). TUMT involves the insertion of a specially designed urinary catheter with a microwave antenna, which heats the prostate and destroys hyperplastic prostate tissue. TUMT allows the avoidance of general or regional anesthesia, and results in minimal blood loss and fluid absorption. In this review, the authors discussed the current indications and outcome of TUMT, including the history of the procedure, the mechanism of action, the indications for TUMT, the pre-operative considerations, the patient selection, the results in terms of efficacy, by comparing TUMT vs. Sham, TUMT vs. Alpha-blocker and TUMT vs. TURP. Finally, the complications are presented, as well as other uses and future directions of the procedure. The authors concluded that TUMT is a safe and effective minimally invasive alternative to treatment of symptomatic BPH.

**Key words:** prostate; prostatic hyperplasia; transurethral microwave thermotherapy; transurethral resection of prostate

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### INTRODUCTION

Transurethral resection of the prostate (TURP) remains the gold standard for treatment of benign prostatic hyperplasia (BPH). In general, while this procedure is safe, patients require a spinal, epidural, or general anesthesia and often several days of hospital stay; the potential morbidity and mortality limits the use of TURP in high-risk patients. Pharmacotherapy has been recommended as a first-line therapy for all patients with mild to moderate symptoms. Unfortunately, long-term outcomes are not fully elucidated, patients must adhere to a strict medication schedule, and outcome indicators are not reached as well or as reliably as TURP. Despite these

inadequacies, patients choose medications over surgery because of the perceived reduced risk of adverse events and the desire to avoid surgery.

This trade-off of risk for efficacy is a common thread running through all elective treatments for BPH. Newer modalities have been aimed at providing alternatives to pharmacotherapy or watchful waiting. Patients are oftentimes enthusiastic if they are offered a one-time method to treat lower urinary tract symptoms secondary to BPH, provided that the method offers reduced risk and allows an efficacy equal to that of medical therapy. One such method is transurethral microwave thermotherapy (TUMT). TUMT involves the insertion of a specially designed urinary catheter with a microwave antenna, which



heats the prostate and destroys hyperplastic prostate tissue. TUMT allows the avoidance of general or regional anesthesia, and results in minimal blood loss and fluid absorption. Clinical trials in the United States and Europe have shown this modality to be safe and effective, with excellent symptomatic relief seen in as little as one outpatient setting using only local anesthesia. However, there is less improvement in urinary functioning seen than with TURP, and long-term follow-up data is not yet available. Clinical indications and treatment parameters for TUMT are still evolving as technology advances and more experience is gained. This manuscript summarizes current knowledge on indications and efficacy of microwave therapy of the prostate.

## PROCEDURE HISTORY

In the 1980s, the use of heat to treat BPH regained clinical interest as alternatives to TURP and open prostatectomy were being explored. The modern use of microwaves has been credited to Yerushalami et al. (1). In 1982, they performed microwave therapy on a patient with prostatic adenocarcinoma (1) and later reported the therapeutic use of microwaves by the transrectal route to treat patients with BPH who were poor operative candidates (2).

The first machines to undergo clinical trials using hyperthermia employed a transurethral catheter in a series of ten 1-hour sessions. Software and instrumentation allowed only a limited and often interrupted delivery of energy to the prostate, with intraprostatic temperatures reaching 40–45°C. Patients reported improved symptomatology, likely due to destruction of the alpha-adrenergic nerve fibers around the prostate, although an objective improvement of voiding parameters was not observed (3), and prostatic cells were not destroyed.

To reliably destroy cells, temperatures greater than 45°C were necessary, which was coined “thermotherapy” (4). Cells would slough away over a period of weeks to months. Unfortunately, the urethral pain threshold was realized to be 45°C. The introduction of urethral cooling allowed these higher temperatures to be used. Although heat treatment pattern differed from device to device, antennae were

designed to allow heat to generally follow the anatomical borders of the transition zone. Both objective and subjective measures produced significant improvement. However, patients invariably had severe prostatic edema and urinary retention, requiring the use of a urinary catheter, which became standard practice after a TUMT.

