

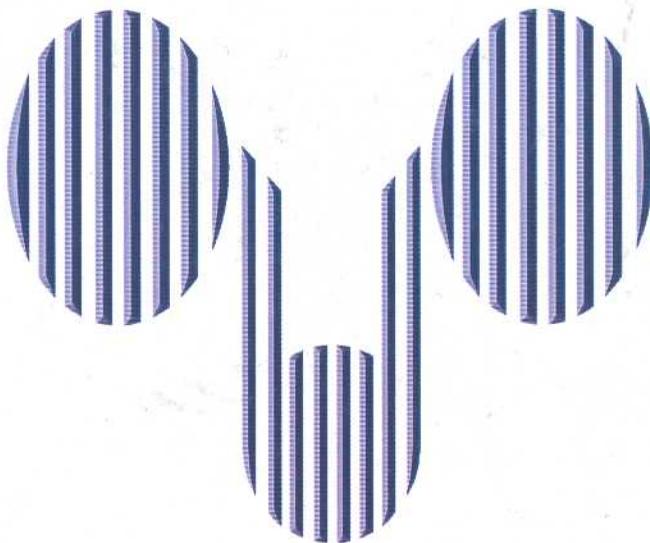
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BRAZILIAN JOURNAL OF UROLOGY

EDITOR'S COMMENT

The July – August 2001 issue of the Brazilian Journal of Urology presents important contributions from USA, Europe and Brazil. The Editor would like to highlight some papers.

Doctors Ames and Older, well known uroradiologists from University of Virginia Health System, Charlottesville, Virginia, USA, present on page 316 an important article on imaging the urinary tract obstruction. The authors state that in the non-acute setting, where urinary tract obstruction is suspected, an ultrasound may be used as the initial screening procedure. To the acute patient, it is now used non-contrast spiral computed tomography as the screening examination for flank pain and suspected ureteral stone. This is faster and more accurate than conventional examinations and provides information regarding non-urologic causes of pain. In children, the approach is somewhat different. Ultrasound is used as the primary screening tool for suspected obstruction. If hydronephrosis is demonstrated, a functional study such as a Lasix renogram is generally performed to evaluate the function of the two kidneys and the severity of the suspected obstruction. Further studies would then depend on clinical consideration such as any need for surgical intervention.

Doctor Graziottin and colleagues, from University of California School of Medicine, San Francisco, California, USA provide our readers with the most comprehensive review on Peyronie's disease published in recent years (page 326). The authors reviewed the incidence, pathology and basic science knowledge of the disease. Also, the natural history, presentation and diagnosis are discussed. The considerations on the non-surgical treatment revealed that the therapeutic advances in Peyronie's disease have not resulted in a reliable cure. The indications for surgical correction include: severe curvature, narrowing or indentation of more than one-year duration, sexual difficulty or partner discomfort because of deformity, or severe penile shortening. Prior to surgery, a detailed evaluation of penile vascular and erectile function is highly recommended. Reconstructive surgery is not recommended in the acute phase of the disease.

Doctor Duarte and co-workers from University of São Paulo, São Paulo, Brazil, report by for first time the use of a cutting balloon catheter for management of urethral strictures in 20 patients (page 358). Doctor Netto Jr., from Unicamp, Brazil, Doctor Preminger, from Duke University, and Doctor Wolf Jr., from University of Michigan, USA, our Consulting Editors, provide important Editorial Comments, which give pertinent considerations on this controversial procedure.

EDITOR'S COMMENT - *continued*

On page 380, Doctor Dénes and associates, from University of São Paulo, São Paulo, Brazil, present an important series of laparoscopy for evaluation and treatment of 85 impalpable testes. Laparoscopy enabled precise diagnosis and when intra-abdominal testis were found, either immediate laparoscopic orchietomy, or primary and staged orchipexy were possible.

Doctor Angulo and co-workers, from University of Alcalá, Madrid, Spain, present on page 386 a surgical modification of the conventional inverted U vaginal flap for correction of severe cystocele or cystourethrocele and associated incontinence, either evident or occult. The technique incorporates anterior colporraphy and a transverse vaginal flap sling to support the bladder neck and treat stress incontinence. The authors studied 41 patients and at a mean follow-up of 42 months presented a success rate of 93% for cystocele repair and 88% for treatment of associated stress incontinence.

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

IMAGING IN URINARY TRACT OBSTRUCTION

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ABSTRACT

There are a wide variety of imaging studies available for evaluation of a potentially obstructed patient. Selection of a specific test over another depends on the acuity of obstruction and the patient's age and renal function. Consideration must also be made for cost of the test, reliability and feasibility of long term follow up by repeated exams. In the non-acute setting where urinary tract obstruction is suspected either on the basis of a rising serum creatinine, history, or prior urinary tract abnormalities, an ultrasound may be used as the initial screening procedure. If ultrasound fails to show any evidence of significant hydronephrosis or hydroureter it is concluded that this patient does not have significant obstruction. Generally, no further studies relative to detecting urinary tract obstruction are performed.

If ultrasound demonstrates the presence of hydronephrosis or hydroureter further studies to determine the point and cause of obstruction are performed, unless the ultrasound examination has clearly demonstrated this, as in the case of an obstructing ureteral stone. In adults, an intravenous pyelography (IVP) is often performed to delineate the point and hopefully cause of an obstruction. If there is good renal function, the IVP will generally be successful in answering these questions. There is not always one "best" way to utilize the multiple studies available and it is often the results of a specific study that will determine if a further study is necessary and which modality to use.

The approach to the patient with acute renal colic has changed over the past few years. Up until recently, these patients were evaluated with either ultrasound or an IVP as the initial study. This is no longer the case as we now use non-contrast spiral computed tomography (CT) as the screening examination for flank pain and suspected ureteral stone. This is faster, more accurate and provides information regarding non-urologic causes of pain.

In children, the approach is somewhat different. Ultrasound is used as the primary screening tool for suspected obstruction. If hydronephrosis is demonstrated, a functional study such as a Lasix renogram is generally performed to evaluate the function of the two kidneys and the severity of the suspected obstruction. Further study would then depend on clinical consideration such as any need for surgical intervention.

Key words: urinary tract; obstruction; imaging; kidney; ureter; calculi
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IMAGING IN OBSTRUCTION

There are numerous studies available to the urologist in the diagnosis and management of obstruction. These include radiographic studies, such as the plain film (kidney, ureter and bladder – KUB), intravenous pyelography (IVP) and retrograde urography, ultrasound, computed tomography (CT),

Lasix renogram, magnetic resonance (MR) urogram and the Whitaker test. Selection of a specific test over another depends on the acuity of obstruction and the patient's age and renal function. Pregnant patients and those with contrast allergy require special provisions. Consideration must also be made for cost of the test, reliability and feasibility of long term follow up by repeated exams. We will explore each imaging

modality listed and then discuss our approach to the patient with suspected obstruction.

PLAIN FILM

Simple radiographic studies such as the KUB have a role, although limited, in the evaluation of obstruction. A single view plain film may be sufficient to diagnose the presence of a ureteral stone. It is low cost with low radiation exposure and may be done rapidly within the urology clinic. The plain film is limited by its low sensitivity for detection of opaque as well as non-opaque stones. Recent studies have shown a sensitivity of about 50% for stone visualization with the abdominal film. Occasionally a suspected ureteral calcification seen on plain film turns out to be a vascular phlebolith when more specific studies are performed (1).

The plain film also provides an easy way to follow the progression of an obstructing stone, even if the diagnosis of stone disease has been made with another imaging modality such as CT scan. Significantly, more stones can be seen on an abdominal film in retrospect following CT (2). Stones larger than 5 mm and with CT attenuation above 300H will likely be detected on abdominal radiography (3).

INTRAVENOUS PYELOGRAPHY

Intravenous pyelography (IVP) plays an important role in the diagnosis of obstruction. It is the classic test which can assess anatomy and to some ex-

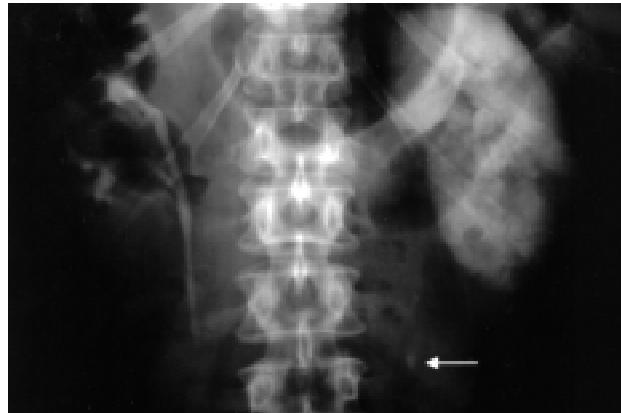


Figure 1 - IVP shows a delayed nephrogram and pyelogram on the left caused by a stone in the mid ureter (arrow).



Figure 2 - IVP shows a delayed nephrogram with extravasation of contrast (long arrow) and a stone with proximal edema blocking the mid ureter (arrow).

tent the function of the kidney. Acute obstruction is identified by the presence of a delayed and often increased nephrogram (Figure-1). Hydronephrosis or hydroureter helps to confirm the diagnosis of obstruction, but are not always visible (1). The level and cause of the obstruction may be determined with the visualization of filling defects or stones (Figure-2) in the renal pelvis or ureter, changes in renal contour and course of the ureters. In addition, bladder pathology may be revealed on IVP, such as filling defects, diverticula and a significant post void residual. Obstructions, which are not obvious initially, may, at times, be revealed after the administration of Lasix during the IVP. This technique is generally reserved for suspected intermittent ureteropelvic junction (UPJ) obstruction.

The IVP requires intravenous contrast and therefore should not be performed in a patient with decreased renal function. We accept creatinine values of 1.5 or lower for patients undergoing IVP in our department. Nephrotoxicity of iodinated contrast is most likely in patients with chronic renal insufficiency especially if diabetes is also present. Patients with contrast allergy need to be premedicated prior to an IVP and should have non-ionic contrast media. The need for the IVP must be balanced against potential risks. It may be wiser to perform alternate studies in certain situations, such as a noncontrast CT scan, ultrasound or magnetic resonance imaging (MRI). The

availability of multiple other modalities not requiring contrast has reduced dependence on the IVP. IVP may be time intensive, requiring delayed films in patients with high-grade obstruction and may not always have sufficient opacification to define the anatomy and point of obstruction. In addition, completion of an IVP requires a significant amount of radiation exposure and may not be ideal for young children or pregnant women (1).

RETROGRADE UROGRAPHY

Retrograde urography, although largely replaced by other imaging studies, can still be useful to delineate the precise location and severity of an obstruction when other studies fail to define the exact point or cause of obstruction. In addition, this study can usually be performed with greater safety in patients who are not candidates for an IVP due to an allergy to contrast media or renal insufficiency. This is not a first line study for patients with obstruction due to the necessity of anesthesia, either general or epidural blockade. However, we often perform retrogrades in the operating room just prior to pyeloplasty or ureteral stent placement to exactly delineate the point of obstruction and to rule out the presence of a second obstruction.

ULTRASOUND

Ultrasound is used extensively to detect hydronephrosis, the primary finding with an obstructed system. It is inexpensive, noninvasive and portable.

Ultrasound is an ideal first line technique to evaluate patients for renal obstruction. It is highly sensitive in detecting dilated systems (Figure-3) and the absence of hydronephrosis is generally a reliable sign that obstruction is not present. An exception is very early obstruction, such as might occur with an acute obstructing stone. Resistive index has been advocated to detect these cases of early obstruction (4) and is occasionally used in our clinic but has not proven to be reliable (Figure-4) (5,6).

Because not all dilated systems represent functional obstruction, ultrasound is therefore not specific. The imaging findings must be correlated with the clin-

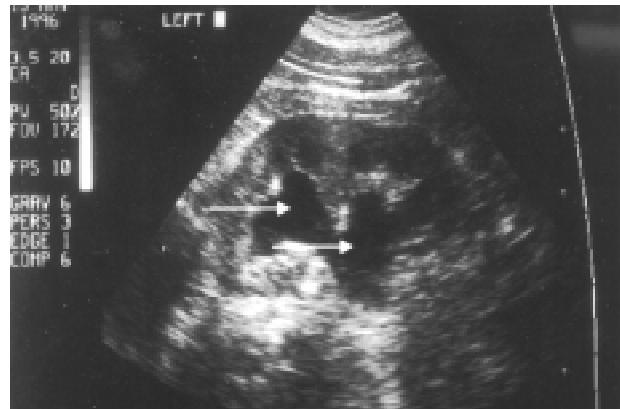


Figure 3 - Renal ultrasound reveals dilation of the renal pelvis and calyces (arrows).

ical picture. Hydronephrosis not due to obstruction can result from prior obstruction, reflux, enlarged extra renal pelvis, bladder over distension or a distensible collecting system in a well hydrated individual. Renal sinus cysts may be mistaken for a dilated renal pelvis on ultrasound, and a skilled ultrasonographer is needed to make this differentiation.

Ultrasound is very accurate in the identification of renal stones that may or may not be visible on plain radiograph, due to either stone composition or size. However, detection of ureteral stones by ultrasound is much more difficult. These stones often go undetected by ultrasound unless they are near the ureteral tunnel (Figure-5). The technical difficulties in detecting stones, operator dependence and relatively low sensitivity for ureteral stone detection with ul-

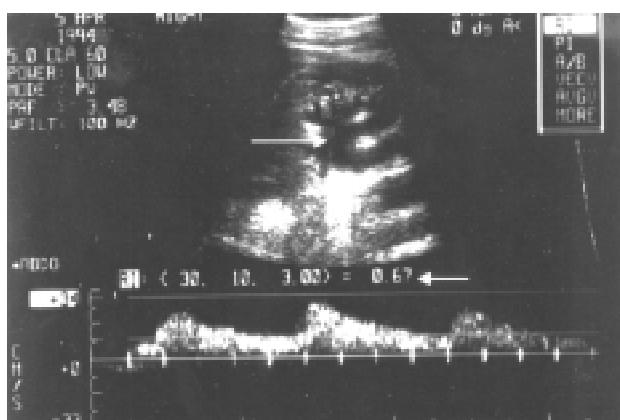


Figure 4 - Doppler ultrasound shows a normal resistive index of 0.67 (arrow) in the face of obstruction and hydronephrosis (long arrow), demonstrating the unreliable nature of the resistive index for diagnosis of obstruction.



Figure 5 - Bladder ultrasound shows a dilated ureteral tunnel (thick arrow) with a stone (arrow) and shadowing distal to the stone (long arrow).

trasound have led to widespread shift to non-contrast spiral CT to evaluate renal colic and suspected acutely obstructing stones.

Prenatal ultrasound is performed routinely and may pick up evidence of hydronephrosis in the developing fetus. In patients diagnosed with prenatal hydronephrosis, ultrasound should be repeated within several weeks of birth to evaluate for persistent hydronephrosis (7).

Because ultrasound is readily available within our clinic, we use it to monitor patients with known obstruction. A caveat to heavy reliance on ul-

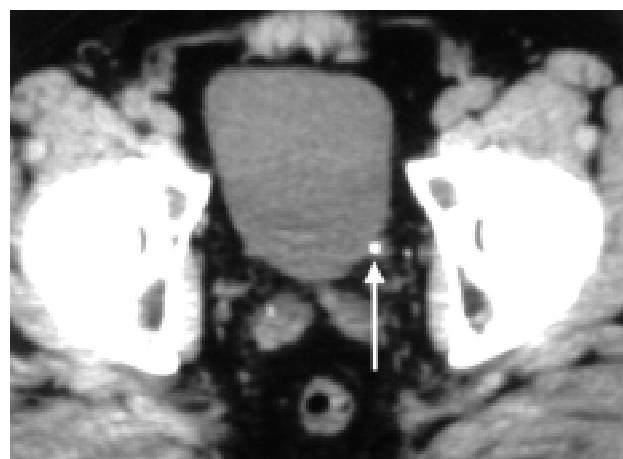


Figure 6 - Non-contrast helical CT scan reveals a stone (arrow) in the distal left ureter, just proximal to the ureteral tunnel.trasound is that ultrasound is extremely operator-dependent. It is ideally performed by personnel experienced in uro-ultrasonography.

The ultrasonographer may also use color Doppler to evaluate the presence of ureteral jets. The periodic “jet” of urine effluxing from the ureteral orifice effectively rules out complete obstruction of the renal system (1,8).

COMPUTED TOMOGRAPHY

Computed Tomography (CT) scans can be performed with or without intravenous contrast. Spi-

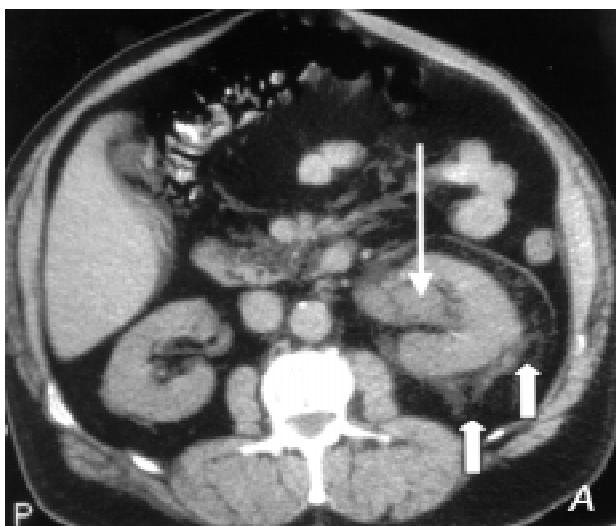


Figure 7 - A)- Non-contrast helical CT scan reveals hydronephrosis (long arrow) and perinephric stranding (thick arrows) caused by B)- A moderate sized stone (long arrow) in the distal ureter.



ral CT scans use 5 mm slices from the level of the kidneys down to the bladder specifically to look for stone disease. It has been shown that the “stone-protocol” CT scan is more effective in precisely identifying ureteral stones than the long time gold standard, the IVP (9,10). CT is ideally suited to detecting obstructing stones and is very effective in distinguishing the stone from other causes of obstruction such as clot or tumor (1). Spiral CT scans may pick up stones that cannot be seen on plain film (KUB) due to stone composition, size or artifacts such as bowel gas. It is also useful to differentiate between calcifications within the vascular system versus the urinary system.

CT diagnosis of a ureteral stone relies on both primary and secondary findings. The primary finding is unequivocal demonstration of a stone within the ureter (Figure-6). Secondary findings, which include hydronephrosis, hydroureter or stranding of the peri-

nephric fat, have a high positive and negative predictive value for the presence or absence of a ureteral stone (Figure-7) (1,11). Perinephric edema has been shown to be predictive of the degree of obstruction (12). However, it should be noted that non-contrasted CT scans could miss other causes of flank pain and hematuria, such as a solid renal mass. It has been suggested that patients with the diagnosis of a suspected ureteral stone that is not seen on CT be followed by a contrasted CT to rule out other diagnoses (13). Potential causes of extrinsic obstruction such as malignancy or aneurysm may also be identified on CT scan (1), (Figure-8). During a dynamic enhanced CT scan, a sign of obstruction is a delay in the nephrogram with persistence of corticomedullary differentiation as compared to the opposite kidney (Figure-8). Although CT picks up most stones, including those that are classically opaque on plain film, it may miss obstruction caused by non-



Figure 8 - A)- Retrograde urogram showing a ureteral stricture (black arrow) and proximal hydroureter; **B)**- Enhanced CT scan shows delayed corticomedullary separation (white arrows) and hydronephrosis (star) on the left; **C)**- A nodal mass (long arrow) surrounds the ureter at the level of the stricture.

opaque indinavir crystals. In patients with HIV on the protease inhibitor, indinavir, presenting with acute flank pain, the absence of a stone on helical CT should be followed with a contrasted CT scan (14).

We occasionally use contrasted CT scans following a spiral (non-contrasted) scan to help define the course of a ureter if we are unsure if a calcification resides within a ureter or a vessel. Contrast CT scans will further assess function of a renal unit and more accurately detail the degree of hydroureteronephrosis.

LASIX RENOGRAM

The Lasix renogram is very useful in the diagnosis and follow up of children with UPJ obstruction.

It is crucial in the identification of an obstructed hydronephrotic kidney versus a non-obstructed hydronephrotic kidney. Previously, it was assumed that any dilatation of an upper urinary system equaled obstruction. We now know that a hydronephrotic kidney may simply represent a dysmorphic or atonic collecting system, which has no functional significance and will not cause renal damage over time. Therefore, all children with suspected UPJ obstruction at our institution undergo diuretic renal scan to determine the functional significance of hydronephrosis. A radionuclide is administered and then the scintillation camera obtains individual counts from each kidney, which are then expressed as a percent of the total. We use ^{99m}Tc -MAG3, which collects

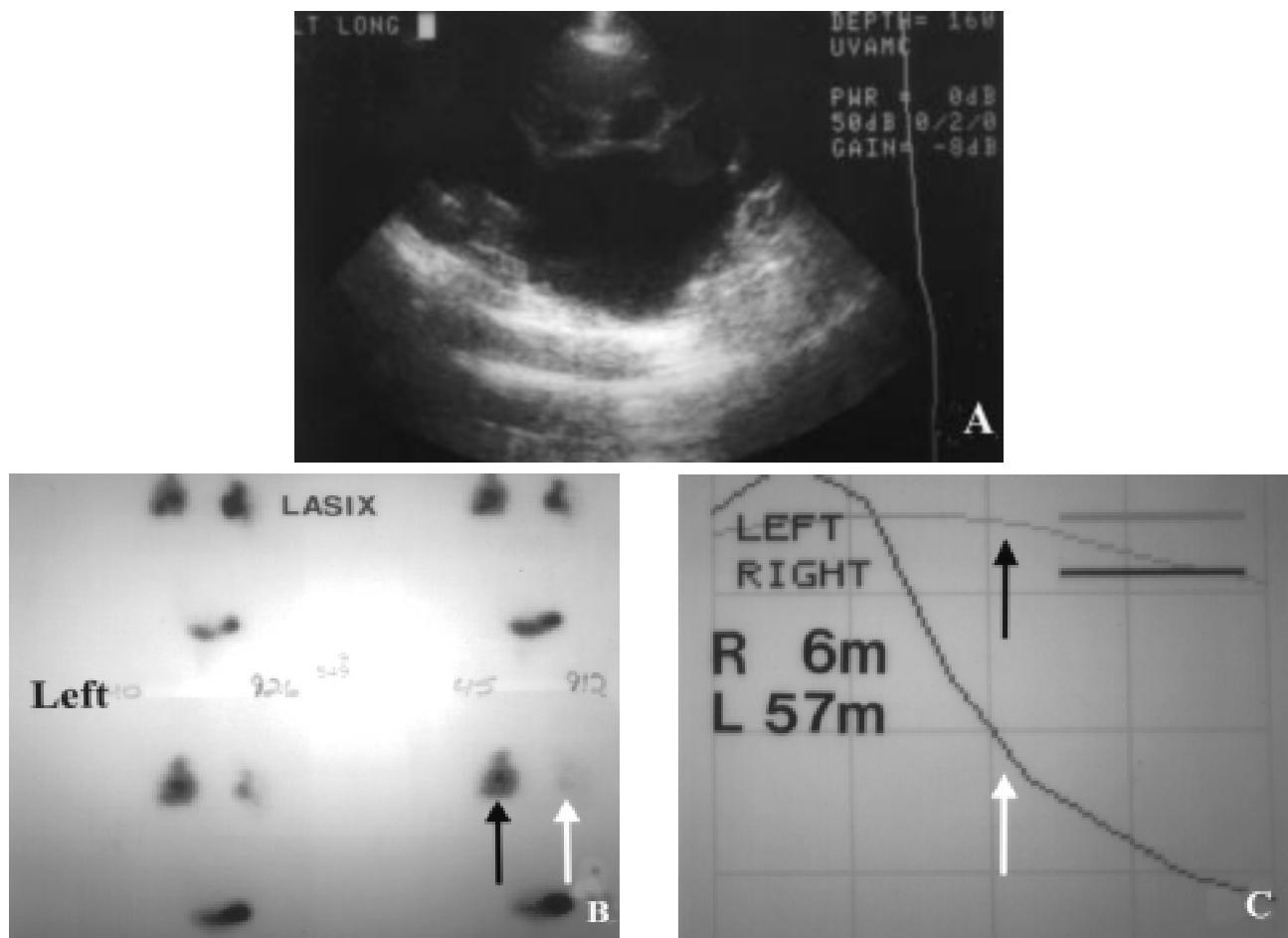


Figure 9 - A)- Renal ultrasound shows dilated pelvis and calyces in a patient with congenital left UPJ obstruction; B)- Lasix renal scan shows delayed washout of left kidney (black arrow) compared to the normal right kidney (white arrow); C)- Washout curves confirm delayed emptying of the left system (black arrow) with an elevated $T_{1/2}$ of 57 minutes compared to the normal right system (white arrow) with a normal $T_{1/2}$ of 6 minutes.

in the collecting system due to tubular secretion and has good uptake in patients with renal insufficiency (1). Diuretics are used as a part of the renogram in order to separate non-obstructive hydronephrosis from obstructive hydronephrosis. A diuretic is given after the radionuclide has accumulated in the collecting system. Then the “washout time” of the radionuclide is determined. In the absence of obstruction, the diuretic will fill the collecting system with urine not containing the radionuclide and the urine that contains radionuclide will be washed out of the system. However, in the presence of obstruction, the radionuclide is not washed out as quickly. The $T_{1/2}$ is a value measured as the time it takes for 50% of the tracer to leave the collecting system. This clearance half-time is based on the slope of the washout curve. A $T_{1/2}$ of less than 15 minutes is normal. In general, a $T_{1/2}$ of greater than 20 minutes represents obstruction. (Figure-9) (15). In addition to the $T_{1/2}$, the Lasix renal scan will also allow estimation of the split renal function. Split function allows the clinician to closely monitor renal function in patients managed conservatively and in postoperative studies (15).

Although the Lasix renogram can supply very useful information, urologists should keep in mind that there are several factors which can make the results unreliable. First of all, poor renal function may cause an inability to respond to the diuretic, resulting in a false delay in washout time. Poor hydration may also limit the response to diuretic (15). Secondly, there is no standard protocol for the administration or the interpretation of the Lasix renogram. Care should be taken when comparing studies performed in two different institutions (16). It is crucial that a standard protocol be developed and maintained at all times within a single center to facilitate comparison of scans over time. At the University of Virginia, we follow the protocol outlined by Conway (17) in an effort to standardize the protocol of performing a Lasix renogram. His guidelines include:

- a)- Oral hydration;
- b)- Bladder catheterization in any patient who cannot void on request;
- c)- Patient at least 1 month old;
- d)- Use of a standard radionuclide-99mTc-MAG3;

e)- Diuretic given at 1mg/kg when the abnormal collecting system is full.

Finally, the diuretic renogram identifies the presence of obstruction but not the cause of obstruction. There is very little anatomic detail provided with the Lasix renogram (1,18).

MAGNETIC RESONANCE UROGRAM

Magnetic resonance imaging provides more detailed anatomy than nuclear renograms without the radiation exposure or the use of potentially nephro-toxic contrast media, which is necessary for IVP. We occasionally employ the MR urogram (MRU) with gadolinium to replace the IVP in a patient with renal insufficiency or contrast allergy or in a patient population that requires reduced radiation exposure (i.e., pregnant women). The MR urogram delineates the presence and degree of hydronephrosis and may pick up filling defects within the collecting system (Figure-10). In a patient with poor renal function, MRU may provide more detailed anatomy than IVP. MR urography has not become popular at most institutions due to several shortcomings. Although there is good resolution of the renal parenchyma and the collecting system, the anatomy of the calices is not seen with optimal detail, as in an IVP. This may miss a diagnosis of papillary necrosis. The diagnosis of a small ureteral stone may also be missed on MRU (19). Patients who are severely claustrophobic or require close hemodynamic moni-

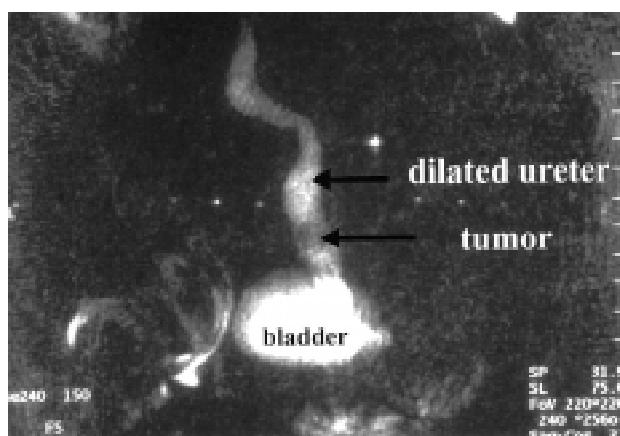


Figure 10 - Magnetic resonance urogram of patient with transitional cell carcinoma in distal ureter. Decreased renal function precluded use of iodinating contrast media.

toring or who are unable to cooperate may be inappropriate for MR. Patients with cardiac pacemakers, cochlear implants, brain aneurysm clips or prosthetic heart valves are not candidates for MR. Finally, MR is limited due to cost and availability (20,21).

WHITAKER TEST

The Whitaker test, a ureteral pressure-flow study, provides a precise but invasive measure of the presence or absence of obstruction in the face of hydronephrosis. It allows direct measurement of ureteral resistance by recording the pressure gradient across the suspected area of obstruction. Results delineate the functional significance of the obstruction. Performance of the Whitaker test requires placement of a catheter in the bladder as well as an antegrade pyelogram needle in the kidney. Contrast is delivered at a constant rate through the needle in the kidney, simulating diuresis, and pressures in the kidney and the bladder are measured. Inaccuracy may be encountered in the face of variable renal anatomy or compliance. Furthermore, the Whitaker test assumes that the obstruction is constant over time, which may produce false negative results (22).

The presence of hydronephrosis does not, in and of itself, imply obstruction. Other causes of hydronephrosis may include: high output by the renal unit, permanent dilation from an old obstruction that has since resolved, vesicoureteral reflux, calyceal dilation of congenital megacalycosis or papillary necrosis, or an extra renal pelvis (23). It is important to document the presence of functional obstruction before any intervention is planned.

URETEROPELVIC JUNCTION OBSTRUCTION

Ureteropelvic junction obstructions may be classified as either chronic or acute. The majority are chronic and congenital in origin although they may not become clinically apparent until childhood or even adulthood (24). Frequently, pathology of the obstructed segment reveals an aperistaltic ureteral segment in which the normal spiral musculature has been replaced by abnormal fibrous tissue and longitudinal muscle

bands. Other causes of chronic UPJ obstruction include congenital stricture, kinks or valves within the ureter caused by infoldings of the mucosa, angulation of the ureteral insertion on the pelvis and aberrant vessels entering directly into the lower pole of the kidney causing external compression of the ureter (22,25).

Acquired causes of chronic UPJ obstruction include vesicoureteral reflux which causes upper tract dilation and tortuosity of the ureter, benign fibroepithelial polyps, transitional cell carcinoma, post operative or post inflammatory scarring and stones (22).

UPJ obstruction is suspected in neonates and infants presenting with a palpable flank mass or hydronephrosis on prenatal ultrasound. Older children and adults may present with flank or abdominal pain that may be intermittent in nature. Alternatively, they may present with urinary tract infections or microscopic hematuria. The diagnosis is confirmed with ultrasound (Figure-9).

In chronic UPJ obstruction, there may be significant loss of renal function before the diagnosis is made. Studies should be performed to consider the amount of renal function still present and how much is salvageable. Lasix renogram studies with split function analysis are crucial for adding this information. Before operative intervention such as pyeloplasty is performed, retrograde urograms may be obtained to delineate the exact site of obstruction and to rule out a second, distal obstruction. This is often done on the same day as the planned repair in order to avoid the use of two general anesthetics.

APPROACH TO THE POTENTIALLY OBSTRUCTED PATIENT

There are a wide variety of imaging studies available for evaluation of a potentially obstructed patient. Our approach to this patient is determined by the clinical setting. In the non-acute setting where urinary tract obstruction is suspected either on the basis of a rising serum creatinine, history, or prior urinary tract abnormalities we will use ultrasound as the initial screening procedure. If ultrasound fails to show any evidence of significant hydronephrosis or hydroureter it is concluded that this patient does not have significant obstruction. Generally, no further

studies relative to detecting urinary tract obstruction are performed.

If ultrasound demonstrates the presence of hydronephrosis or hydroureter further studies to determine the point and cause of obstruction are performed, unless the ultrasound examination has clearly demonstrated this, as in the case of an obstructing ureteral stone. In adults, we will often perform an IVP to delineate the point and hopefully cause of an obstruction. If there is good renal function, the IVP will generally be successful in answering these questions. If there is reduced renal function due to a long-standing obstruction, or for other reasons, the IVP may not provide sufficient visualization of the collecting structures to define the etiology of the obstruction. In these instances retrograde pyelogram is performed which, if technically successful, will usually define the point of obstruction. If the etiology is intrinsic to the urinary tract further studies are generally not necessary. If, however, the studies demonstrate what appears to be an extrinsic cause of the obstruction, computed tomography, with contrast if possible, is performed to look for evidence of mass lesions (Figure-8C) or fibrotic change. There is not always one "best" way to utilize the multiple studies available and it is often the results of a specific study that will determine if a further study is necessary and which modality to use. Although not used often at our institution, MRI urography can demonstrate both intrinsic and extrinsic abnormalities related to the urinary tract and is particularly helpful in those patients in whom contrast cannot be used.

Our approach to the patient with acute renal colic has changed over the past few years. Up until recently, these patients were evaluated with either ultrasound or an IVP as the initial study. This is no longer the case as we now use non-contrast spiral CT as the screening examination for flank pain and suspected ureteral stone. This is faster, more accurate and provides information regarding non-urologic causes of pain. In most cases, the non-contrast study will determine the presence and cause of obstruction, especially if due to a ureteral stone. If an obstruction secondary to a ureteral stone is identified and the stone is to be followed, we will often obtain an abdominal film for the purposes of follow-up. Unfortunately, only

approximately 70% of stones detected on CT scanning will be demonstrable on an abdominal film even in retrospect. If the obstructing stone cannot be identified on an abdominal film and follow-up imaging is necessary because of the patient's clinical course then either a follow-up non-contrast spiral CT or in some cases an IVP can be obtained to assess the persistence and degree of obstruction as well as the position of the stone.

If the non-contrast spiral CT shows no evidence of a ureteral stone but does show hydronephrosis or hydroureter, correlation is made with clinical findings to determine if this may represent passage of a stone prior to the CT scan. If this is the case, clinical follow-up will determine further imaging. Otherwise, IVP will be performed to evaluate for other causes of obstruction.

In children, our approach is somewhat different. Ultrasound is used as the primary screening tool for suspected obstruction. If hydronephrosis is demonstrated, a functional study such as a Lasix renogram is generally performed to evaluate the function of the two kidneys and the severity of the suspected obstruction. Further study would then depend on clinical consideration such as any need for surgical intervention.

In summary, multiple techniques exist for the evaluation of renal obstruction. Each patient must be evaluated on an individual basis with consideration of the acuity of obstruction and the special needs of the patient. Certain centers may not have access to helical CT scanners, nuclear medicine capabilities or a MRI. Techniques must be reliable and accessible to allow the clinician to follow the disease over time.

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PEYRONIE'S DISEASE

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ABSTRACT

Peyronie's disease can be considered an exaggeration of the wound repair process and is linked to penile trauma. Although a better understanding of the pathophysiology of the disease was achieved recently, the best alternative to treat the patients remains a dilemma. Pain, shortening, plaque and erectile dysfunction are clinical characteristics of this disease, and solution to patients complains should steer the therapy. Non-surgical treatment is offered to patients with pain, plaque or deformity of less than one year. Surgical treatment should be delayed until the process become stabilized. Surgery is indicated in patients with stable and severe deformity of more than one year of duration and for patients who have penile shortening, narrowing or indentation, or a combination of the above that preclude normal sexual intercourse. If the patient is also impotent and fails to respond to non-surgical treatment, we recommend a penile prosthesis insertion.

Key words: penis; penile induration; Peyronie's disease; impotence

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INCIDENCE AND BACKGROUND

Peyronie's disease (indurato penis plastica) is characterized by the formation of fibrous plaques within the tunica albuginea. In 1561, Fallopius first reported the disease, which later bore the name of the surgeon to King Louis XV of France, Francois Gigot De la Peyronie, who popularized the disease entity in 1743. Peyronie's disease is estimated to affect 0.4 to 3.5% of adult male patients worldwide (1-4). Autopsy studies have suggested a much higher incidence of subclinical plaques or fibrotic lesions noted in the penis. These plaques impede expansion of the tunica during erection resulting in penile bending. In some extreme cases, these plaques may induce a collar-like or an hourglass-like appearance in the erect penis with dense calcified areas.

Peyronie's disease has been reported to occur in association with Dupuytren's contractures, plantar fascial contractures, tympanosclerosis as well as trauma, urethral instrumentation, diabetes, gout, Pagets' disease, and the use of beta-blockers (5). This condition can occur in a familial pattern (6). There is

a 10 to 40% chance that the descendent of a patient with Dupuytren's contracture will develop that problem, and a 15% chance that a man so afflicted will develop Peyronie's disease.