To improve outcomes even further, high-energy thermotherapy was introduced. Temperatures greater than 70°C were reached, causing thermoablation of prostatic tissue. Today, several different microwave devices are in use around the world, including the Targis (Urologix, Inc., Minneapolis, Minnesota, USA), Prostatron (Technomed Medical System, Lyons, France), Prostalund (Lund Instruments AB, Lund, Sweden), Prostatecare (Bruker Medical, Wissembourg, France), Urowave (Dornier MedTech America, Kennesaw, Georgia, USA), PRIMUS U+R (Tecnomatix, Monheim, Germany), and the LEO Microthermer (Laser Electro Optics, London, UK).

## MECHANISM OF ACTION

TUMT uses an external power source creating microwaves at a frequency of 915–1296 MHz. Tissue penetration of microwaves leads to electromagnetic oscillations of free charges and the polarization of small molecules, such as water, resulting in the release of kinetic energy, which increases the temperature of the tissue. Cell necrosis, vascular injury, and apoptosis ensue. Urethral cooling in part protects the prostatic urothelium from these effects.

## INDICATIONS FOR TUMT

It is widely agreed upon that patients with mild to moderate symptoms should be treated with medical therapy initially, reserving invasive therapies for those with more severe symptoms, those failing medical management, and for patients choosing invasive therapy over medical management. As the criterion standard for invasive therapy, TURP is offered to most patients. Initially, only patients with severe symptoms who were poor anesthetic risks were

offered TUMT. Indications have now been expanded to include patients who prefer an outpatient setting rather than for a hospital stay due to the ease of use, minimal anesthesia requirement, and potentially rapid recovery.

## PRE-OPERATIVE CONSIDERATIONS

### Patient Selection

A thorough clinical evaluation is vital to assess the presence and degree of voiding dysfunction and/or the role played by BPH. The patient's past urologic history along with surgical risks and concomitant medical problems need to be evaluated. A history of sexually transmitted diseases, kidney stones, trauma, previous catheterizations, genitourinary cancer, renal insufficiency, neurologic disease, and neurogenic bladder may influence the treatment options. Medical conditions that may influence bladder functioning mimicking BPH-type symptoms include diabetes and neurological diseases. Surgical risks predominantly are due to renal failure, coronary artery disease, and cerebrovascular disease. Medicines containing alpha-sympathomimetics, such as over-the-counter cold remedies, enhance bladder outlet obstruction. A family history should focus on a history of urologic cancer, and a social history should focus on risks for cancer such as a smoking history and occupational exposure.

The physical examination should be systematic and meticulous, focusing on the presence or absence of distended bladder, urethral stenosis, meatal stenosis, and anal area and rectal tone. The prostate is evaluated for its size, the presence or absence of nodularity, laterality, consistency, and landmarks.

### Laboratory Studies

A hemoglobin determination and platelet count are not specifically required prior to TUMT unless the patient has a history of anemia, coagulation disorder, or as suggested by the history and physical examination. Patients with a renal insufficiency (baseline creatinine greater than 1.7 mg/dL) due to post-renal obstruction may benefit more from a more definitive procedure such as TURP. A determination

of serum PSA level may be important in the evaluation of the absence of prostate cancer. Unlike TURP, no specimen is submitted to pathology after TUMT. Even with a normal PSA and negative biopsies, patients are at risk for prostate cancer, which may be observed on the chips. If clinically suggested, transrectal biopsies should be performed, as alternative therapies may be suggested. Studies using baseline PSA as a predictive factor for TUMT success are varied. In addition, all patients should have documented negative culture before any urethral instrumentation to decrease the risk of urosepsis.

### Imaging Studies

A transrectal ultrasound (TRUS) is suggested before performing TUMT, for patients with prostate volumes estimated to be less than 25 cc or greater than 100 cc respond poorly to TUMT. Renal ultrasound should be performed if there is a history of urinary retention, have evidence of renal insufficiency, or there is hematuria.

### Diagnostic studies

A cystourethroscopy is mandatory to evaluate the urethra for stricture disease, prostatic length, and degree of prostatic hypertrophy. Patients with lateral lobe hypertrophy respond much better to TUMT than those with middle lobe hypertrophy or a median bar, as marked middle lobe enlargement distorts the heating pattern. The urethra and bladder urothelium should also be evaluated for evidence of tumors and stones. The location of the ureteral orifices should be noted.