Contemporary thinking suggests Peyronie's disease represents a localized aberration of the wound healing process. Pathologically, Peyronie's plaques begin with fibrin deposition and end up like scars. Clinical data, anatomical pathology, and bioengineering analysis all implicate trauma as an initiation factor in Peyronie's disease (7,8). Fibrin deposition is recognized as one of the initial consequences of microvascular injury, and it may be the precursor to Peyronie's plaque formation (9).

The search for a genetic link for Peyronie's disease has yet to identify a genetically predisposed population. However, there are reports associating this condition and Paget's disease of the bone, Dupuytren's contracture, and specific HLA subtypes (6,10-12). Studies of Peyronie's patients have implicated an autoimmune component (13,14). It is likely that a certain proportion of men in this age group respond to mechanical tunical stress and microvascular trauma

with an aberrant or hyperactive wound healing response (7,8,15,16). Thus, there may be a subpopulation whose genetic background is such that response to wound healing predisposes development of Peyronie's plaques.

PATHOLOGY AND BASIC SCIENCE

Pathologically, Peyronie's disease is associated with perivascular round cell infiltration, which can be found within the tunica albuginea (17). Fibrin deposition, presumably from microvascular injury, has also been found in relation to Peyronie's plaques, but not in normal or scarred tunica from individuals without Peyronie's disease (9). Plaques consist of dense collagenous connective tissue with reduced and fragmented elastic fibers. In about one third of patients, radiologically or sonographically demonstrable dystrophic calcifications are present (18). The scar tissue of Peyronie's disease contains excessive amounts of type III collagen, which renders it particularly responsive to the wound contraction process (19).

One of the most likely causes of Peyronie's disease may be repeated tunical mechanical stress and microvascular trauma. Excessive bending during erection or blunt trauma to the erect penis may result in bleeding into the subtunical spaces or tunical delamination at the point where the septum integrates into the inner circular layer of the tunica albuginea (7,8,15). Such microvascular trauma may come from sexual intercourse; either with the woman on top or an accident during penetration where the man misses the vagina and injures the penis. Microvascular trauma or subtunical bleeding can result in fluid and fibrinogen in the subtunical layers. The resulting fibrin deposits may be key in the initiation of a wound healing response, which encompasses pain, hematoma, and subsequent inflammatory response with recruitment of macrophages and neutrophils (9,16,20). These cells, in response to clot formation, release a variety of cytokines, autocoids and vasoactive factors, which may precipitate a fibrotic reaction. The unique anatomy of the tunica albuginea with its multiple sublayers of dense fibrous tissue and hypovascularity may «trap» the inflammatory reaction. This may pro-

long the process to months or years and therefore foster the formation of Peyronie's plaque.

There has yet to be a detailed examination of the cell types involved in the pathogenesis of Peyronie's disease. Transforming growth factor-b1 has a pleotropic effect on fibroblast function by increasing transcription and synthesis of collagen, proteoglycans and fibronectin while also increasing synthesis of tissue inhibitors of collagenase, which prevents connective tissue breakdown. A role for TGF-b1 has been proposed in the pathogenesis of Peyronie's disease (21-23). Finally, in the later stages of healing, the connective tissue is remodeled by specific collagenases and proteases. In Peyronie's disease, defects in overproduction of collagen and other tissue remodeling mechanisms may result in an inability to resolve the injury and in plaque formation.

NATURAL HISTORY AND PRESENTATION

In most cases, onset is associated with an active phase, consisting of painful erections, a palpable plaque and bending of the penis. Up to a third of patients with Peyronie's disease present with painless curvature. Whether the onset of deformity associated with the active phase is gradual or sudden, pain usually resolves and the pathologic process itself seems to stabilize after 12 to 18 months. A relatively quiescent secondary phase follows, which is characterized clinically by painless stable deformity, and pathologically by mature scar. Earlier report characterized Peyronie's disease as a process of gradual spontaneous resolution (24). More recent data do not support the above conclusion (25). Painful erection almost always resolves with time; penile deformity usually does not.

The reported incidence of erectile dysfunction in Peyronie's disease is variable. Bystrom & Rubio reported that 52% of 106 patients had coital difficulties and 17% had poor penile rigidity distal to the plaque (26). However, only 8% of patients described coital difficulties at the initial presentation suggesting that this was probably a late feature of the disease. Stecker & Devine found abnormal nocturnal penile tumescence in 29% of patients with Peyronie's disease with suspected organic impotence although

in only 5% of patients could the Peyronie's disease plaque be the sole cause of the dysfunction (27). Other series have reported an incidence of erectile dysfunction of 19% (28). Amin et al. discovered that out of 208 patients investigated routinely by color Doppler ultrasound for erectile dysfunction, 20% had undiagnosed Peyronie's disease (29).

It is clear, therefore, that erectile dysfunction in Peyronie's disease is common and is usually due to 1 or more of 4 factors; psychological or performance anxiety, severe penile deformity, a flail penis, or impaired penile vascular function (30). The deformity of the penis may be so severe that penetration is difficult, painful or impossible. This is more likely to occur if the deformity is in a ventral or lateral direction, where deviation from the normal angle of vaginal entry is maximal. There is a small group of patients with extensive Peyronie's disease who have circumferential plaques and a degree of cavernous fibrosis causing a flail penis. Tumescence is absent from this segment and if extensive it may result in a hinge effect and an unstable penis. Erectile dysfunction may be due to concomitant vascular disease that occurs in 30% of patients with Peyronie's disease (31) or to veno-occlusive dysfunction (32,33). Most studies have used both color Doppler ultrasound and cavernosometry to investigate the impaired erection in Peyronie's disease. Lopez & Jarow showed that out of 76 patients, 36% had arterial disease and 59% had veno-occlusive dysfunction (34). Others have also suggested there is a mixture of arteriogenic and venogenic factors (33,35). It is thought that the venous leakage may occur through the emissary veins that pass near the Peyronie's plaque into the dorsal vein of the penis. The reduced compliance of the tunica albuginea of the plaque prevents the normal compression of these veins during erection and therefore does not compress the venous channels.

Peyronie's disease typically presents with one of the following 4 complaints: painful erection, penile deformity or shortening during erection, presence of a plaque or induration on the shaft of the penis, or erectile dysfunction. Almost all patients have either a well-defined plaque or an area of induration that is palpable on physical examination which 38-62% of the patients are unaware of (26,28,36,37). The plaque is usually

located on the dorsal surface of the penis with a corresponding dorsal penile deformity. Lateral and ventral sited plaques are not as common but result in more coital difficulty, as there is a greater deviation from the natural coital angle. Penile pain may be present with erection or during sexual intercourse. The pain is not severe in nature but may interfere with sexual function. Spontaneous improvement in pain usually occurs as the inflammation settles.

DIAGNOSIS

Peyronie's disease is usually apparent by patient history and physical examination. The medical history should include time and mode of onset (sudden or gradual), course of disease (stable or progressive), history of penile surgery, urethral instrumentation or trauma, medication or drug abuse and family history of Peyronie's disease or Dupuytren's contracture. Risk factors for erectile dysfunction should also be obtained.

A detailed psychosexual history should include penile rigidity during erection, shortening, induration, hourglass constriction, or pain with or without erection. Other important information should also be determined such as ability to have intercourse, adequacy of erection (rigidity and duration), frequency of intercourse, libido, and psychological impact. A photograph of patient's erect penis to identify the extent, direction, and character of erectile distortion is helpful.

Examination of the penis is facilitated by its gentle stretching. This will help identify the size, location and consistence of plaques which may be helpful in determine the stage of the disease and monitoring its progression. The patient should also be examined for the presence of Dupuytren's or plantar fascial contractures. Further diagnostic studies should include photography or drawing of the erect penis after intracavernous injection or vacuum erection device. The stretch length of the penis should also be documented.

Many patients have mild symptoms and reassurance, particularly that the palpable lump is not cancer, is all that is necessary. The majority of patients with Peyronie's disease may be managed with-

out vascular investigation. Penile curvature, especially in young patients, may cause severe psychological distress, which may need to be corrected. Patients usually give an accurate description of their deformity to within 10-20° (38,39). However, when planning a surgical correction of the deformity, documentation of the deformity during erection either by intracavernosal injection of a vasoactive agent or a vacuum device is very helpful.

When the site and size of the Peyronie's plaque needs to be assessed, ultrasound usually will suffice and is particularly helpful in monitoring the progress of medical treatment (2). Patients who also complain of impaired erections, further evaluation is essential. Color duplex sonography performed before and after intracavernous injection of a vasoactive agent allows for assessment of the structure of the corpus cavernosum, tunica albuginea and the cavernous arterial and venous function (40). Color duplex ultrasound is also excellent in detecting collateral arterial connections between dorsal, cavernosal and spongiosal arteries. Dynamic infusion cavernosometry can be used as an adjunct to duplex ultrasound to confirm the diagnosis of veno-occlusive dysfunction (41). Finally, in rare cases MRI can be used for detailed evaluation of penile anatomy prior to surgical intervention.

During the evaluation of patients with Peyronie's disease, other causes of bending and induration of the penis must also be considered. These differential diagnoses include: congenital curvature of the penis, chordee with or without hypospadias, penile dorsal vein thrombosis, cavernosal fibrosis secondary to local trauma, leukemic infiltration of the corpora cavernosa, ventral curvature secondary to urethral instrumentation, benign or malignant primary or secondary tumors, late syphilitic lesion, and penile infiltration with lymphogranuloma venereum.

NON-SURGICAL TREATMENT

The initial approach to treatment should be conservative. Many patients with a minor curvature and normal erectile function can be given reassurance with no invasive diagnostic tests or treatments. Medical management is indicated for patients with a

greater degree of curvature or symptoms. Non-surgical treatments can be divided into systemic, local, or intra-lesional therapies.

Vitamin E is a commonly used oral therapy for Peyronie's disease. In 1948, Scott & Scardino (42) reported a beneficial effect on treatment of 23 patients with vitamin E, a tocopherol with antioxidant properties. The proposed dose was 200 to 300 mg per day. In 1990, Gelbard et al. compared the effects of the vitamin E treatment and natural progression of the Peyronie's disease (25). They noted no significant differences between the 2 groups with respect to pain, bend, ability for intercourse, and over-all perception of disease progression. At this time however, vitamin E continues to be the primary mode of treatment due to its mild side effects and low cost, despite the lack of controlled study showing its benefits.

Potassium aminobenzoate (Potaba) has been studied for the oral treatment of Peyronie's disease (43,44). Its mechanism of action, though not well understood, is decreasing fibrogenesis by decreasing serotonin through increased tissue utilization of oxygen and increased activity of monoamine oxidase. The most extensive review of this therapy of 2653 patients has found it to be successful in 57% of patients (45). The dosage is 20 grams a day for 3 months. Due to Potaba's modest results in literature, relatively high cost, and high side effect, enthusiasm for the use of this medication is cautiously guarded.

Several small, uncontrolled, short-term reports suggest mild to moderate benefit using oral Tamoxifen (46). It has been suggested that Tamoxifen facilitates the release of transforming growth factor-beta (TGF- β) from fibroblasts (47). TGF- β has been shown to play a central role in regulating immune response, inflammation and tissue repair by deactivating macrophages and T lymphocytes. Tamoxifen results in a reduced inflammatory response and, therefore, diminished angiogenesis and fibrogenesis (48). Tamoxifen dosage is 20 mg twice a day with minimal reported side effects of gastrointestinal distress and alopecia.

Colchicine therapy is the most recently reported oral therapy for Peyronie's disease. Akkus et al., in an uncontrolled study, showed a decrease in plaques size and an improvement in penile curvature

in approximately 50% of the 24 patients they treated (49). The main side effect of colchicine is gastrointestinal upset with diarrhea reported in 33% of subjects. Recommended dosing is 0.6 to 1.2 mg daily during the first week of treatment followed by an increase to 1.8 to 2.4 mg for three months. Colchicine is an anti-microtubular agent, which inhibits the proliferation of inflammatory cells and fibroblasts. It can also increase collagenase activity and reduce collagen synthesis (50-52). We currently use colchicine as our first line agent in the treatment of acutely acquired Peyronie's disease.

Based upon anti-inflammatory properties, as well as decreased collagen synthesis by unclear mechanisms, steroids have been used as an intralesional therapy for Peyronie's disease. Several short-term non-controlled subjective studies have reported good responses using various steroids (37,53-55). Nevertheless, we do not recommend intralesional steroids in the treatment of Peyronie's disease. This type of therapy has many local side effects including local tissue atrophy and skin thinning while offering only an inconsistent improvement in well-established curvature. Steroid injections ultimately make surgery more complex due to the difficulty in subsequent separation of tissue planes.

In a randomized placebo controlled study, purified intralesional clostridial collagenase was shown to have some benefit over placebo for mild to moderate degrees of Peyronie's disease. In more severe curvature however, the response to treatment was not statistically significant (56). Its mechanism of action is via altering collagen content of penile plaque. This drug is currently being evaluated for approval for use in the United States of America.

Orgotein, an anti-inflammatory metalloprotein with pronounced superoxide dismutase activity, has been used by several groups in Europe (57-60). Reports of subjective benefits are as high as 80-90%. It is not available in USA and has been taken off the market in several European countries due to its significant toxicity.

The potential use of interferons as an intralesional therapy for Peyronie's disease has been demonstrated (61). In fibroblasts derived from Peyronie's plaques, the addition of interferons decreased the rate of proliferation in a dose-dependent

fashion, decreased the production of extracellular collagen, and increased the production of collagenase. Several clinical trials of intralesional interferon for Peyronie's disease have been published (62-64). Objective improvement in deformity was considered small with mean improvement of 20 degrees. Patients with small plaques (< 4 cm) were more likely to have a better response. All patients experience brief influenza-like side effects.

The calcium channel blocker verapamil was first reported as an intralesional therapy by Levine et al. and Rehman et al. (65-67). Penile shaft narrowing, decreased in 100% of patients, but curvature improved in only 42%. Fifty-eight percent reported that their sexual performance had improved. Overall, 83% noted that the disease had arrested or improved with no recurrence of symptoms or deformity within the eight months follow-up period. Verapamil and other calcium channel blockers affect cytokine expression associated with early phases of wound healing and inflammation and increase the proteolytic activity of collagenase (68). Matrix remodeling is enhanced by human fibroblasts in burn scars and vascular smooth muscle cells in vitro (49,69). Goals of this treatment are to stabilize disease process and reactivate a more normal remodeling process, yielding gradual improvement in deformity. Multiple doses, 10 mg injected every 2-4 weeks for 12 weeks, are given over time. The main side effect is ecchymosis. This is currently the most frequently used intralesional therapy for Peyronie's disease.

Iontophoresis was examined as a means of enhancing topical delivery of verapamil (10 mg) and dexamethasone (4 mg) with a local electric field in 15 patients with Peyronie's disease. At 5 months follow-up, penile pain resolved in 66%, curvature improved in 53% and plaque size reduced or softened in 40% of cases (70). Local penile lithotripsy has also been proposed as topical therapy for Peyronie's disease with limited numbers of patients reporting subjective results (71). The rationale for this approach is not known. Topical verapamil cream has also been advocated for Peyronie's disease. However, we cannot comment on its use because of the lack of analyzable data.

Overall, therapeutic advances in Peyronie's disease have not resulted in a reliable cure. This may

be due to an incomplete understanding of the basic pathophysiology of this disease and the lack of an animal model for study. Recent advances in the understanding of disorders of wound healing have allowed forward strides in the understanding of this disease and offer new therapies, such as the injection of calcium antagonists and interferon. Recent reports of the involvement of TGF- β in human Peyronie's disease and the induction of Peyronie's like condition by injecting TGF- β into the rat's tunica albuginea may help provide a new strategy in combating the disease.

SURGICAL TREATMENT

The indications for surgical correction include: severe curvature, narrowing, or indentation of more than one year's duration, sexual difficulty or partner discomfort because of deformity, or severe penile shortening. Surgical correction of penile curvature is reserved for those who fail conservative measures. There is a considerable variation in the deformity that makes penetration difficult. In young men particularly with congenital deformities the bend causes more psychological distress than physical disability and it may be necessary to correct curvature as little as 20-30 degrees. In contrast, an older man with a stable relationship and partner is better able to cope with a more severe degree of deformity. Of note, a ventral deformity causes more difficulty in vaginal penetration than a dorsal or lateral one.

Prior to surgery, a detailed evaluation of penile vascular and erectile function is highly recommended. Reconstructive surgery is not recommended in the acute phase of the disease. In the past, many penile implants have been performed in patients with normal penile rigidity to treat severe curvature. In the current era, penile implants should be reserved for Peyronie's patients who have severe erectile dysfunction that does not respond to non-surgical erectile dysfunction therapy. The surgical treatments for penile curvature are classified into 3 different categories: tunical shortening procedures, tunical lengthening procedures, and prosthetic procedures.

Shortening procedures are reconstructive techniques performed on the convex surface of the

penis at the site opposite to the penile plaque. These procedures are the easiest to perform and require the least expertise. Patient selection is extremely important. Shortening procedures are most appropriate for patients with useful erections, adequate penile length, and without hourglass deformity. Reed Nesbit first described the correction of congenital erectile deformities by shortening the opposite side of the penis by the excision of an ellipse of tunica albuginea (72). The Nesbit technique was re-introduced for Peyronie's disease in 1979 (73). In a review of 359 men operated upon between 1977 and 1992, 295 (82%) had good results and were able to have intercourse after correction with this technique (74). A literature review has confirmed these favorable results (30). The overall results of the Nesbit procedure have improved in the operations performed after 1985. This is thought to be due to better patient selection (74). With increasing time after the operation, there is a decrease in satisfaction with the results of the Nesbit procedure. The most common complication of this procedure as with all shortening procedures is loss of penile length. This complication, however, does not preclude the great majority of men from having sexual intercourse. Others complications reported include erectile dysfunction, penile hematoma, penile narrowing or indentation, urethral injury, herniation, suture granuloma, numbness and phimosis (74).

A modification of the Nesbit procedure was described by Lemberger et al. (10) and further refined by Yachia (75). The approach is similar to the Nesbit procedure but instead of removing an ellipse of tunica, a long longitudinal or multiple smaller longitudinal incisions are made in the corpora cavernosa. These incisions are then closed horizontally in a Heineke-Mikulicz fashion in order to correct the angle of penile curvature. Many authors claim a high percentage of good results with this technique reporting satisfaction rates between 79-95% (10,75-81). The complications of this procedure are similar to those reported for the Nesbit technique.