The maximal voiding rate (Q<sub>max</sub>) is a noninvasive but nonspecific electronic recording of urinary flow rate. This is mainly used to monitor response to treatment, although patients may have a weak urinary stream due to an inadequate detrusor contraction rather than bladder outlet obstruction. An adult man without evidence of obstruction should have an average velocity of 12 cc/sec and an average peak velocity of 20 cc/sec. The prediction capacity of Q<sub>max</sub> for outcome remains a matter of debate.

Symptom indices (including the AUA score, IPSS, Madsen quality of life, and Boyarsky) are available and are used to confirm the components of

the patient's history, evaluate and quantify the patient's response to treatment, and to compare the results of research protocols. Studies have failed to document a strong correlation between symptom scores and physiologic changes due to BPH.

A post-void residual (PVR) volume is often measured. While this does not predict surgical outcome, it may be used to determine how closely patients need to be followed. Patients with high PVRs have slightly higher rates of failure of watchful waiting and are at an increased risk of complications such as urinary tract infections and renal failure. A pressure-flow study should be performed in patients whose voiding velocity and PVR measurements are not sufficient to determine the presence or absence of bladder outlet obstruction or poor detrusor contraction. This is the study of choice in patients with a history of neurologic disease or other problems that affect the bladder and may confound the diagnosis, and for patients with normal flow rates but bothersome symptoms.

A cystometrogram (CMG) using either gas or liquid may be of value for patients with known or suspected neurological impairment. While it is less specific than pressure-flow studies, it allows the evaluation of bladder capacity, evidence of uninhibited detrusor contractions, and an estimation of bladder compliance. Patients who have adequate bladder contractions have better outcomes after TUMT. A urethral pressure profile measures pressures along the length of the urethra. In patients with known or suspected urethral obstruction, this test helps determine the location of the lesion. Finally, videourodynamics may be useful for patients with complex causes of outlet obstruction or for cases where the sites of obstruction need to be identified. Patients with neurogenic bladders may benefit as well as patients undergoing an evaluation for incontinence.

## HISTOLOGICAL FINDINGS AFTER TUMT

Bostwick & Larson (5) studied the results of TUMT on 3 dogs, showing that there was periurethral coagulative necrosis acutely, which began to resolve within 18 days. The capsule and urethra were deemed

to be intact. Mauroy et al. (6) reported maximal coagulative necrosis at 8 days. Bdesha et al. (7) reported a significant decrease in alpha-1 adrenoreceptors after TUMT. Khair et al. (8) performed radical prostatectomies on at 7 days and 1 year later after TUMT, reporting that hemorrhagic necrosis and devitalized tissues without inflammation was observed in benign, stromal, and cancerous areas early on, with a mean volume of necrosis being 8.8 cc (average 22% of the tissue), but that only nonspecific chronic inflammation and a desquamous metaplasia with evidence of periurethral fibrosis remained at one year. The mean volume of necrosis remaining was 0.2 cc, which was less than 1%, implying that cells were sloughed away.

## CONTRAINDICATIONS

All patients undergoing transurethral procedures must have a documented sterile urine culture and must be evaluated for prostate or urothelial cancer if clinically suspected. Patients with neurogenic bladder voiding dysfunction should have their underlying neurogenic problem evaluated and treated.

Contraindications specific to TUMT are evolving as the technology changes and outcomes are studied further. Patients with a history of TURP or pelvic trauma should not undergo TUMT because of potential alterations in pelvic anatomy. Patients with glands that are smaller than 25 gm. or a prostatic urethral length of less than 3 cm respond poorly to TUMT, as do patients with glands greater than 100 gm or patients with a prominent median bar.

Other contraindications include patients with penile prosthesis, severe urethral stricture disease, Leriche syndrome/severe peripheral vascular disease, or an artificial urinary sphincter. Patients with pacemakers and defibrillators need clearance from their cardiologist concerning turning their pacemakers off during therapy.

Hip replacement is no longer a contraindication. Acute urinary retention was previously thought to be a contraindication to TUMT; however, high-energy TUMT has shown to be promising in this population, although efficacy has yet to be determined. Those presenting in retention

tend to be ill with greater co-morbidities; thus, they might benefit from the less invasive nature of TUMT.

## PREOPERATIVE DETAILS

In preparation for TUMT, patients need to be counseled about the risks, benefits, alternatives, and expectations of the therapy. Patients who have a urinary catheter in place or had recent urinary tract manipulation should be placed on appropriate antibiotics. The patient should have nothing by mouth for 6 hours prior to the therapy. An appropriate oral analgesic (such as ibuprofen, ketorolac, or morphine) and an anxiolytic (benzodiazepine) may be administered prior to the procedure.

The patient is brought to the therapy suite and asked to void to completion. The bladder is emptied by straight catheterization, and 40 cc of sterile water is placed within the bladder. 10-20 cc of 1-2% Xylocaine gel is inserted within the urethra for anesthesia. The treatment catheter is then placed within the urethra, confirmed by return of the sterile water and by transabdominal or transrectal ultrasound, and the balloon is inflated. This catheter has a curved tip, a temperature sensor, and a microwave unit near the tip. The distal ports include those for balloon inflation, urine drainage, coolant, microwave cable, and fiber optic connector. The rectal probe (if used) is inserted and continuously monitors the rectal temperature.

## POSTOPERATIVE DETAILS

Out patients and practice are such that all patients are catheterized following TUMT. They return to the clinic for a trial of decatheterization, varying by the protocol used. As prostatic edema is nearly universal after microwave therapy, there are a high number of patients that fail the initial decatheterization trial if performed too early.

Post-treatment convalescence is relatively rapid, with most patients able to void in less than 3 days at home and a mean recovery time of 5 days at home. Catheterization is required in approximately 60% of patients after low-energy Prostatron 2.0 and 100% of the high-energy Prostatron 3.5, and often

this is extended for over 2 weeks. Patients are typically catheterized for a minimum of 2 days after Targis thermotherapy. Patients with larger prostates are more prone to catheterization because of increased edema. The slow process of improvement is characteristic of high-energy transurethral microwave thermotherapy. Coagulated tissue must be absorbed and the treated area must be reorganized before sufficient voiding is achieved. Patients may notice an improvement over a period of many months. Patients are advised to watch for the inability to void, painful voiding, high fevers, abdominal pain, or other problems.

Some patients are maintained on alpha-blockade for a period of time after TUMT. Studies have shown that these patients have improved symptomatology early on over those not on alpha-blockade (9), and also have a lower incidence of retention. Another option includes the placement of a temporary prostatic bridge catheter, which is effective and well-tolerated option that provides a better immediate peak flow, IPSS, and quality of life compared to no stent if the patient has adequate detrusor contraction (10,11).

## RESULTS

### Efficacy

Microwave thermotherapy has been around long enough for both short and medium-term results to be reported (Table-1). In general, patients have noticeable symptomatic improvements as shown by a reduction in symptom scores, although complementary objective improvements have not occurred as regularly (12-26). Long-term follow-up in patients undergoing low-power TUMT reveals subjective symptom score improvement, although for only limited duration in most cases; in the long-term, only a minority of patients showed benefit from treatment. Retreatment rates are substantial, reportedly 57-84% by 5 years. Using the low-energy Prostatron Prostatsoft 2.0, Ohigashi et al. (25) reported a estimated of 67% retreatment rate with 5 years with only 11% "satisfied" with treatment, while Tsai et al. (20) reported an overall retreatment rate of 84.4% in 5 years using Prostatecare. In both of these studies, patients with high peak flow rates (i.e. > 6.5 cc/sec)