Wedge resection or incision of the tunica requires extensive dissection of the neurovascular bundle or the corpus spongiosum. A simplified approach for correcting penile curvature is to perform

plication on an erect penis produced by intracavernous injection of papaverine or alprostadil (82). Plication is a simple, outpatient procedure, which takes approximately 30 minutes under local anesthesia. Tissue incisions or removal or dissection of the neurovascular bundle or urethra is not necessary (Figure-1). Some authors described high recurrence rates and poor results with prolonged follow-up. The literature reports significant variation in results ranging from 38-100% satisfactory results (83-87). Gholami et al. recently reported 98% satisfaction rate with over 90 patients

followed for one to five years (88). Complications of plication surgery include loss of penile length, phimosis, penile narrowing, erectile dysfunction, suture granuloma and palpable suture lumps on penis (85,86,89).

Tunical lengthening procedures use reconstructive techniques to correct penile curvature while restoring the length of the curved, shortened penis. This surgery is performed on the concave, diseased side of the penis and requires plaque excision or incision with grafting. Lengthening of the tunica with graft place-

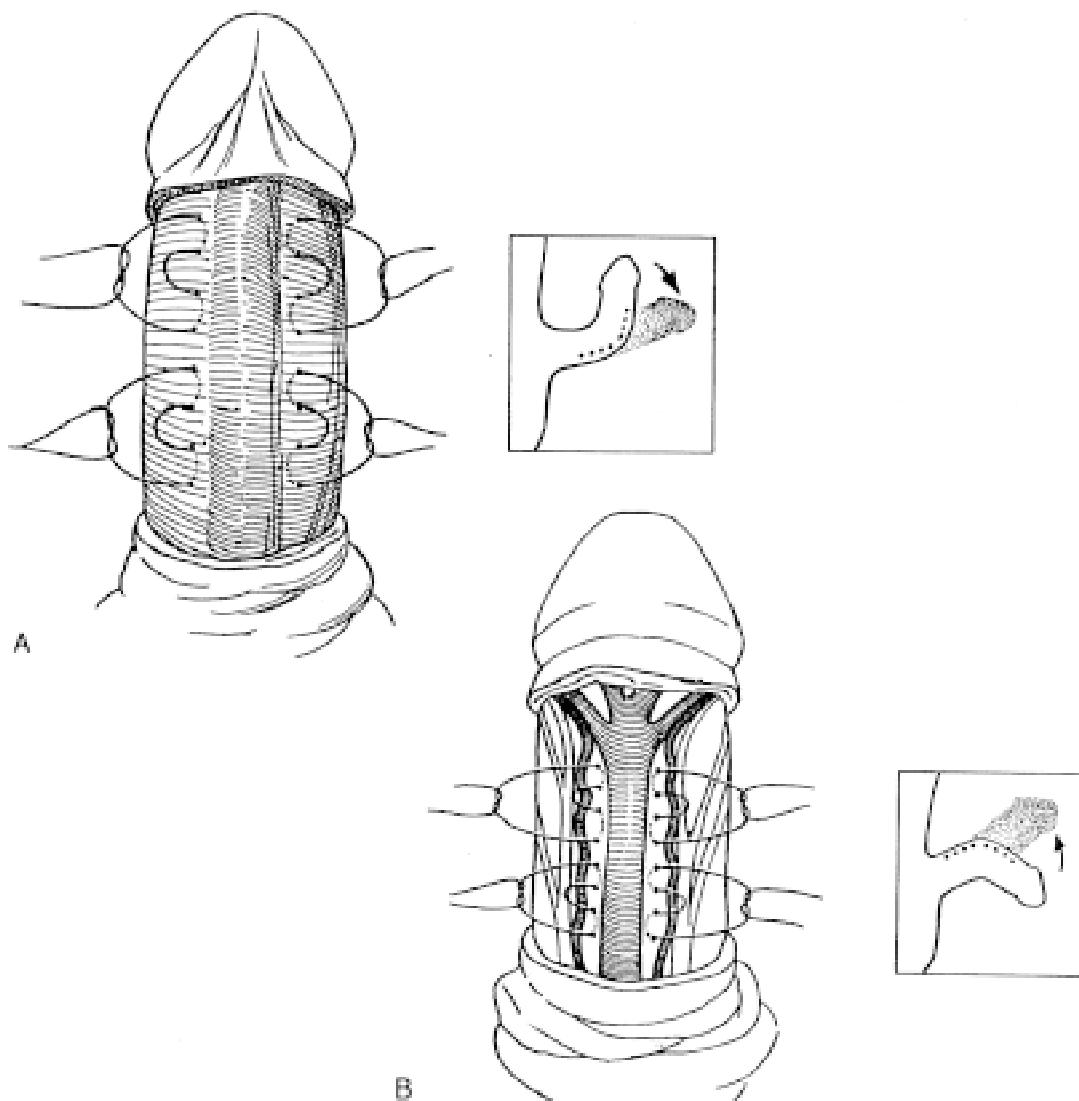


Figure 1 - Plication procedures performed on a papaverine induced erect penis. Dissection of neurovascular bundles is not necessary. The location of paired non-absorbable plication sutures is shown. A)- Perispongiosal for dorsal curvature; B)- Between dorsal vein and dorsal arteries for ventral curvature. The suture entry sites are marked with a marking pen before suture placement. (ref. 82).

ment is indicated in patients with severe curvature resulting in a shortened and deformed penis with penile narrowing or hourglass deformities. Lengthening can also be done on patients that present with recurrent curvature after other surgical procedures. These procedures are the most difficult to perform and require the greatest expertise. Few investigators have experience with more than 50 patients. The replacement of diseased tunica albuginea in Peyronie's disease was largely unsuccessful until the use of dermal graft first described by Bystrom & Rubio (26) in Scandinavia and by Devine & Horton (90) in the United States.

Subsequently, many autologous tissues (temporalis fascia, dura mater, tunica vaginalis and dorsal or saphenous vein), cadaveric tissue (dermis, fascia or pericardium) and synthetic materials (Dacron and Gortex) have been used with different results. Excision of the plaque has been the standard approach. However, it is now known that the pathologic process of Peyronie's disease extends far beyond the plaque and removing a large area of tunica albuginea may impair erectile function (90-92). A review of the literature shows that there is great variability in the outcome of plaque excision with the most common problem being erectile dysfunc-

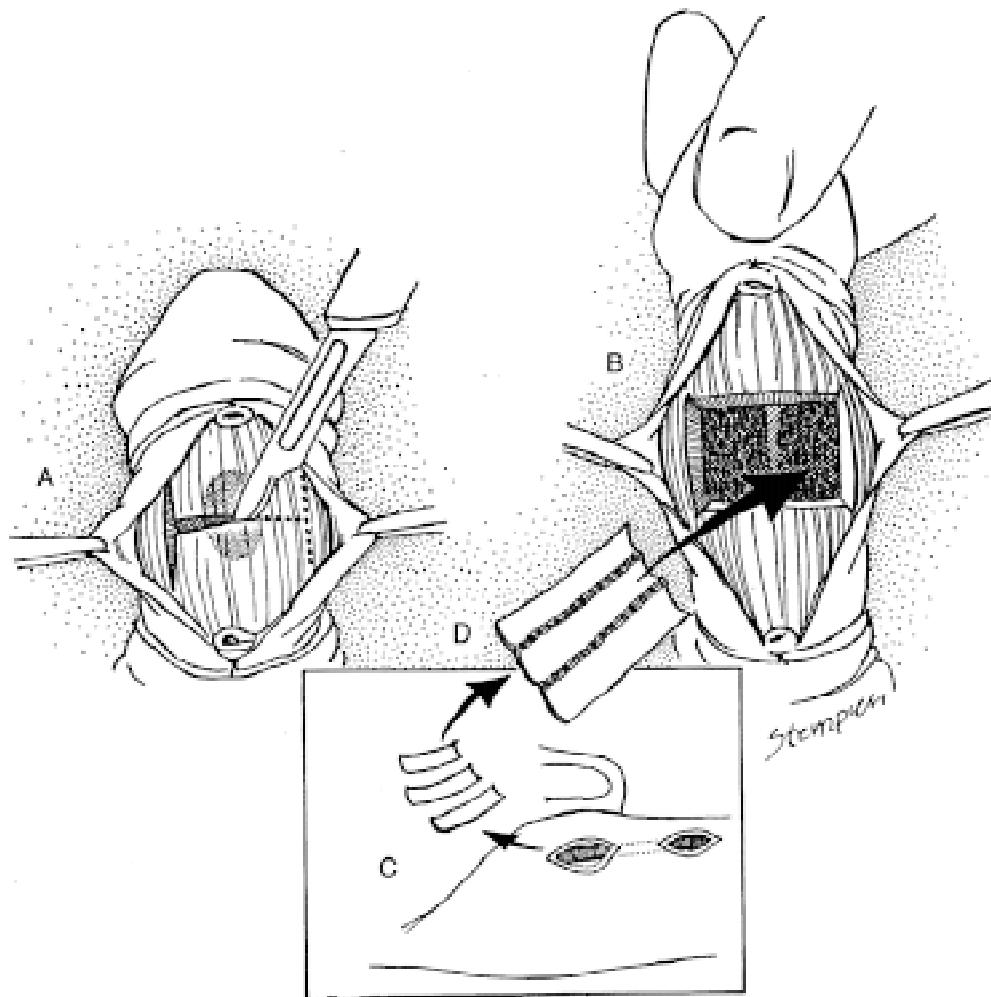


Figure 2 - H-incision and saphenous vein grafting. A)- Dissection of neurovascular bundles (medial to lateral) with tenotomy scissors under 3x or 5x magnification loupes. B)- H-shaped transverse relaxing incision in center of plaque for correction of penile curvature; C)-The tunical defect is measured by stretching the penis longitudinally and transversely; D)- A segment of saphenous vein is resected, opened, cut into several pieces and stapled together with vascular clips. The vein graft is sutured to the tunical defect with the endothelial surface facing the inside of the corpus cavernosum (ref. 96).

tion (26,32,92). Due to the high incidence of erectile dysfunction, contracture of the graft, late recurrence and poor long terms results, the excision of the plaque and grafting is less performed today (93).

In 1991, Gelbard & Hayden (94) proposed plaque incision and grafting rather than excision, decreasing some of the complications of excising the tunica albuginea. The less the tunica and its underlying erectile tissue are altered, the better the postoperative erectile rigidity. No perfect graft material has been described for replacing the diseased tunica albuginea. Lue et al. report on their experience with the use of saphenous vein graft in 112 patients with Peyronie's disease (Figure-2). Successful straightening was accomplished in 95% of the patients with 13% of potent men complaining of decrease in erectile function (95,96).

Patients with Peyronie's disease and impotence, which does not respond to medical management, are usually treated with penile prostheses with or without excision or incision of the plaque. Literature review (91,93,97,98) shows excellent results provided men have realistic expectations. Although there may be some intrusion of the plaque on the corporal bodies, this usually does not cause any difficulty in the implantation. Historically, a penile prosthesis would be performed on any patient who had a penile deformity but without erectile dysfunction. With advances in the medical treatment of erectile dysfunction, prosthesis surgery is now reserved as the final treatment option or in those with severe erectile dysfunction. In most patients with mild to moderate curvature, insertion of a penile prosthesis tends to straighten the penis and no additional procedures are necessary. However, in cases of severe deformity, incision and grafting the diseased tunica albuginea with synthetic material grafts or cadaveric tissue may be necessary during prosthesis placement. The use of operative molding of the penis over the prosthesis is helpful in order to give good correction of the deformity (99).

CONCLUSION

Peyronie's disease remains one of the most perplexing diseases in urology. With continued basic research in wound healing and scarring, our under-

Table 1 - Non-surgical treatment: oral therapy.

Placebo Control	N Patients	Dose	Mean Follow-up	Pain Improvement	Curvature Improvement	Plaque Size Reduction	Side Effects
Vitamin E N	23	200-300mg/d	9 mo.	12/12 (100%)	18/23 (18%)	21/23 (91%)	None
Vitamin E Y	59	NR	NR	NSD	NR	NR	None
PABA N	2653	12g/d x3 mo.	NR	NR	NR, 53% subj. improvement	NR	Anorexia, N/V
PABA N	32	12g/d x3 mo.	8-24 mo.	8/18 (44%)	18/31 subj.(58%)	18/32 subj.(56%)	GI
Tamoxifen N	36	20mg bid x3 mo.	6 w	16/20 (80%)	11/31 obj.(35%)	12/35 obj.(34%)	Dec. libido, flush., dec. ejac. vol.
Colchicine N	24	0.6-2.4mg incr. dose qd	2-5 mo.	7/9 (78%)	7/19 subj. (37%)	12/24 obj.(50%)	Diarrhea, liver toxicity, nausea

NR = Not recorded, NSD = No Significant Difference, NA = Not Available

Modified from Lue et al. (100)

Table 2 - Non-surgical treatment: intralesional therapy, topical, iontophoresis.

	Placebo Control	No. Patients	Dose	Mean Follow-up	Pain Improvement	Curvature Improvement	Plaque Size Reduction	Side Effects
Dexamethasone	N	21	0.4% qmo x6 months	NR	86%	76% subj.	76% subj.	Ecchymosis
Triamcinolone	N	45	2mg q6 wks x6 injections	4 years	17/45 (38%)	NR	14/45 (31%)	NR
Collagenase	N	31	470-2370 u injection	9.8 mo	13/14 (93%)	16/31 (52%)	20/28 (71%)	Ecchymosis, corporeal rupture None
Orgotein	N	22	4mg qmo x6	NA	19/22 (86%)	NR	NR	
Orgotein	N	18	8mg qmo x8	N/A	15/15	7/18 (39%)	NR	Severe hypotension
Verapamil	N	14	10mg q2 wks x12 weeks	8 mo.	91%	42% subj.	30% obj.	Ecchymosis
Verapamil	N	38	10mg q2 wk x12 inj.	2 weeks	97%	76% subj. 54% obj.	23% obj.	Decreased sensation, hematoma
Verapamil	Y	14	10mg qwk x6 mo.	3 mo.	NR	NSD	NSD	Ecchymosis
Interferon	N	25	1 M IU qwk x5 weeks	6 mo.	24/25 (96%)	1/25 (4%)	7/25 (28%)	Influenza-like symptoms
Interferon	N	10	1.5 M IU qod x3 weeks	6 weeks	60%	60% subj 60% obj.	30% obj.	Influenza-like symptoms
Iontophoresis Verapamil and Dexamethasone	N	15	Verap - 10mg Dexam - 4mg 20 min qod x3 weeks	5 months	66%	53%	40%	NR

NR = Not recorded, NSD = No Significant Difference, N/A = Not Available

Modified from Lue et al. (100)

standing and management of this frustrating disease will improve. Initial treatment of Peyronie's disease should be conservative with expectant therapy and medical management. Once the penile curvature and plaque have stabilized, patients with severe deformity may be offered surgery depending on their symptoms and complaints. Patient selection is key to proper treatment. Less experienced surgeons should limit themselves to medical management or simple surgical management of the disease including plication or Nesbit procedures. Tunical lengthening procedures or complicated penile prosthesis should be reserved for surgeons with familiarity and expertise in this type of reconstruction. Education of the pathogenesis and natural history of the disease will allow the patient and his partner to make an informed decision in regards to his treatment options and expected outcomes.

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TELOMERASE ACTIVITY IN LOCALIZED PROSTATE CANCER: CORRELATION WITH HISTOLOGICAL PARAMETERS

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ABSTRACT

Objective: Telomerase is an enzyme responsible for lengthening the telomere, active during the embryonic development and detected, in the adult life, only at low levels in germinative cells and some stem cells. Tumor cells need to be immortalized and the reactivation of telomerase activity, or alternative mechanisms for lengthening the telomeres is necessary for tumor progression. Some studies have correlated telomerase activity with bad prognostic parameters in prostate cancer. Our objective is to detect telomerase activity in invasive prostatic adenocarcinoma and to correlate its presence with the stage, histological differentiation, and volume of the cancer in radical prostatectomy specimens. As well as in PIN adjacent to the cancer.

Material and Methods: Tissue samples from 75 patients submitted to radical prostatectomy for localized prostate cancer were studied using the telomeric repeat amplification protocol (TRAP).

Results: Telomerase activity was detected in 29% of 21 high grade PIN and in 80% of 54 invasive cancer. There was no statistically significant difference between the telomerase-positive and telomerase-negative groups in Gleason grade, tumor volume or tumor stage.

Conclusion: We conclude that telomerase activity is common in prostate cancer and may appear early in the development of the disease. Its presence is unrelated to classical prognostic parameters.

Key words: prostate; prostatic neoplasia; prognosis; telomerase

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INTRODUCTION

The enzyme telomerase is important for the immortalization of cancer cells because it maintains the telomeres (1). Telomeres cap the ends of chromosomes and protect the DNA from recombination, fusion, and loss of terminal sequences during replication. They consist of tandem repeats of a G-rich sequence (TTAGGG in vertebrates) up to 15 kilobases long (2). With each round of DNA replication the telomeres become 100 base pairs (bp) shorter because the RNA primers that initiate polymerization of a new DNA at the 3' single strand tail are then degraded, leaving a gap that is never filled in (3). When the telomere reaches a critical length, a

cell becomes senescent and unable to divide. If the cell is forced into mitosis by an oncogene, the complete loss of the telomeres results in massive fusion of chromosomes, and the cell dies by apoptosis. This mechanism, which is called the mitotic clock, has been implicated in the control of cell proliferation, and is believed to work as a tumor suppressor (4).

Telomerase, an enzyme capable of elongating telomeres, was discovered in 1985 (5). It is a ribonucleoprotein composed of an RNA primer (3'-CAAUCCCAAUC-5'), that hybridizes with the end of the telomere, and an enzyme with reverse transcriptase activity (5). Telomerase is normally expressed only by germ cells and, at low levels, by some stem cells; it is repressed in somatic tissues (6).

The maintaining of telomere length by the re-expression of telomerase has been described in more than 85% of malignant human tumors (1), as well as other alternative mechanism for it (7), and it is considered an essential step in tumor progression, promoting cell immortalization.

The re-expression of telomerase is believed to be one step in the transformation of benign prostatic epithelium to prostatic intraepithelial neoplasia (PIN) and has been detected in 16% of the cases (8), as well as in benign prostatic hyperplasia (BPH) adjacent to invasive adenocarcinoma (9,10).

There is no definitive prognostic parameter for prostate cancer. Histological differentiation, tumor volume, tumor stage, and DNA ploidy are important for prognosis, but some cases behave unpredictably. This lack of predictability is inconvenient when different therapeutic approaches should be considered (11,12). If telomerase has a role in prostate cancer, perhaps its detection could be useful for prognosis.

We wanted to determine the frequency of telomerase expression in samples of PIN and invasive cancer from 75 prostate cancer patients submitted to radical prostatectomy, and to examine the relationship of telomerase expression to prognostically important tumor characteristics (stage, histological differentiation, and tumor volume). To this purpose, we used the telomeric repeat amplification protocol (TRAP) (13), a very sensitive method based on a polymerase chain reaction, to detect telomerase activity.