**Table 1** - Results of TUMT, based on time since treatment.

Study (reference)	Study (reference)	# Patients	Mean Symptoms Score*	Qmax	Retreatment Rate
<b>1 year</b>	<b>1 year</b>				
Eliasson (15)	Eliasson (15)	120	12.1 to 6.6 (Madsen)	9.7 to 11.1	n/a
De Wildt (13)	De Wildt (13)	85	13.9 to 5.8 (Madsen)	9.9 to 14.9	6.7% (5/74)
De la Rosette (12)	De la Rosette (12)	105	12.6 to 8.0 (IPSS) 20 to 9.2 (IPSS)	9.5 to 15.3	none
<b>2 years</b>	<b>2 years</b>				
Thalmann (16)	Thalmann (16)	162	23 to 3 (IPSS)	6 to 14.5	13% 1 yr, 22% 2 yr
D'Ancona (17)	D'Ancona (17)	301	18.9 to 7.9 (IPSS)	9.7 to 13.8	7%
<b>3 years</b>	<b>3 years</b>				
Robinette (18)	Robinette (18)	320	17 to 6 (IPSS) 11 to 4 (Madsen)	11 to 16.0	86%
Ramsey (19)	Ramsey (19)	152	20.2 to 8.4 (AUA)	8.5 to 12.7	None
<b>4 years</b>	<b>4 years</b>				
Blute (21)	Blute (21)	216	14 to 7 (Madsen)	n/a	39% (11% surgical, 28.7% medical)
Glass (22)	Glass (22)	67	10.2 to 6.2 (Boyarsky)	7.9 to 11.5	31% (25% surgery, 6% medical)
Hallin (23)	Hallin (23)	187	12.2 to 7.7 (Madsen)	10.1 to 8.2	51.9% (17% surgery, 41% medical)
<b>5 years</b>	<b>5 years</b>				
Tsai (20)	Tsai (20)	45	n/a	n/a	84.4% (32.7% surgery, 46.7% med)
Keijzers (24)	Keijzers (24)	231	12.1 to 7.6 (Madsen)	9.0 to about 11	58% (41% surgery, 17% medical)
Ohigashi (25)	Ohigashi (25)	102	17.6 initial to n/a (IPSS)	8.8 initial to n/a	67% estimated
Daehlin (14)	Daehlin (14)	91	22.4 to 12.9 (IPSS)	9.9 to 9.4	59% (21% surgical, 38% medical)
Francisca (26)	Francisca (26)	1094	15.2 to 8.6 (Madsen)	8.7 to 11.1	57% (26% surgery, 31% medical)

\*Note: Change in mean symptoms score is listed

Q max: Mean maximal flow rate (cc/sec)



and short urethral lengths (i.e. < 40 mm) had a lower risk of receiving additional treatments after TUMT. Interestingly, in both studies, older patients (i.e. > 64 years old) similarly had a decreased rate of retreatment. Keijzers et al. (24) similarly reported a decreased risk of retreatment in patients with pre-treatment maximal urinary flow greater than 10 cc/sec, Madsen symptom score less than 15, post-void residual urine less than 100 cc, and age greater than 65 years.

In comparison, higher energy protocols appear to result in symptomatic improvement similar to that of lower energy protocols yet the improvement in uroflowmetry is much more pronounced. This appears to be in trade-off for greater irritative symptomatology and longer duration of catheterization (12). In patients with good initial responses to treatment, which is achieved in approximately 80%, TUMT provides better long-term subjective and objective results. Improved urinary flow, decreased post-void residual urine volume and urodynamic parameters appear to remain stable at 2 years. In a two-year follow-up using the Targis, Thalmann et al. (16) reported that only 22% required additional treatments. In the remaining patients, the IPSS decreased from an average of 23 to 3 at 6 months, while the maximal flow rate increased from 6 ml/sec to 14.5 at 6 months. Both results remained durable through 24 months. Post-void residual volumes also appear to be markedly decreased after high-energy TUMT, as well as demonstrable decreases in detrusor opening pressures and median detrusor pressure at maximum flow rate (17). De la Rosette et al. (12) reported that 6 months after treatment with the ProstateSoft 3.5, patients had an average decrease in the IPSS from 20 to 9.3, an increase in flow rate from 9.4 cc/sec to 14.6 cc/sec, an average catheter time of 18 days, and no serious complications.

### **TUMT vs. Sham**

Several small studies of randomized controlled trials comparing TUMT versus sham treatments (Table-2) are available, and generally show improvement of TUMT over sham. In the largest study (220 men), Roehrborn et al. (27) reported a decrease in AUA symptom score from 23.6 to 12.7 after TUMT,

compared to 23.9 to 18 in the sham group, while the Qmax increased from 7.7 to 10cc/sec and 8.1 to 9.8 cc/sec in each group respectively. Blute et al. (28) and Larson et al. (29) similarly reported a significant improvement in the TUMT group compared to sham treatment using the ProstateSoft 2.0 and Targis respectively. After reporting their results, de Wildt et al. (30) commented that “a beneficial effect of heating at thermotherapy temperatures is conclusive and further sham studies would be unethical”. In contrast, neither Nawrocki et al. (31) nor Mulvin et al. (32) showed any significant improvement of TUMT over sham treatment in their studies using the Prostatron 2.0 and Targis respectively.

### **TUMT vs. Alpha-blocker**

When compared to alpha-blockade, TUMT is associated with an initially poorer outcome but eventually better result. Djavan et al. (33,34) prospectively studied 51 patients undergoing high-energy TUMT and 52 patients on terazosin therapy. Terazosin appeared to have a more rapid onset of action, and had its maximal effects observed at 6 weeks of therapy. In contrast, the maximal effect of TUMT was not observed until after 6 months of therapy. Those patients on terazosin therapy similarly were reported to have a more favorable change in the IPSS, peak flow, and quality of life at 2 weeks compared to TUMT. However, by 1, 4, and 6 months, while there was a significant improvement in both cohorts, all patients were more improved with TUMT. At 18 months, the IPSS, Qmax, and quality of life was 35%, 22%, and 43% better in the TUMT group. Alpha-blocker therapy was associated with more adverse events (17/52) compared to TUMT (7/51). Patients on alpha-blockade complained of dizziness, asthenia, headaches, and lack of effectiveness, prompting discontinuation in 11.5% of patients. In addition, there was a sevenfold greater treatment failure rate seen in the terazosin group.

### **TUMT vs. TURP**

There have been several trials comparing TUMT and TURP (Table-2). In generally, these studies have shown TUMT to be an effective modality, but in no way duplicated the results of TURP in terms

**Table 2** - Results of studies comparing outcomes of TUMT against Sham, Alpha-blocker, and TURP.

<b>TUMT compared to Sham</b>					
<b>Study (ref.)</b>	<b>Device</b>	<b># Patients</b>	<b>Follow-up</b>	<b>Change in Symptom Score</b>	<b>Change in Qmax (cc/sec)</b>
Roehrborn (2)	Urowave	147	6 months	23.6 to 12.7 (AUA)	7.7 to 10
	Sham	73		23.9 to 29	8.1 to 9.8
Blute (28)	Prostasoft 2.0	78	3 months	13.9 to 6.3 (Madsen)	7.2 to 11.5
	Sham	37		14.9 to 10.8	7.4 to 9.4
Larson (29)	Targis	125	6 months	20.8 to 10.5 (AUA)	7.8 to 11.8
	Sham	44		21.3 to 14.3	7.8 to 9.8
DeWildt (30)	Prostatron 2.5	47	1 year	13.7 to 4.2 (Madsen)	9.2 to 13.4
	Sham	46		12.9 to 8.2	9.6 to 10.5
Nawrocki	Prostatron 2.0	38	6 months	19 to 9.5 (AUA)	8.83 to 9.94
	Sham	40		18 to 9.5	9.44 to 9.49
	No treatment	42		18 to 17	8.79 to 8.47
Mulvin (32)	Targis	20	3 months	24.2 to 14.1 (AUA)	12.8 to 14.6
	Sham	20		21.0 to 9.6	10.0 to 12.4
<b>TUMT compared to Alpha-blocker</b>					
<b>Study (ref.)</b>	<b>Device</b>	<b># Patients</b>	<b>Follow-up</b>	<b>Change in Symptom Score</b>	<b>Change in Qmax (cc/sec)</b>
Djavan (33)	Targis				
	Terazosin	51	6, 18 months	19.4 to 6.8, 7.0 (IPSS)	8.3 to 13.9, 13.8
		52		18.9 to 11.0, 11.3	8.9 to 11.6, 11.3
<b>TUMT compared to TURP</b>					
<b>Study (ref.)</b>	<b>Device</b>	<b># Patients</b>	<b>Follow-up</b>	<b>Change in Symptom Score</b>	<b>Change in Qmax (cc/sec)</b>
Ahmed (34)	TURP	30	6 months	18.4 to 5.2 (AUA)	9.5 to 14.6
	Prostatron 2.5	30		18.5 to 5.3	10.1 to 9.1
D'Ancona (35)	TURP	21	30 months	13.8 to 2.6 (Madsen)	9.3 to 19.1
	Prostatron 2.5	31		13.3 to 5.8	9.3 to 15.1
Floratos (37)	TURP	66	1, 2, 3 years	20 to 3, 4, 5 (IPSS)	7.8 to 24.5, 23, 24.7
	Prostatron	78		20 to 8, 9, 12	9.2 to 15.5, 14.5, 11.9
Daulstrad (37)	TURP	32	2 years	13.6 to 1.2 (Madsen)	8.6 to 17.7
	Prostatron 2.0	37		12.1 to 2.3	8.6 to 12.3
Wagrell (38)	TURP	46	12 months	20.4 to 7.1 (IPSS)	7.9 to 15.2
	Prostalund	100		21 to 7.2	7.6 to 13.3