MATERIAL AND METHODS

Seventy-five patients with prostate cancer, clinically staged T1c-T2 were submitted to radical prostatectomy at the Sirio Libanes Hospital from March 1998 to March 1999. Immediately after the gland was removed it was sent to the laboratory, and a thin, 1-cm² square fragment of glandular tissue was frozen at -80°C in liquid nitrogen. After this, the prostate was fixed in formalin for 4 hours, surgical margins were stained with India ink, and the whole gland, including the bladder neck and prostatic apex,

was submitted for pathological evaluation of surgical margins and extraprostatic infiltration. Serial 3-mm cuts were taken from each prostatic lobe. The seminal vesicles and pelvic lymph nodes were also submitted, and cuts were examined for tumor involvement. Extraprostatic infiltration was defined as tumor infiltrating the adipose tissue or neurovascular plexus. The Gleason score was used for histological classification. The tumor volume was evaluated as described by Humphrey et al. (1). Briefly, a grid was placed below the slides, on which the area involved by the tumor had been previously sketched out. The percentage of tumor on a slide was determined by dividing the number of squares involved by tumor by the number of squares occupied by the whole section on the slide. Tumor volume was defined as the mean percentage of tumor in the prostate gland (the percentage of tumor on each slide divided by the number of slides from the prostate gland). Tumors were staged according to the TNM classification (1992) (15).

Before telomerase activity was assessed a section of the frozen prostate fragment was stained with hematoxylin and eosin and examined microscopically by the pathologist in order to confirm the presence of invasive cancer or PIN. Ten 10-μm sections of the frozen prostate fragment were cut in a cryostat and used for the telomerase assay.

The TRAPeze Telomerase Detection Kit (Intergene, Purchase NY, USA) and the methods described in the kit were used for detection of telomerase activity. To extract RNA and protein, the samples were incubated for 30 minutes on ice in 200 μL of CHAPS (3-[(3-cholamidopropyl) dimethylammonio]-1-propanane sulfonate) lysis buffer (10 mM Tris-HCl, 1 mM MgCl₂, 1 mM EGTA, 0.1 mM benzamidine, 5 mM β-mercaptoethanol, 0.5% CHAPS, and 10% glycerol) containing RNase inhibitor (RNAGuard®, Pharmacia Biotech, Uppsala, Sweden) at 200 units/mL. The samples were then spun in a microcentrifuge at 12,000g for 20 minutes at 4°C, and the supernatant was retained as the extract.

To detect telomerase activity, the TRAPeze kit follows the telomeric repeat amplification protocol (13), except that it does not require a wax

barrier hot start. For each sample, 2 µL of the RNA-protein extract was added to a 48-µL reaction mixture containing 10X TRAP Buffer (200 mM Tris-HCl, 15 mM MgCl₂, 630 mM KCl, 0.5% Tween 20, and 10 mM EGTA), 50X dNTP mix, TS primer (5'-AATCCGTCGAGCAGAGTT-3'), TRAP primer mix (RP primer, K1 primer, and TSK1 template), Taq polymerase (Amersham Pharmacia Biotech, Uppsala, Sweden), and distilled water. The reaction mixture also contained a 36-bp positive control to allow recognition of false negatives, which could result if an inhibitor of Taq-polymerase were present. All measures to prevent RNA degradation were taken. In a thermocycler block (Perkin Elmer GeneAmp Thermal Cycler 9600, Foster City, California, USA), a 30-minute incubation at 30°C was provided in which telomerase (if present) could hybridize with and extend the TS primer. Then a polymerase chain reaction was run for 30 cycles of 30 seconds at 94°C, 30 seconds at 59°C, and 30 seconds at 72°C to amplify the first extension, adding 6 base pairs per cycle.

To identify a positive or negative assay, 20 µL of the amplification product was submitted to electrophoresis for 2.5 hours at 200 V on a 10% nondenaturing polyacrylamide gel in 0.5X Tris-borate-EDTA (TBE) buffer was used. The gel was then silver-stained according to the method of Budowle et al. (16). Briefly, the gel was placed in 10% ethanol for 5 minutes, oxidized in 1% nitric acid for 3 minutes, placed in 0.012 M silver nitrate for 30 minutes, and reduced in a solution containing 0.28 M sodium carbonate and 0.019%

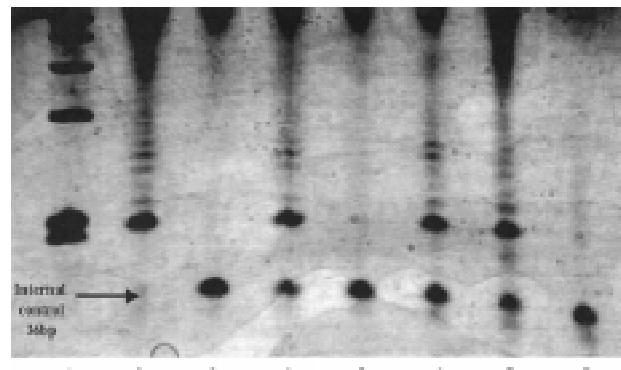


Figure - Detection of telomerase activity in extracts of invasive prostate cancer. Lane 1, ladder 50bp. Lanes 2, 4 and 6, show telomerase activity characterized by a ladder pattern with 6bp increment in bands. Lanes 3 and 5 show 2 negative cases. Lanes 7 and 8, have the positive and negative control, respectively.

formalin until bands developed. Placing the gel in 10% glacial acetic acid for 2 minutes stopped reduction, and the gel was then placed in distilled water. Samples that exhibited a ladder beginning at 50 bp with 6-bp increments were considered positive (Figure). Since the telomerase is a heat sensitive enzyme, the negative control is one tumor sample submitted to a heat treatment (85°C) for 10 minutes.

The relationship between stage and telomerase activity was analyzed with the Pearson Chi-square test. The Gleason score and tumor volume of patients with or without telomerase activity were compared using the Mann-Whitney test because of the non-normal distribution of the numbers. P-values less than 0.05 were considered statistically significant.

Table - Gleason score, tumor volume and tumor stage for carcinomas telomerase-positive and telomerase-negative.

	Telomerase-positive	Telomerase-negative	
Gleason score (median-range)	6.3 (4 - 10)	6.2 (4 - 9)	p = 0.733
Tumor volume % (median-range)	19 (0.3 - 56)	12 (0.7 - 53)	p = 0.193
Stage			
pT2	25 (58%)	7 (64%)	p = 0.990
pT3	18 (42%)	4 (36%)	

RESULTS

The pathological stage was pT2 for 49 (65%) patients and pT3 for 26 (35%) patients. Only one patient presented lymph node metastasis, and was staged T3cN1. The mean Gleason score was 6, and the median 5. Twenty-seven (36%) patients had high-grade tumors (Gleason ≥ 7), and 48 (64%) had low-grade tumors (Gleason ≤ 6).

For 21 patients the specimen submitted to the TRAP assay contained only high grade PIN. For the remaining 54 patients the assayed specimen contained only invasive adenocarcinoma.

Telomerase activity was found in 43 (80%) of the invasive cancer specimens. There was no correlation between Gleason score and Telomerase activity. The enzyme activity was positive in 81% (26/32) of well differentiated tumors (Gleason 4-6), in 80% (4/5) of Gleason grade 7 tumors and in 76% (13/17) of poor differentiated tumors. The results of telomerase activity detected in the invasive carcinoma and tumor stage, tumor volume and Gleason score are shown in Table. Telomerase activity was found in 6 (29%) of the PIN specimens. The characteristics of the invasive carcinoma adjacent to those PIN areas were: The median of Gleason score was 5 for either group, telomerase-positive and telomerase-negative. The median of tumor volume was 11% for telomerase-negative PIN and 3.5% for telomerase-positive PIN. Seventy three percent and 100% of telomerase-negative and telomerase-positive cases, respectively, were staged pT2. The presence or absence of telomerase activity in PIN did not correlate to the tumor stage ($p = 0.429$), tumor volume ($p = 0.310$) or Gleason score ($p = 0.619$) of the invasive carcinoma adjacent to the PIN lesion.

DISCUSSION

Our results show that the re-expression of telomerase occurs early in the development of prostate cancer, since we found telomerase activity in one third of the samples of PIN. Koeneman et al. (8) found telomerase activity in 16% of 25 cases of PIN, a frequency much lower than ours, that can be partially

explained by technical problems, since the authors, different from all previous studies, have found much lower telomerase activity in carcinoma, also (69%). They claim the presence of non- neoplastic cells, telomerase negative, interfering in the results, and suggest that the microdissection of the specimen could enrich the sample with tumor cells, telomerase positive, increasing the frequency of telomerase positive lesions. Currently there is no way to identify patients with PIN who will progress to invasive cancer or who already have invasive cancer that was not reached by the biopsy. We cannot assess from our study whether telomerase activity in a PIN specimen predicts prostate cancer, because all of our cases had invasive cancer. We can, however, point out that the absence of telomerase activity in a PIN specimen certainly does not rule out cancer elsewhere in the prostate gland.

Other cancer precursors, such as oral leukoplakias, express some telomerase activity, as does some normal lung tissue from lung cancer patients and its detection has been useful for surveillance of these patients (17,18). It has also been suggested that telomerase detection by the TRAP assay could be used for early detection of cancer in brushings, fine needle aspiration biopsy specimens, or voided urine (19-21).

Telomerase activity has been detected in 11% to 38% of biopsies containing only benign tissue (22,23). The presence of telomerase activity in BPH adjacent to cancer suggests that this information could be used to indicate patients who are more likely to have cancer elsewhere in the prostate or to develop it later. Since the TRAP assay is extremely sensitive, and can detect very few cells telomerase-active, we assume that the recovering of telomerase activity occurs previously to morphological alterations, and should be a marker for patients potentially vulnerable to develop prostate cancer.

Telomerase activity was detected in 80% of our invasive adenocarcinoma samples, and we were unable to correlate the re-expression of telomerase with the Gleason grade, tumor volume or tumor stage.

Telomerase activity has been reported in 84 to 90% of prostate cancer (9,10). Sommerfeld et al.

(9) who were the first to detect telomerase activity in prostate cancer described the presence of it in all lymph node metastasis and the absence of it in 4 cases with organ-confined disease, suggesting that there could be a relationship between telomerase activity and unfavorable prognosis. Lin et al. (10) unlike us were able to correlate telomerase activity with histological differentiation: they found telomerase activity in 38% of well-differentiated prostate cancers, and in 91% of poorly differentiated prostate cancers. Also, they found strong telomerase activity in metastatic prostate cancer in lymph nodes and bones. Our study is the larger and strictly standardized. We included only surgical specimen obtained by radical prostatectomy, performed by the same team (MS), examined by the same pathologists (KRML, LHCL), and the whole gland was submitted for the evaluation of the prognostic parameters. The lack of correlation between telomerase activity and prognostic parameters could be related to the high prevalence and early occurrence of this phenomenon, and the follow-up of the patients could bring more information about the relevance of this event.

In other solid tumors telomerase activity has been associated with unfavorable characteristics or outcomes. Telomerase activity has been found in 92% of malignant ovarian tumors but only 17% of borderline tumors of the ovary (24). A lower survival rate and advanced stages have been described for telomerase-expressing gastric carcinomas (25). In meningiomas telomerase activity has been reported to predict recurrence (26). Some cases of stage 4S neuroblastoma with undetectable or low levels of telomerase have regressed spontaneously, suggesting that the lack of telomerase contributes to a favorable outcome (27).

Because telomerase is normally expressed only by germ cells and, at low levels, by some stem cells, it has been proposed that telomerase inhibitors could be used to treat cancer without affecting normal somatic cells (28). Antisense strategies directed toward the RNA template component of telomerase (29) and inhibitors of the reverse transcriptase (30) have been described. A recent, novel approach has been to use cationic porphyrins that interact with the

telomeric G-quadruplex inhibiting telomerase and preventing elongation of the telomere (31). However, there are tumors without telomerase activity in which telomeres are maintained by some alternative mechanism (7). Therefore, it will be important to identify those cancers that depend on telomerase for immortalization, as it is only these cancers that may be vulnerable to telomerase inhibitors.

In conclusion, our results demonstrate that the re-expression of telomerase is an early and frequent event in prostatic carcinoma, with telomerase activity present in 29% of our PIN specimens and 80% of our invasive cancer specimens. We could not find any correlation between telomerase activity and histological differentiation or tumor stage, parameters that reflect cancer behavior. The prognostic value of telomerase activity remains open for further investigation.

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QUANTITATIVE MORPHOLOGICAL CHANGES IN THE PROSTATE EPITHELIUM OF PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

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ABSTRACT

Purpose: To analyze the modifications in prostatic glands, using as morphometric parameter the number of acini and the height of the epithelial cell layer, comparing samples of prostates obtained from patients with benign prostatic hyperplasia (BPH) with normal prostates (NP) from young adults.

Material and Methods: Samples were obtained from eight patients aged 63 to 79 years, submitted to open prostatectomy due to prostatic enlargement and obstructive clinical symptoms. A histopathologic analysis confirmed the diagnosis of BPH in all specimens. Controls consisted of the transitional zone of prostates obtained during necropsy of 8 adults aged 18 to 30 years. The samples were stained by hematoxilin-eosin and Gomori's trichrome. The epithelial layer area as well as the maximum, mean and minimum heights were determined on 25 random fields per prostate, comprising about 228.9 acini per prostate. We counted and measure 3663 acini in the two groups, using histomorphometrical software. The data was then analyzed by GraphPad InStat Software.

Results: There was a significant decrease in the maximum (23.59%), mean (27.99%), and minimum (30.38%) epithelium heights. The control data and the BPH samples, respectively, were: 1)- 0.0252 ± 0.0069 (mm) and 0.0178 ± 0.0023 (mm) for the epithelium area ($p < 0.05$), 2)- 55.20 ± 5.78 (μm) and 42.18 ± 3.84 (μm) for the maximum height ($p < 0.05$), 3)- 9.58 ± 1.71 (μm) and 6.67 ± 1.45 (μm) for the minimum height ($p < 0.05$), 4)- 27.72 ± 3.20 (μm) and 19.96 ± 2.07 (μm) for the mean epithelium height ($p < 0.05$).

Conclusions: The modifications in the height of the epithelial cell layer are significant, with its decrease suggesting changes in the secretory activity of the epithelium cells of the hyperplastic prostates compared to the secretion of normal prostates.

Key words: prostate; prostatic hyperplasia; epithelium; morphometry
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INTRODUÇÃO

A arquitetura histológica da próstata é centrada em dois componentes principais: o estroma fibromuscular e o componente glandular ou parenquimatoso (1). A hiperplasia prostática benigna (HPB) é um crescimento tecidual destes elementos histológicos que acarretam profundas modificações na organização da próstata (2).

As doenças do aparelho reprodutor masculino, embora não estejam restritas à próstata,

tem neste órgão o seu componente mais afetado. Evidências histológicas de HPB estão presentes em aproximadamente 90% das biópsias da glândula, realizadas em indivíduos após 60 anos, fazendo dessa doença uma inevitável consequência da idade (3).

Recentemente tem havido um aumento no interesse por tratamentos não invasivos. Esse tratamento tem como alvo os diferentes elementos histológicos que compõem a próstata (1,4). Um conhecimento mais preciso dos constituintes teciduais e suas alterações na HPB contribui não somente para

o entendimento da gênese desta patologia como para a escolha da melhor terapêutica entre os diversos métodos disponíveis (1).

São poucos os trabalhos encontrados na literatura que utilizam métodos de histomorfometria na análise dos diferentes elementos histo-arquiteturais da próstata humana. Os poucos estudos quantitativos mostraram comparações realizadas entre HPB e câncer prostático (5) ou entre diferentes amostras de HPB (6-8) ou ainda entre HPB e próstatas fetais (9), sem no entanto, comparar os resultados obtidos em HPB com próstatas normais. Persiste ainda uma grande divergência sobre o principal elemento tecidual envolvido no crescimento prostático. Se ele é de origem epitelial (ductos ou ácinos prostáticos) (10,2) ou proveniente da proliferação de células do estroma. Este último conceito é o mais aceito atualmente (11,12).

Um estudo estereológico recente, levado a efeito em nosso laboratório (13), corrobora os achados de outros pesquisadores (11,12,14,15) sobre um aumento significativo do estroma (tecido muscular e tecido conjuntivo). Este estudo difere dos demais por ter realizado a comparação de amostras de tecido prostático analisando exclusivamente a zona de transição da próstata.

O presente trabalho tem por objetivo quantificar e determinar as mudanças estruturais ocorridas nos ácinos das glândulas hiperplásicas e comparar com ácinos da zona de transição de próstatas de indivíduos jovens.

MATERIAL E MÉTODOS

Amostras de tecido prostático da zona de transição de próstatas hiperplásicas foram coletadas de 8 pacientes cujas idades variaram entre 63 e 79 anos (idade média de 72 anos), submetidos a prostatectomia aberta. Todos esses pacientes apresentavam sintomatologia obstrutiva e diagnóstico histopatológico de HPB, excluindo assim a presença de qualquer foco de neoplasia maligna na amostra estudada. O material controle consistiu de 8 próstatas obtidas em autópsias de indivíduos jovens normais com idade entre 18 a 30 anos (idade média de 22),

vítimas de morte traumática. Durante a autópsia, verificou-se que a “*causa mortis*” não implicava em comprometimento dos órgãos urogenitais.

Foi estabelecido um critério de tempo entre a hora da morte e a retirada do material. No grupo controle esse período não excedeu 6 horas. Durante a retirada das amostras da zona de transição das próstatas do grupo controle respeitou-se as orientações anatômicas propostas por McNeal et al. (16). Logo após a sua retirada, os fragmentos da zona de transição das próstatas do grupo controle sofreram uma primeira clivagem e foram fixados em Bouin por 24 horas. Em seguida foram desidratados em soluções crescentes de álcool, clarificados em xanol e incluídos em parafina. Todas as amostras de HPB foram coradas com hematoxilina-eosina e examinadas por um patologista para a detecção de focos neoplásicos.

De cada próstata foram retirados 5 fragmentos, que originaram 5 cortes diferentes de 5 µm de espessura, sendo corados pelo tricrômico de Gomori. De cada corte foram analisados e medidos todos os ácinos de 5 campos diferentes perfazendo um total de 25 áreas teste analisadas em cada próstata.

Aquisição e Análise de Imagens

As imagens para análise foram obtidas em aumento de 40 vezes em um microscópio óptico Olympus acoplado a uma câmera de vídeo Sony CCD, sendo as imagens dos campos microscópicos transferidas para um monitor Sony KX14-CP1.

Após a seleção e ajuste focal das imagens no monitor de vídeo, estas eram convertidas em sinais digitais e transferidas para um computador. Para a análise quantitativa utilizou-se o software Image Pro-plus (Media Cibernetics). Este programa semi-automático possibilitou circunscrever os limites basais e luminais do epitélio (Figure). Os parâmetros morfométricos estabelecidos foram:

- A área total do epitélio (ATE) em µm², convertidos para mm:

ATE (mm) = LB - SL, onde LB (µm²) = limite basal e SL (µm²) = superfície luminal

- As alturas epiteliais máxima (AEmax), mínima (AEmin) e média (AEme), (Figure).

Os dados obtidos foram analisados no software Graphpad InStat (Graphpad). Utilizou-se o

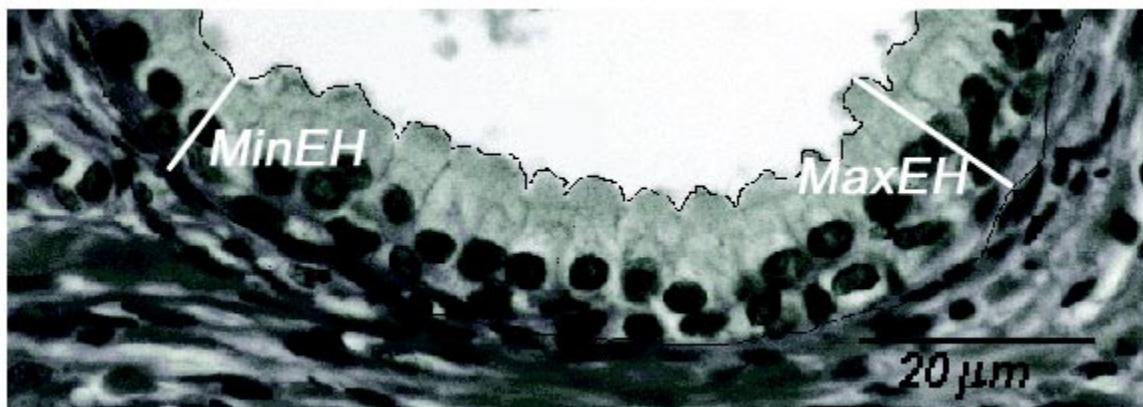


Figure - Histologic section demonstrating the method of obtaining linear measurements in the epithelium of the prostatic acini (hematoxylin-eosin, X 400). MinEH = minimum epithelial height, MaxEH = maximum epithelial height.

teste de Kolmogorov-Smirnov para verificar-se se os dados encontravam-se dentro da distribuição normal, e o teste “t” não pareado para demonstrar a diferença entre os grupos de próstata normal e com HPB, e determinar se essa diferença era significativa. Considerou-se um $p < 0.05$ como significativo.

RESULTADOS

No presente trabalho, em média, foram contados e medidos o epitélio de 5.2 ácinos por mm^2 nas próstatas com HPB e 4.37 ácinos por mm^2 no grupo controle. Nossos achados mostraram uma diminuição significativa de 29.37% (Table-1) na área ocupada pelo epitélio nos ácinos com HPB. As alturas dos epitélios revelaram também um decréscimo

significativo nos ácinos hiperplásicos. Os dados mostraram uma redução de 30.38% para a menor altura epitelial e de 23.59% para a maior altura. A altura média foi reduzida em 27.99% (Table-2). Além disso, a observação dos cortes de HPB mostraram que a maioria dos ácinos hiperplásicos apresentavam em seu interior grânulos que se condensam em concreções (corpora amilacea), o que não foi observado nas próstatas do grupo controle.

DISCUSSÃO

Trabalhos qualitativos e quantitativos sobre HPB normalmente não levam em consideração o fato de que a próstata é um órgão histologicamente heterogêneo. Autores que fizeram estudos morfométricos sobre o componente epitelial (15,17) coletaram amostras aleatoriamente sem levar em consideração as diferenças existentes entre as distintas regiões prostáticas. As análises levadas a efeito no presente trabalho referem-se exclusivamente à zona de transição, reduzindo em muito a possibilidade de alteração dos dados devido a componentes histológicos de outras regiões.

McNeal (10) e Price et al. (2), propõem que as formações nodulares encontradas na HPB também se encontram relacionadas a modificações do parênquima prostático. Isto é confirmado por Iczkowski & Bostwick (4) que descreveram

Table 1 - Total area of the acinar epithelium in the transition zone (TZ) of the prostate, in normal prostates (NP) and in benign prostatic hyperplasia (HPB). Eight patients were studied in each group.

Prostate (TZ)	Epithelial Area (mm^2)
Groups	Mean \pm SD
BPH	$0.0178 \pm 0.0023^*$
NP	0.0252 ± 0.0069

* $p = 0.0126$, as compared to NP.

qualitativamente alterações histopatológicas encontradas no epitélio. Apesar de se conhecer o comprometimento do componente epitelial foram encontrados poucos trabalhos na literatura consultada, contendo dados morfométricos a respeito do epitélio em particular e dos ácinos como um todo, da zona de transição da próstata (4,10,15). Nossos dados indicam uma diminuição significativa da área total ocupada pelo epitélio sugerindo fortemente uma alteração no mecanismo secretor destas células. Tal fato é corroborado por Cohen et al. (18,19) que realizaram análises qualitativas sobre o comportamento glandular em próstatas com câncer e HPB e demonstraram, nessas patologias, a presença do glicosaminoglicano (GAG) queratan sulfato sendo produzidos pelas células epiteliais. Como este GAG representa um dos principais componentes das concreções prostáticas (19) é possível supor que exista uma relação entre estas modificações de natureza morfológica assinaladas no presente trabalho e a secreção prostática.

Table 2 - Height of the acinar epithelium in the transition zone (TZ) of the prostate in normal prostates (NP) and in benign prostatic hyperplasia (HPB). Eight patients were studied in each group. It was calculated the maximum epithelial height, the minimum epithelial height and the mean between the maximum and minimum heights for each group.

Prostate (TZ)	Epithelial Height (μm)
Groups	Mean \pm SD
BPH (minimum)	6.67 \pm 1.45**
NP (minimum)	9.58 \pm 1.71
BPH (maximum)	42.18 \pm 3.84*
NP (maximum)	55.2 \pm 5.78
BPH (mean)	19.96 \pm 2.07*
NP (mean)	27.72 \pm 3.20

* $p = 0.0001$; ** $p = 0.0025$, as compared to the respective NP values.

CONCLUSÕES

A diminuição significativa da altura e da área ocupada pelo epitélio no ácino hiperplásico é um fenômeno constante. As modificações na secreção de

ácinos em próstatas com HPB, descritas na literatura, encontram um respaldo morfológico nos achados do presente trabalho.

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CORRELATION BETWEEN URINARY FLOW RATE, QUALITY OF LIFE AND INTERNATIONAL PROSTATE SYMPTOM SCORE [I-PSS] IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA (BPH)

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ABSTRACT

Purpose: This study aimed to find a correlation between urinary flow rate, quality of life and I-PSS.

Material and Methods: A total 288 with benign prostatic hyperplasia (BPH), who showed inferior urinary tract symptoms and had increased prostate volume, was studied. They answered a translated and validated version of the I-PSS questionnaire during individual sessions at the urology outpatient unit, without the intervention of the researchers. In addition, they had their urinary flow rate evaluated in two different occasions, with a period of one week between the two exams. In the data analysis, the maximum urinary flow rate (Qmax) was correlated with the score of symptoms obtained in each session. The data collected in the second session, regarding I-PSS scores, quality of life and maximum flow rate were statistically correlated.

Results: The correlation between I-PSS and Qmax was found to be low, but statistically significant ($r = -0.223$, $p < 0.05$). Even when the sample was stratified according to the degree of severity of symptoms (low, moderate or severe), no significant correlation was found in any groups. The correlation between I-PSS and the quality of life was significant ($r = 0.664$, $p < 0.001$), which showed that patients with more severe micturition complaints reported poorer quality of life.

Conclusion: The degree symptoms severity in the inferior urinary tract has a direct impact on the quality of life in BPH patients, but it has a low correlation with maximum urinary flow rate. Micturition symptoms and urinary flux rate are determined by distinct variables; therefore, they should be analyzed in independent ways.

Key words: prostatic hyperplasia; flowmetry; urodynamics; quality of life

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INTRODUÇÃO

A hiperplasia prostática benigna (HPB) é doença de alta prevalência e freqüente causa de morbidade em homens após os 50 anos de idade, sendo a ela atribuída a grande maioria dos sintomas do trato urinário inferior (STUI) (1). Os métodos de avaliação da HPB, objetivos e subjetivos, são utilizados não só no diagnóstico, mas também na

indicação terapêutica e no acompanhamento dos pacientes. Os métodos objetivos mais utilizados são urofluxometria, medida do resíduo urinário e estudo pressão/fluxo. Dentre eles, o mais empregado é a urofluxometria, principalmente pela sua natureza não invasiva e sua viabilidade através de urofluxômetros modernos e de boa sensibilidade (2).

Na prática clínica, não se utilizam estudos urodinâmicos complexos e tampouco biópsias para

indicar o tratamento para um paciente. Baseamo-nos, fundamentalmente, nas queixas miccionais apresentadas pelo paciente. Essas são subjetivas e interferem de forma diversa na qualidade de vida de cada indivíduo (3).

Considerando a importância dos sintomas como fator primordial na indicação do tratamento da HPB e a falta de uma sistematização de critérios para indicar o tratamento, assim como para comparar resultados dos diversos tratamentos em diferentes países, a Associação Americana de Urologia desenvolveu um questionário para avaliar STUI que, em 1991, ao ser anexada com uma questão sobre qualidade de vida, passou a se chamar I-PSS (4).

Esperar-se-ia que, na vigência do tratamento, a melhoria dos padrões objetivos de avaliação fosse acompanhada da melhoria dos sintomas clínicos, o que, no entanto, não foi observado em alguns pacientes (5,6) e nos levou a estudar melhor a correlação entre urofluxometria, I-PSS e qualidade de vida.

MATERIAL E MÉTODOS

Foram avaliados, consecutiva e prospectivamente, 288 pacientes, com idade de 50 anos ou mais e diagnóstico clínico de HPB, ou seja, próstata aumentada pelo toque retal, que procuravam o ambulatório de urologia com algum dos sintomas do trato urinário inferior. A coleta dos dados ocorreu no período de 1 de novembro de 1996 a 31 de maio de 1998.

Na primeira consulta, os pacientes realizaram urofluxometria e responderam ao questionário, devidamente validado para a língua portuguesa (7), individualmente e sem intervenção dos pesquisadores. Uma semana depois, retornaram ao ambulatório para que fossem repetidos os mesmos procedimentos.

Foram excluídos do estudo os pacientes com diagnóstico ou história prévia de estenose de uretra, retenção urinária, bexiga neurogênica, neoplasia de próstata suspeita ou confirmada (nódulo duro ao toque, PSA maior que 4 ng/ml), cirurgia de próstata e

cirurgias pélvicas de grande porte. Também foram excluídos os indivíduos com deficiência mental ou visual severas, ou que não concordaram em participar do estudo.

Na aferição dos dados, a medida de fluxo máximo (Qmax) foi correlacionada com o escore obtido no momento correspondente. O fluxo máximo foi medido através de urofluxômetro de disco modelo urodyn, tipo 22G03, fabricado pela Dantec. O exame foi realizado em ambiente privado, e o paciente apresentava algum desejo miccional. Foram desconsiderados os exames cujo volume urinário foi menor que 150 ml ou maior que 500 ml e, para as análises estatísticas de correlação, optamos pelas medidas de Qmax e I-PSS realizadas durante a segunda visita (5,6). Para a análise dos dados utilizamos o coeficiente de correlação de Pearson; o nível de significância adotado foi de $\alpha = 0.05$.

RESULTADOS

Da amostra de 288 pacientes, 38 não compareceram para a segunda visita e, destes, 69 pacientes foram excluídos da análise de urofluxometria por terem volume urinário maior que 500 ml ou menor que 150 ml. Portanto, a correlação de I-PSS e a questão sobre a qualidade de vida foram analisada em 250 pacientes e I-PSS e a urofluxometria em 181 pacientes. A idade média dos 250 pacientes foi de 64.8 anos, variando entre 51 e 84 anos.

Constatou-se que houve significativa, porém baixa, correlação entre escore total de sintomas e fluxo máximo ($r = -0.223$ e $p < 0.05$). Mesmo quando estratificamos a amostra, conforme a severidade de sintomas, em leve ($r = -0.172$ e $p = 0.316$), moderado ($r = -0.187$ e $p = 0.09$) e severo ($r = -0.124$ e $p = 0.32$), observamos que não houve correlação significante em nenhum dos grupos.

A correlação entre escore total de sintomas (I-PSS) e questão sobre qualidade de vida foi significativa ($r = 0.664$ e $p < 0.001$). Os pacientes com queixas de STUI mais severas referiram pior qualidade de vida.

DISCUSSÃO

Até o presente momento, os estudos brasileiros utilizavam o escore em português simplesmente através da tradução literal, a partir do original em língua inglesa. O escore ainda não tinha sido submetido à validação transcultural e psicométrica na língua portuguesa. Neste trabalho, utilizamos o escore I-PSS em português devidamente validado (7).

Netto et al., em 1993, publicaram estudo sobre 104 pacientes com idade entre 40 e 94 anos e STUI. Utilizou o escore I-PSS somente traduzido e não encontrou diferença significativa nas respostas, quando o questionário era auto-administrado pelo paciente ou respondido com o auxílio do médico entrevistador. Também concluiu que a faixa etária e a escolaridade não comprometiam a aplicação de escores clínicos (8). Em nosso estudo orientamos que, quando o paciente apresentasse dificuldade para responder o questionário, deveria receber o auxílio de familiar ou acompanhante e não dos pesquisadores, já que estes estariam envolvidos na realização da urofluxometria. O conhecimento prévio de uma das variáveis pelo pesquisador poderia vir a ser fonte de viés na coleta dos dados.

Barry et al., em 1995, analisaram repetidos I-PSS e Qmax encontrando variações de até 4.9 pontos no I-PSS e 4.1 ml/s de Qmax. Alertaram para o perigo de se realizar apenas uma medida desses dados para uma decisão terapêutica (9). Em nosso trabalho, realizamos as medidas de urofluxometria e administraramos o questionário de sintomas sempre em duas ocasiões. Optamos pela análise dos dados coletados na segunda visita, porque acreditamos que, nesse momento, os pacientes teriam maior familiaridade com o questionário e com o equipamento de urofluxometria.

Em nossa análise de dados, encontramos significativa correlação entre I-PSS e qualidade de vida (QL) ($r = 0.664$ e $p < 0.001$), coincidindo com os dados de Bosch et al. e Sagnier et al. (5,10). Isso sugere que a intensidade dos STUI é fator importante na determinação da qualidade de vida do paciente com HPB.

Na década de 70, vários autores já questionavam a correlação entre sintomas e fluxo miccional, mas não havia um questionário devidamente validado ou, então, foram utilizados outros que não o I-PSS.

Estudos mais recentes, como os de Barry et al. (3), Bosch et al. (5), Ko et al. (11) e Batista-Miranda et al. (12), que já utilizaram o I-PSS como medida de severidade de sintomas, não encontraram correlação entre escore e fluxo máximo. Somente nos estudos de Garraway et al. (1) e Chute et al. (13) a correlação foi significante, porém baixa como em nossos resultados. Nesses trabalhos, também foram excluídos pacientes com volume urinado menor que 150 ml ou maior que 500 ml. Provavelmente, essa discordância de dados da literatura deve-se, basicamente, à seleção dos pacientes. De qualquer modo, tanto nos dados de literatura como em nossos resultados, existe o consenso de que a correlação de fluxo máximo e sintomas (STUI), quando existente, é muito baixa, e esses parâmetros devem ser considerados de forma independente. O conhecimento de um parâmetro não permite inferir sobre o outro.

Clínica e intuitivamente, acreditávamos que HPB era a causa básica de obstrução infravesical e dos sintomas anteriormente denominados de prostatismo (14). Hoje sabemos que HPB é doença complexa e nem sempre a obstrução e os sintomas aparecem juntos.

Quando analisamos cada questão do I-PSS de forma independente e correlacionamos com fluxo máximo, os resultados também não diferem dos anteriores. Ou seja, quando existe a correlação é baixa. Mesmo quando analisamos, isoladamente, o sintoma “jato fraco” que corresponde à questão número 6 do escore I-PSS, e, inicialmente, pensávamos referir-se especificamente a fluxo, encontramos uma correlação que apesar de significante, foi baixa ($r = -0.192$ e $p = 0.010$). Isto nos leva a crer que a simples impressão de jato fraco, percebida e declarada pelo paciente através do I-PSS, não corresponde aos achados objetivos medidos através da urofluxometria. Os demais sintomas como hesitação (Q1), micção incompleta (Q2),

intermitênciam (Q4) e noctúria (Q7) também não demonstraram correlação com fluxo máximo tanto em nossos dados como nos de outros autores (5,15).

Estudos futuros ainda devem determinar a verdadeira origem dos STUI. Até lá, os testes objetivos com parâmetros anatômicos e, principalmente, fisiológicos relacionados com HPB, ainda são indispensáveis.

CONCLUSÃO

A severidade dos sintomas (STUI), medida através do I-PSS, em língua portuguesa tem, apesar de significante, baixa correlação com os valores de fluxo máximo em pacientes com diagnóstico clínico de HPB, pois, sintomas miccionais e fluxo urinário são determinados, provavelmente, por variáveis diferentes.

A correlação entre o escore total I-PSS e a questão sobre qualidade de vida sugere que o tratamento dos sintomas melhore significativamente a qualidade de vida dos pacientes.

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MANAGEMENT OF URETHRAL STRICTURES WITH ACUCISE CATHETER

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ABSTRACT

Purpose: To evaluate the use of a cutting balloon catheter (Acucise catheter) for the management of urethral strictures.

Material and Methods: Twenty male patients with urethral stricture were treated; of these, 13 had undergone previous treatment unsuccessfully. The patients presented with a weak urinary stream, voiding symptoms, maximum urinary flow lower than 15 ml/s, and the retrograde and urinary urethrocystography indicated a urethral stricture less than 20 mm in length. Location of the stenosis and consequent positioning of the balloon were assessed through urethroscopy and fluoroscopy. The metallic guide wire was placed at the 12 o'clock position and an electrocautery incision made. Clinical criteria, results of urinary flowmetry and the urethrocystography – prior to treatment and after six months were classified as: improved, unchanged and worse.

Results: Eighty-five percent of the patients reported clinical improvement following the internal urethrotomy with the Acucise catheter. According to the evaluation by urinary flowmetry, in six patients (30%) results were considered good, in 4 (20%) the outcome was fair and in 10 (50%), poor. However, 71.4% of the 7 patients that had not undergo previous treatment evidenced good and fair outcomes. In 75% percent of the patients there was a radiological improvement and no cases of worsening of conditions were found.

Conclusions: The use of the Acucise catheter proved to be simple and safe, and it may be considered favorably as a new therapeutic option.