Note: Symptom score and Qmax represent the mean scores

of objective or subjective parameters. For example, Ahmed et al. (35) reported that 60% of a cohort of 30 patients reported symptomatic improvement after TUMT, but none had objective relief of obstruction. In comparison, 100% of the patients in the TURP cohort showed relief of obstruction. At a longer follow-up of 2.5 years, d'Ancona et al. (36) reported that TURP performed better than TUMT using both subjective (Madsen score improvement of 76% after TURP compared to 56% after TUMT) and objective (flow rates increased 105% after TURP compared to 62% after TUMT) parameters. Floratos et al. (37) showed that these differences became more pronounced with time, as patients undergoing TURP continued to improve in both subjective and objective parameters after 1, 2, and 3 years, which was not the case in the TUMT group. Further procedures were required in 19.8% of patients undergoing TUMT, compared to 12.9% of the TURP group at 33 months.

In an attempt to bridge this gap, Wagrell et al. (38) compared patients undergoing TURP to those undergoing TUMT with the ProstaLund Feedback Treatment, which provides a feedback system based on intraprostatic temperatures during treatment. In 133 patients with a minimum of 12 months follow-up, good outcomes were reported in 82% and 86% of the patients in the TUMT and TURP respectively, and symptoms score and maximal flow rate improvements appeared to be similar. Whether or not this remains durable in the long-term remains to be seen.

Adverse effects of the 2 modalities vary. In general, patients requiring further procedures after TUMT were due to therapy failure, while after TURP was due to complications. Mild and moderate adverse events were more common in the TUMT group, but serious adverse events were more common (17% vs. 2%) in the TURP group. The complication rate of TURP in these series varied, and was generally due to bleeding and clot retention, urinary retention, urinary tract infections, urethral strictures, and retrograde ejaculation. In contrast, patients undergoing TUMT were at higher risk for severe urinary urgency, urinary retention, and many required secondary procedures. The average catheter time was 3 days with TURP, 1-3 days with low-energy TUMT and 3-14 days using high energy TUMT.

The reported rate of changes in sexual function is 17% with TUMT compared to 36% with TURP, which is higher in older men. One of the most common adverse effects is retrograde ejaculation. This is reportedly observed in 48-90% of patients after TURP and 0-28% of patients after TUMT, although even alpha-blockers are associated with a risk of retrograde ejaculation. If explained prior to therapy, this complaint is generally not a concern to most patients.

Arai et al. (39) reported a 26.5% rate of erectile dysfunction for TURP and 18.2% with TUMT using a high-energy protocol. Overall, satisfaction with sex life seems to be higher in patients who have had TUMT than in patients who have had TURP, with patients undergoing microwave thermotherapy reported as being "very satisfied" in 55% versus 21% of TURP. However, only 27% of this population is satisfied with their urinary flow after TUMT compared to 74% of patients who are satisfied after TURP.

### **TUMT in patients in urinary retention**

Because patients presenting with urinary retention generally are older, have a larger prostate volume, and have more renal insufficiency, they are at increase anesthetic risk, increased risk for secondary procedures, and risk for bleeding. In the past, TUMT was thought to be contraindicated because of a high failure rate. However, with the advent of high-energy TUMT, patients are now offered this less-invasive therapy. Djavan et al. reported a 94% success rate at 12 weeks in 31 patients presenting in retention (40), although the 1-year retreatment rate is estimated to be 25% (41). Schelin reported that 80% of their cohort was relieved of an indwelling catheter after TUMT, and those who failed all had large median lobes or protruding lateral lobes into the bladder (42). Robinette et al. (18) reported that 44 of 60 patients in retention were able to void spontaneously at 6 months after therapy with the Prostatron 2.0 or 2.5, as were 32 of 35 followed at 12 months.