Key words: urethra; urethral stricture; urethrotomy; Acucise catheter

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INTRODUCTION

Despite the advances, urethral stenosis still represents one of the most common and challenging medical problems (1). Reports of treatment for urethral strictures can be found in Hindu texts dating back to 6 centuries before Christ (2). However, less invasive management methods, with lower rates of recurrence continue to be investigated.

Urethral strictures are basically treated by various techniques including urethral dilations (3-5), cold knife internal urethrotomies (6,7), laser internal urethrotomy (8-10); self-expandable prostheses (11,12) urethroplasties with a primary termino-

terminal anastomosis (13,14) or substitution urethral reconstruction using skin flaps or grafts in one or two-stage repairs (15-19).

Urethral dilation is the oldest method used for the treatment of urethral stricture. However, several authors and patients may prefer to treat urethral stenosis with periodic dilations performed in the hospital, in the office or at home as self-catheterization. The drawback of this approach is possible lesions to the epithelium with increased fibrosis. Urethral balloon dilations have been indicated as advantageous because they promote a uniform dilation and cause little local trauma (5,20).

Cold knife urethrotomy has been widely employed (6). However, stenosis recurrence rates have been high with this method (21), up to 82% of cases (22). Stricture recurrence rates following internal urethrotomy are equivalent to those seen with urethral dilations (23,24).

Based on satisfactory clinical results obtained with the use of the Acucise cutting balloon catheter (Applied Medical Technologies, Laguna Hills, CA) for the treatment of pyeloureteral junction and ureteral stenosis the authors realized the use of the Acucise catheter for management of urethral stenosis disease.

The method not described before has the advantage of combining the principles of balloon dilation with an incision using the Acucise catheter. The urethral incision is uniform, limited to the diameter of the balloon and to the length of the metallic wire of the catheter.

MATERIAL AND METHODS

Between December 1997 and October 1998, 20 male patients with partial stenosis of urethra no longer than 20 mm and with maximum urine flow under 15 ml/s were submitted to internal urethrotomy with an Acucise catheter. Patient age ranged from 15 to 83 years, mean 59.5 years. Seventeen patients (85%) were Caucasian (white) and 3 were LatinNegro (15%). The most frequent complaints were a weak urinary stream (90%) and voiding symptoms (85%). Time of disease from onset of symptoms to surgery ranged from 6 to 144 months, mean 37 months.

Only 7 (35%) of the 20 patients studied had not been submitted to any previous urethral treatment. In the remaining 13 patients, 5 (25%) had undergone cold knife internal urethrotomy and 9 (45%) had been submitted unsuccessfully to various methods of treatment for stenosis of urethra. Regarding location, data evidenced: there were 14 (70%) cases of strictures of the bulbar urethra, 5 patients (25%) had a penile urethra stricture and there was one case of stricture of the membranous urethra (5%) (Table-1). As for extent, findings indicated: up to 5 mm, 4 patients (20%); between 6 and 10 mm, 13 patients (65%) and from 11 to 20 mm, 3 patients

Table 1 -Urethral stricture location.

Urethral Stricture Location	No. of Patients	%
Membranous	1	5
Bulbar	14	70
Penile	5	25

(15%) (Table-2). The most commonly detected etiology was iatrogenic: there were 13 (65%); 2 cases of traumatic stenosis (10%); in 4 patients (20%) it was not possible to determine the etiology, and in 1 patient (4%) stenosis occurred following neourethroplasty (Table-3). Previous treatment for urethral stenosis in these patients included: a single cold knife internal urethrotomy in 5 patients (25%); internal urethrotomy followed by periodic dilations in other 5 patients (25%); 1 patient had been managed with dilations only; 2 patients had been submitted to a termino-terminal urethroplasty followed by periodic dilations. Seven patients had not been submitted to any treatment prior to the procedure using the Acucise catheter (35%) (Table-4).

Eighteen patients were given spinal anesthesia and in 2 patients sedation was used. All patients were given 1 g of intravenous cephalotine at the beginning of the procedure. Surgery was performed with the patient in the lithotomy position and it started with a retrograde urethrography using a fluoroscope with a "C-arm" at a 60° angle relatively to the patient. A urethroscopy (Figure -1) was carried out next for identification of the stenosis location (21F cystoscope). A 0.028F guide wire was passed to the stricture and taken along the urethra as far as the bladder. An Acucise catheter was passed over the guide wire to the stenosis site. The metallic wire of the Acucise catheter was directed toward the most

Table 2 - Extent of urethral stricture.

Extent of Urethral Stricture (mm)	No. of Patients	%
1 - 5	4	20
6 - 10	13	65
11 - 20	3	15

Table 3 - Etiology of urethral stricture.

Etiology of Urethral Stricture	No. of Patients	%
Iatrogenic	13	65
Undetermined	4	20
Traumatic	2	10
After neourethroplasty	1	5

anterior part of the urethra, at the 12 o'clock position (Figure-2). At this time, the balloon (Figure-3) was inflated using 2.2 ml of contrast material; under fluoroscopy it was possible to observe the constriction ring between the extremities of the balloon. The electrocautery was then used after being regulated at 75 watts for 5 seconds. During the incision fluoroscopy allowed the surgeon to follow the disappearance of the constriction ring caused by the urethral stenosis. The balloon was maintained inflated for 10 minutes for hemostatic purposes (Figure-4). After that, the balloon was deflated, the catheter removed and the cystoscope introduced into the bladder (Figure-5). An 18F urethral Foley catheter was then inserted and left in place for a period of 10 days postoperatively. Average time of procedure was 45 minutes. The patients were discharged from the hospital on the same day of the procedure. During the monthly follow-up data were collected from patient information as to their ability to urinate and from the urinary flowmetry and, after a six-month period, from the retrograde and urinary urethrocystography.

Success of internal urethrotomy using an Acucise catheter for treatment of urethral stenosis was assessed according to the following criteria: patient information (improved, unchanged and worse) and

urinary flowmetry (maximum urine flow: good > 15 ml/s; fair: 10 to 15 ml/s and poor: < 10 ml/s). Retrograde and urinary urethrocystographies carried out prior to the treatment and six months after the procedure were compared and classified as: improved (enlarged caliber of the stenosis and reduction of the dilation proximally), unchanged and worse.

The variables were analyzed statistically (Friedman and Mann-Whitney non-parametric test), and the rate considered significant was 0.05 (p).

**Figure 1 - Cystoscopic visualization of the urethral stenosis.**

RESULTS

Concerning pre and postoperative signs and symptoms, results of the internal urethrotomy with Acucise evidenced improvement in 17 cases (85%), 2 cases remained unchanged (10%) and in one condition grew worse (5%).

Considering the maximum urine flow, and comparing pre and postoperative results one month after the internal urethrotomy using the Acucise

Table 4 - Previous treatment for urethral stricture.

Previous Treatment for Urethral Stricture	No. of Patients	%
Cold knife internal urethrotomy only	5	25
Cold knife internal urethrotomy plus dilatation	5	25
Dilatation only	1	5
Termino-terminal urethroplasty	2	10
No previous treatment	7	35

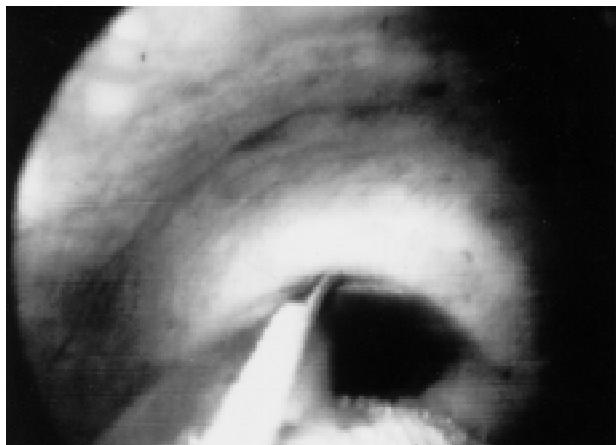


Figure 2 - The Acucise catheter is placed at the site of stenosis with the cutting wire at the 12 o'clock position. At this time the hot electrode cuts linearly.

catheter, data revealed an average increase from 7.5 ml/s to 13.4 ml/s. During the six-month follow-up period the increase in the maximum urine flow remained statistically stable. The maximum urine flow was considered good (Max Q > 15 ml/s) in 6 patients (30%) and fair (Max Q 10 to 15 ml/s) in 4 patients (20%). In 10 patients (50%) results were poor (Max Q < 10 ml/s). However, in the patients that had not been submitted to any previous treatment (7 patients) success rates were good (57.1%) and fair (14.3%) in 71.4% of cases. Comparing outcomes in

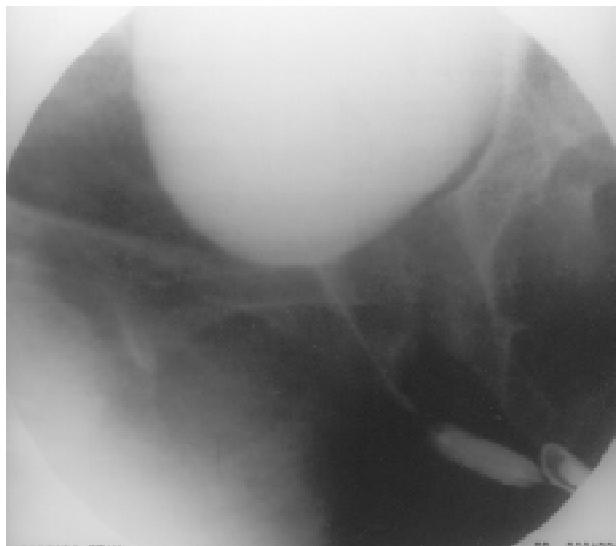


Figure 3 - Image obtained by fluoroscopy showing the balloon inflated with 2.2 ml of iodinated contrast liquid, at the site of the urethral stenosis, before the incision with the metallic wire.

patients without previous treatment with the stricture recurrence rates a statistical tendency was observed to a less favorable evolution in the operated cases ($p = 0.0842$). Results were also compared regarding extent of the urethral stenosis. The 4 patients with a stricture up to 5 mm were compared with the other 16 cases and no statistical difference could be found in these two groups. Likewise, the results in patients with iatrogenic urethral stenosis were compared with the non-iatrogenic cases and no statistical difference was evidenced between the 2 groups. With regard to location, in this study the stricture occurred most frequently in the area of the bulbar urethra: 14 cases; as to other locations, penile or membranous, no significant statistical difference was found.

Results of the internal urethrotomy with Acucise were evaluated by a retrograde and urinary urethrocytography performed 6 months following the procedure. The radiographic study revealed improvement in 16 cases (75%); 4 cases remained unchanged (25%).

A noted postoperative complication was fever in 3 patients after catheter removal; these patients were successfully treated on an outpatient basis with norfloxacin. Outcome in these cases was poor. Bleeding, edema or urinary incontinence was not observed.



Figure 4 - Image obtained by fluoroscopy of the inflated balloon after the internal urethrotomy with the Acucise catheter.

DISCUSSION

The development of more effective and lasting techniques for the treatment of urethral strictures by means of minimally invasive procedures continues to represent an important area of research.

Despite being widely employed, cold knife internal urethrotomy as a treatment modality for urethral stenosis is related to high rates of stricture recurrence (25) to the point that some authors consider urethral dilation equivalent in efficiency to this procedure, but with lower costs (26). In this sense, in order to improve results of urethral dilations several authors have recommended the use of dilating balloons; the feasibility of this method has been demonstrated, and it is associated with high success rates (5,20).

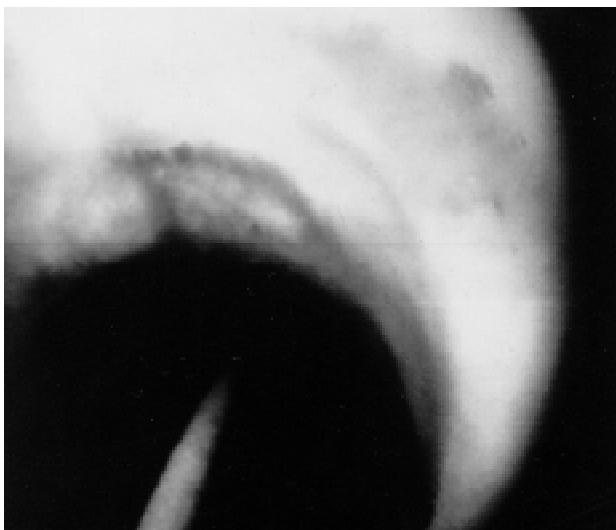


Figure 5 - Visualization of the urethral stenosis site after the internal urethrotomy with the Acucise catheter allowing the passage of a 21F cystoscope.

The use of dilating balloons attached to a cutting wire, or the Acucise catheter, for the treatment of urethral stenosis was not previously described.

During the preliminary stage of the present study the authors discussed potential risk of lesion to the sphincter using the Acucise urethrotomy catheter in the area of the bulbomembranous urethra. However, this complication has been considered a remote

possibility due to the diameter, limited to 24F, of the balloon when inflated. In fact, in this study no patients developed urinary incontinence. As in observations made by Giannakopoulos et al. (1997) (27) no complications were observed with the Acucise catheter relative to the use of electric current. The incision via metallic wire is linear, uniform and limited to the 3 cm of the balloon length; tissue lesions beyond these limits or in depth injuries are therefore unlikely. No occurrences of extravasation of the irrigation fluid or bacteriemia were observed in the patients treated. Fernandes et al. (1993) (28) considers that the use of balloons for the treatment of urethral stenosis has the advantage of promoting a lower absorption of fluids.

As for results, based on information given by the patients, the authors could observe higher success rates (85%) than the good and fair rates indicated by the urinary flowmetry (50%). The urine flow measures used in the investigation of the low urinary tract can reveal variations relative to urinary volume, sex, age and position taken by the patient.

The six-month follow-up was considered too short; however, most stricture recurrences take place within this period (22,25,29,30). A study based on the pre and postoperative retrograde and urinary urethrocystographies indicated results considered better in 15 cases (75%).

When results from the clinical evaluation and flowmetry and urethrocystography were compared it was observed that there was a greater correlation between the clinical and the radiographic evaluation (88.2%) than between the clinical evaluation and the urinary flowmetry (58.8%). There was also a small correlation between the urethrocystography and the urinary flowmetry (66.6%).

In the present study only 7 patients (35%) had not been submitted to any previous treatment for urethral stenosis; in 5 of them good and fair results were achieved (71.4%). On the other hand, in 13 patients with recurrent stenosis the evaluation by urinary flowmetry revealed a failure rate of 65%. The medical literature reports that patients with recurrent stenosis are also considered of worse prognosis for endourologic treatment (21).

The cost of the Acucise catheter must be taken into account. Each catheter was used at least 5 times

and resterilized with glutaraldehyde, decreasing its cost. Furthermore, reduction in costs as a whole is achieved with the overall smaller time of the procedure and the lower rates of complications, and probable recurrence rates of stenosis. As this is an initial study, the Acucise catheters were reused after being sterilized. In the future, with the advances in technology, less expensive adequate catheters can be developed. In this case, the catheters will be used only once.

In fact, this is a first study using balloon and a cutting wire with the advantage that this technique is very easy to perform, safe because is a linear cut limited to 24F without irrigation, and less traumatic to the urethra. The cost may be reduced with new developments of the appropriate catheter.

CONCLUSIONS

Management of urethral stenosis by internal urethrotomy using the Acucise catheter proved to be a simple and safe procedure, and can be considered a new minimally invasive therapeutic option. The risks of complications are few and no bleeding neither incontinence was observed. This can be a new and beneficial therapeutic alternative. Further studies are necessary with longer follow-up and comparing it with other outpatient procedures.

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EDITORIAL COMMENT - I

This article represents an original approach to urethral stenosis. However, there are some controversial aspects like the fluoroscopic control of the Acucise position and its relation to the urethral sphincter (membranous and bulbar urethra).

Cold knife urethrotomy has a high recurrence rate in cases of intense scar tissue down the spongy tissue. Also the urethral balloon dilation is not able to solve this problem. Therefore, how the combination of urethral dilation and electrocautery will work across the periurethral scar tissue is indeed not clear.

Another intriguing point is the reuse of the Acucise for so many times without any technical problem with the device.

The last but not the least is the high price of the Acucise catheter, even with repeated sterilization and reuse of the device.

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simple and safe method of treating benign urethral strictures.

The authors comment briefly on the cost of the Acucise catheter. While the authors have decreased the cost of the device by repeat sterilization and reuse of the device, this technique would not be allowed in many operating rooms across the world. In fact, the Acucise device is quite expensive costing greater than \$1500 US and therefore if only single use were allowed, the procedure would be cost prohibitive.

My overall concern of this particular study is the expense and potential problems related to reuse of a clearly disposable device. It is one thing to reuse balloons or catheters, which do not rely on electrical current for their proper performance. However, reuse of the Acucise with repeat sterilization may indeed cause problems with the electrical current and the cutting capabilities of the device.

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EDITORIAL COMMENT - II

In this study, the authors describe their technique of Acucise incision of benign urethral strictures. Their results were fair overall, but do provide an interesting use of the Acucise device.

Following Acucise incision, 85% of the patients reported clinical improvement in their voiding parameters. By uroflowmetry, 50% of patients had either a good or fair improvement. Moreover, 75% of the patients demonstrated radiological improvement following Acucise incision. There were no significant complications in the patients treated with the Acucise device. The authors conclude that the Acucise catheter can provide a

EDITORIAL COMMENT - III

This study is the first report of a series of urethral strictures treated with a cutting balloon catheter (Acucise catheter). Of the 20 patients treated, of whom 13 had undergone prior treatment for urethral stricture, 85% reported clinical improvement but by objective urinary flowmetry the results were considered good in only 30%. The authors' conclusion was favorable towards the technique.

Although in some settings one-time use medical devices are resterilized and reused, this is generally limited to devices with simple contours and without complex interfaces. Wires, catheters, and dilators can likely be resterilized safely, but to apply resterilization to a cutting balloon catheter, with its complex shape and internal surfaces, might expose the surgeon and patient to significant risk of failure

of the sterilization or the equipment. This practice should not be recommended without further testing. In addition, the final contentions that the cutting balloon catheter provides shorter procedure time, lower complication rate, and lower rate of recurrence are not at all supported by data in the manuscript. An additional disadvantage of the technique described is the need for fluoroscopy, which adds considerably to the instrumentation burden of the urethrotomy. In

summary, the authors have not provided data that are in any way suggestive that internal urethrotomy with a cutting balloon catheter would be superior or even equivalent to other standard techniques.