### **COMPLICATIONS**

During the procedure, patients commonly experience mild perineal warmth, mild pain, and a

sense of urinary urgency. However, only 5% of patients reported their pain as being severe during Targis therapy. Despite this, more than one half of these patients required substantial oral analgesics during treatment. Higher energy protocols appear to have a slightly higher level of initial pain due to the initial higher power, which appears to resolve and return to the same level of comfort as the lower-energy protocols soon into treatment.

Reports of complications vary, and range from 0 to 38%, based on the study and the investigators' criteria for complications. For example, Ohigashi et al. reported no serious side-effects in 91 patients treated with low-power over 5-year follow-up (25). Others report complications including acute urinary incontinence, urinary tract infection, and urinary retention. The risk for urinary tract infections rises with each day of catheterization. In addition, the necrotic tissue that remains in the prostatic fossa after TUMT may increase the risk of colonization and infection. Treatment morbidity of higher energy protocols is moderate and consists mainly of the need for catheterization and a higher percentage of retrograde ejaculation (17).

Erectile dysfunction after TUMT is rare if a patient is previously normal, but is commonly observed in patients with prior erectile difficulties. Although causes have not been fully elucidated, psychogenic factors, bladder neck trauma, and neurogenic voiding dysfunction probably play a role. Lower-energy TUMT protocols have a lower incidence of erectile dysfunction compared to higher-energy protocols but at the expense of better urinary results. Francisca et al. (43) reported no change in sexual performance after low-energy TUMT when compared to a sham procedure in 147 patients.

A variety of other rare but reported complications following TUMT occur. This includes, but is not limited to, urethrorectal fistula (44), bladder perforation, and improper catheter placement. An emphysematous prostatic abscess (45) has been reported after low-energy TUMT in a 55-year old man with diabetes mellitus and cirrhosis. Proper intra-treatment physician and nursing observation are vital to decrease these risks.

## OTHER USES AND FUTURE DIRECTIONS

Microwave therapy may be of value to treat other types of prostate pathology. For example, several investigators are using TUMT to treat chronic prostatitis (46). Microwave therapy is known to be lethal to many microorganisms because microwaves are used to sterilize urinary catheters and surgical scalpels. Patients with nonbacterial prostatitis who are non-responders to traditional therapy may benefit from TUMT. Early results are promising, with a 25% complete and sustained improvement and 50% mild improvement in a group of 45 patients using TUMT.

In the future, because of the risk factors for patients with symptomatic BPH, patients may be better stratified in order to determine the optimal choice of therapies (i.e., pharmacotherapy vs. TURP vs. TUMT vs. other method). Responders and non-responders may be differentiated better by prostatic biopsy. The optimal combination of preoperative medicines may allow for an increase in comfort. The optimal time and energy requirements for therapy will decrease morbidity. The long-term results of the balance between patient tolerability and efficacy need to be evaluated adequately in a controlled setting.

Currently underway is the MIST trial, which is a prospective, National Institute of Health-sponsored trial comparing the outcomes of transurethral needle ablation - TUNA, TURP, or combination medical therapy (alpha-blocker and 5-alpha reductase inhibitor). The end-points and goals of this study are to evaluate the perioperative morbidity (i.e. pain), complications, and long-term outcomes of these three options in the treatment of BPH.

## CONCLUSIONS

TUMT is a safe and effective minimally invasive alternative to treatment of symptomatic BPH. TUMT can be performed in a 1- to 2-hour office visit without IV sedation. This is a good alternative for patients who are at high surgical and anesthetic risk. It is not effective for patients with a large median lobe or a very large prostate and results in less urinary flow patterns than TURP.

Enthusiastic reassessment of procedures that may reduce local and overall morbidity and maintain or improve immediate and long-term physiologic results is understandable and laudable. Currently, the limited number of patients, evolving selection and technical approaches, hampers assessment of these efforts and the limited period and nature of the follow-up information provided. In summary, this minimally invasive therapy appears to balance efficacy against tolerability, and this balance might be tenuous for patients in the long term.

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