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DOUBLE INFERIOR VENA CAVA ASSOCIATED WITH RENAL CELL CARCINOMA

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ABSTRACT

Introduction: Anomalies of the inferior vena cava (IVC) occur infrequently and if unidentified can lead to life-threatening situations with significant morbidity during surgical exploration in the retroperitoneum. Most anomalies remain asymptomatic until recognized in surgery. Double inferior vena cava has been associated with horseshoe kidneys, cloacal exstrophy and renal neoplasms. The authors describe a case of double IVC confirmed during surgical treatment for renal cell carcinoma of the right kidney.

Case Report: A 71 year-old man, admitted with a palpable mass in the right upper quadrant and hematuria. There was no weight loss or intestinal disturbance. Ultrasound showed a heterogeneous mass on the upper pole of the right kidney. The computed tomography (CT) scan confirmed a solid lesion, suggesting a renal neoplasm and an image of double IVC. The magnetic resonance imaging did not demonstrate tumor thrombus into the right inferior vena cava. The patient underwent a right radical nephrectomy, by a thoracoabdominal approach and was discharged from the hospital on postoperative day 6 with none intra or postoperative complication. The patient is on ambulatory follow-up with no signs of local or distant recurrence.

Discussion: Formation of inferior vena cava is a complex process that involves multiple steps. Caval development begins in the sixth week and progresses rapidly, with formation of all three precursor venous systems by the eighth week of fetal life. Double inferior vena cava is caused by persistence of all or parts of both subcardinal vessels. Anomalous venous tend to be dilated and tortuous, making injury more likely. Intraoperative trauma may cause life-threatening hemorrhage. Although duplication of the IVC are not common and have no clinical significance, its recognition are important when surgical procedures involve structures of the retroperitoneum.

Key words: vena cava; anomalies; double inferior vena cava; renal cell, carcinoma
Braz J Urol, 27: 367-369, 2001

INTRODUÇÃO

Anomalias da veia cava são patologias raras, com incidência entre 0.5% e 3%. Duplicação da veia cava inferior é pouco comum, tendo incidência de 1.5 a 3% em relatos de autópsias (2,3). Esta entidade tem sido evidenciada em associação com rins em ferradura (1), extrofia de cloaca (1) e durante explorações cirúrgicas para tratamento de neoplasias renais (2,3).

Os autores apresentam um caso de duplicação de veia cava inferior, confirmado durante tratamento cirúrgico de carcinoma de células renais do rim direito.

RELATO DO CASO

Paciente do sexo masculino, de 71 anos, apresentando sensação de incômodo na região lombar direita e hematúria macroscópica há 6 meses. Ao exame físico bom estado geral, apresentando massa palpável em hipocôndrio direito. Negava perda de peso ou alteração do ritmo intestinal.

Realizado ultra-som abdominal e urinálise que evidenciaram massa heterogênea, de 13 x 15 cm, em polo superior do rim direito e hematúria. Radiografia do tórax apresentava-se normal, sem evidência de metástases. A tomografia computadorizada revelou

lesão expansiva sólida em pólo superior do rim direito, sugestiva de neoplasia renal com ausência de linfonodos regionais aumentados ou metástases, porém a veia cava apresentava-se deslocada pelo tumor com imagem de duplicação ao nível de L3-L4 (Figure-1). Foi realizada ressonância nuclear magnética que confirmou duplicação da veia cava inferior bem como excluiu a presença de trombos tumorais no seu interior.

O paciente foi submetido à nefrectomia radical e linfadenectomia regional à direita através de toracofrenolaparotomia. A dissecção do retroperitônio e dos grandes vasos confirmou a anomalia de duplicação da veia cava inferior (Figure-2). O laudo histopatológico confirmou carcinoma de células renais de pólo superior do rim direito, com invasão da gordura peri-renal e sem linfonodos acometidos. Não ocorreu nenhuma complicação intra ou pós-operatória, e o paciente encontra-se em acompanhamento ambulatorial, sem evidência de recorrência local ou à distância no seguimento de 6 meses após a cirurgia.

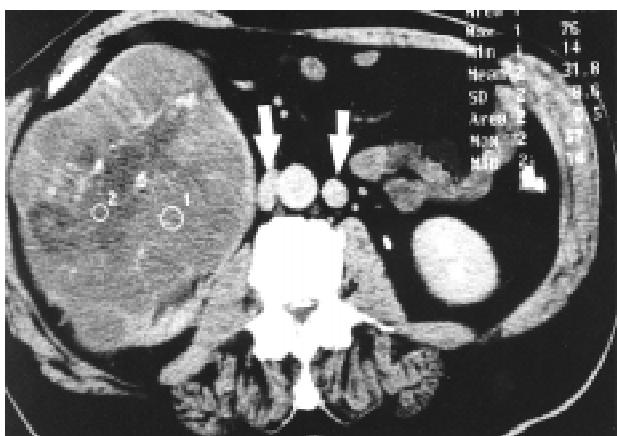


Figure 1 - Computed tomography of the abdomen demonstrating a right renal neoplasm and an image of double inferior vena cava. The right and the left vena cava are located on each side of the aorta (arrows).

DISCUSSÃO

A formação da veia cava inferior é um processo complexo que envolve várias etapas. Três sistemas venosos completos se desenvolvem (veias cardinais anteriores e posteriores, veias subcardinais

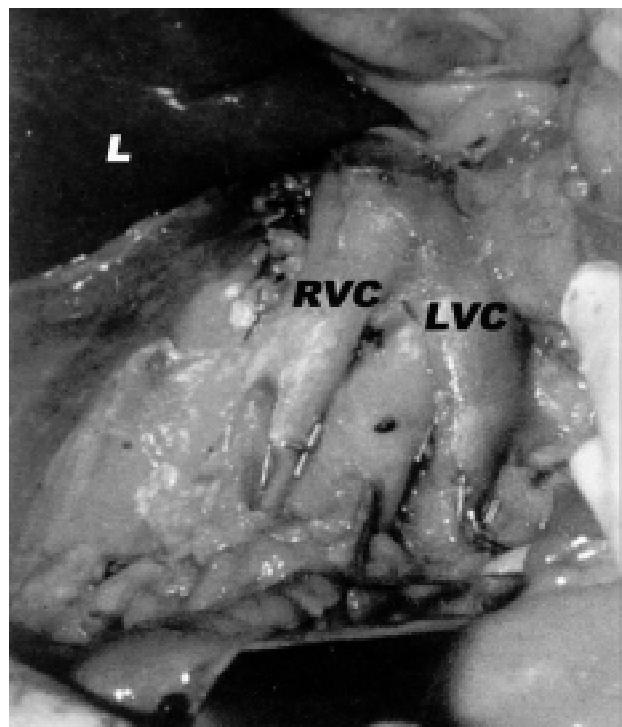


Figure 2 - Intraoperative aspect after right radical nephrectomy. Double inferior vena cava on the level of the porta hepatic, with the right gonadal vein draining into the right vena cava and the left renal vein into the left vena cava. L = liver, RVC = right vena cava, LVC = left vena cava.

e veias supracardinais) e seletivamente regridem para a formação da veia cava inferior e suas tributárias. Este desenvolvimento se inicia na 6a. semana de vida fetal e progride rapidamente, com formação dos 3 sistemas precursores em torno da 8a. semana (1,3).

Existem 4 grandes malformações da veia cava inferior: transposição da veia cava inferior, duplicação da veia cava inferior, colar renal circum-aórtico e veias renais retro-aórticas (3).

A duplicação da veia cava inferior é originada da persistência de ambas ou parte das duas veias subcardinais. Uma dupla veia cava direita é formada devido à persistência de ambas as veias subcardinais: dorsal e ventral. A duplicação geralmente é abaixo das veias renais, porém variações são comuns. Usualmente a veia cava direita é dominante, e a veia cava esquerda se anastomosa a esta pela frente ou por detrás da aorta, e podem estar presentes anomalias concomitantes das veias renais. Anomalias venosas tendem a se dilatar e se tornarem

tortuosas, o que as torna extremamente fáceis de serem lesadas, transformando assim, o traumatismo intraoperatório uma condição de risco de vida (1).

Em exames de tomografia computadorizada a duplicação da veia cava inferior pode ser erroneamente interpretada como adenopatia retroperitoneal, sendo a incidência em exames relatada em torno de 0.3 a 1% (2,3). A continuidade de duas estruturas redondas de cada lado da aorta (“double cava sign”), deve ser confirmada em cortes consecutivos da veia renal esquerda até a 4a. vértebra lombar (2).

Embora a duplicação da veia cava inferior seja incomum e não apresente significado clínico, seu reconhecimento é importante quando procedimentos radiológicos ou cirúrgicos envolverem estruturas do retroperitônio. Os cirurgiões devem ter em mente a possibilidade de

anomalias da veia cava inferior, em especial a duplicação, quando realizarem cirurgias retroperitoneais.

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PROSTATIC AND RENAL SYNCHRONOUS NEOPLASMS

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ABSTRACT

Objective: Renal and prostate neoplasms are frequent urological malignancies. The association between these two diseases may change patients' prognosis. Two cases of primary prostate cancer associated with synchronous renal tumor are reported.

Case reports: Case 1)- A 66 year-old white man, with lower urinary tract symptoms (LUTS) for 4 months, developed acute urinary retention. The ultrasonography revealed a 5 cm tumor in the left kidney. PSA level was 58.6 ng/ml and a prostatic biopsy revealed prostate adenocarcinoma. The abdominal and pelvic computed tomography (CT) scan demonstrated left renal tumor with enlarged pelvic lymph nodes. The bone scan was negative for metastasis. The patient underwent left radical nephrectomy with pelvic lymphadenectomy. The pathologic examinations revealed renal adenocarcinoma and prostate metastasis to pelvic lymph nodes. The patient was placed on androgen blockage for prostatic neoplasm. At a 19-months follow-up, there are no signs of local recurrence or distant metastasis of renal tumor. Case 2)- A 71 year-old white man presented left lumbar pain and LUTS. There was no hematuria, weight loss or anemia. The ultrasonography and the abdominal CT scan showed a small heterogeneous mass (4.5 x 3.1 cm) on the left kidney. The PSA was 22.0 ng/ml and a prostatic biopsy confirmed prostatic adenocarcinoma (Gleason VIII, 5 + 3). The bone scan was negative for metastasis. The patient underwent left radical nephrectomy, bilateral pelvic lymphadenectomy and radical retropubic prostatectomy. The pathologic examinations confirmed both renal and prostate adenocarcinoma. At a 6-months follow-up, there are no signs of local recurrence or distant metastasis of renal tumor and the PSA level is under 0.4 ng/ml.

Comments: Patients with prostate cancer seems to have an elevated risk for developing other genitourinary malignancies. Until now, it remains controversial the need for carefully follow-up of patients with prostate cancer, about developing a second primary genitourinary neoplasms.

Key words: prostate; kidney; prostatic neoplasms; kidney neoplasms; synchronous malignancies
Braz J Urol, 27: 370-372, 2001

INTRODUÇÃO

As neoplasias de rim e próstata são tumores urológicos freqüentes. A associação destas duas neoplasias, quando do diagnóstico, pode mudar o prognóstico do paciente. Tumor sincrônico é definido como o 2º. tumor primário diagnosticado até 6 meses do primeiro tumor primário, sendo que após 6 meses é definido como tumor metacrônico (1).

Neoplasias primárias múltiplas foram pri-

meiramente descritas em 1889 (1). Em exames de necropsia, a incidência de neoplasias primárias múltiplas é em torno de 5%, sendo que em pacientes com neoplasia prostática esta incidência atinge até 27% (1). A concomitância de neoplasia primária de próstata e rim varia entre 3 e 7% (2,3).

Os autores relatam 2 casos de pacientes com neoplasia prostática primária associada a tumor renal sincrônico.

RELATO DOS CASOS

Caso 1 - L.A.C., 66 anos, branco, aposentado, apresentando polaciúria e nictúria há 4 meses e retenção urinária com necessidade de cateterismo uretral há 1 semana. Realizado ultra-som urinário que revelou próstata de 33 g e lesão sólida de 5 cm de diâmetro no pólo inferior do rim esquerdo. A dosagem de PSA foi de 58.6 ng/ml e o toque retal mostrou próstata de consistência pétrea difusamente. A biópsia prostática revelou adenocarcinoma prostático moderadamente diferenciado. A tomografia computadorizada de abdome e pelve demonstrou lesão sólida, heterogênea, de 5 cm em pólo inferior do rim esquerdo, além de linfonodos obturadores aumentados à esquerda. A cintilografia óssea foi negativa para metástases.

O paciente encontrava-se em bom estado geral sendo submetido a nefrectomia radical esquerda e linfadenectomia obturadora bilateral em 28/09/1999. Evoluiu bem, tendo alta no 6º dia pós-operatório. O laudo histopatológico revelou adenocarcinoma renal limitado à fáscia de Gerota, sem acometimento de linfonodos peri-hiliares (pT2NoMo) e adenocarcinoma prostático moderadamente diferenciado metastático para linfonodo obturador esquerdo (D1). Foi instituído bloqueio androgênico com análogo LH-RH, sendo que atualmente encontra-se em bloqueio androgênico total (análogo LH-RH e ciproterona), sem evidências de recidiva local ou à distância da neoplasia renal, continuando em acompanhamento ambulatorial após 19 meses de seguimento.

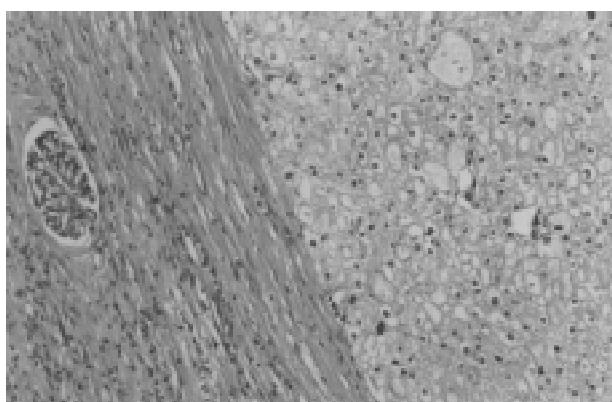


Figure 1 - Case 2: Renal cell carcinoma of the left kidney (HE X100).

Caso 2)- J.A.Q., 71 anos, branco, vigilante, procurou serviço médico com queixas de dor lombar, tipo cólica, à esquerda, há aproximadamente 2 anos, com piora nos últimos meses. Relatava ainda diminuição do jato urinário e polaciúria há 4 anos, sem hematúria, perda de peso ou infecção urinária. Ao exame apresentava-se em bom estado, hígido, exame físico normal. O toque retal demonstrava uma próstata pouco endurecida, sem nódulos.

Realizou ultra-som que revelou lesão heterogênea e hipoecóica em 1/3 médio do rim esquerdo, sugestiva de processo expansivo e próstata de 36 g. Dosagem do PSA de 22.0 ng/ml. Encaminhado para realização de biópsia trans-retal que revelou adenocarcinoma prostático Gleason VIII (3 + 5) no lobo direito (T1cNoMo). Tomografia de abdome confirmou a lesão renal como sugestiva de neoplasia, com 4.5 x 3.1 cm de diâmetro e cintilografia óssea foi negativa para metástases.

O paciente foi submetido a nefrectomia radical esquerda, linfadenectomia obturadora bilateral e prostatectomia radical retropúbica em 24/10/00. Evoluiu bem no período pós-operatório, tendo alta no 6º dia. O laudo histopatológico revelou adenocarcinoma renal limitado à Gerota, sem acometimento ganglionar (pT2NoMo) (Figure-1), e adenocarcinoma prostático Gleason VIII no lobo direito, não havendo acometimento dos linfonodos obturadores (pT2a No Mo) (Figure-2). No momento encontra-se bem e em acompanhamento ambulatorial com PSA < 0.4 ng/ml após 6 meses da cirurgia.

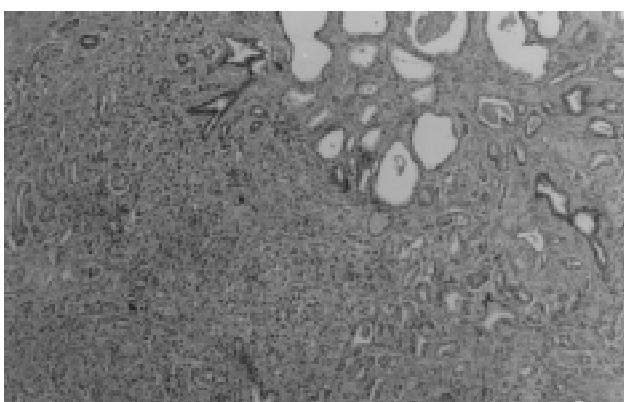


Figure 2 - Case 2: Adenocarcinoma of the prostate; Gleason VIII (5+3) (HE X40).

DISCUSSÃO

Em um estudo com 161 pacientes tratados com radioterapia para câncer prostático localizado, identificou-se 18 pacientes (14.75%) com tumores múltiplos associados a um tumor prostático primário, sendo que em apenas 2 (1.24%), o tumor secundário era genitourinário. Neste estudo, em 72% dos pacientes com neoplasias múltiplas, a neoplasia inicial era prostática, indicando que o câncer prostático parece preceder os outros sítios com os quais encontra-se associado (1).

Outros autores analisando 3675 registros médicos de pacientes com câncer prostático, identificaram 220 com outras neoplasias primárias, sendo que em somente 17 (7.72%) a segunda neoplasia primária era de origem renal. Destes 17 casos, 7 eram carcinoma de células renais, 5 adenocarcinomas, 3 carcinomas de células transicionais e dois tumores não foram histologicamente identificados (2).

Homens que desenvolvem câncer da próstata em idade menor que 70 anos, têm até 51.8% de chances de desenvolver outra neoplasia primária, e após os 70 anos este risco não é tão significante. Homens brancos também apresentam uma maior incidência de uma segunda neoplasia primária após câncer da próstata (2). Outra constatação é de que o risco de desenvolver outra malignidade genitourinária após diagnóstico do câncer prostático (até 34%), diminui com o tempo, sendo a maioria no primeiro ano e um número insignificante após 3 anos (2).

Em 164 pacientes tratados com radioterapia para câncer prostático localizado e estadiados cirurgicamente, identificaram-se 43 (26.21%) com tendo uma segunda neoplasia primária. Destes 43, apenas 5 pacientes (3.04 %) apresentavam neoplasia renal primária sincrônica (3).

É possível que os segundos tumores primários observados em muitos destes estudos, foram evidenciados somente devido ao diagnóstico inicial de câncer prostático. Os fatores que predispõem o indivíduo a neoplasias múltiplas podem ser hereditários ou adquiridos. Somente estudos direcionados às possíveis causas etiológicas de

neoplasias múltiplas em pacientes com câncer da próstata, podem confirmar a real necessidade de seguimento cuidadoso de pacientes com câncer prostático quanto à possibilidade de desenvolverem outra neoplasia primária.

*Dr. Pedro Gustavo Ferreira Falcão
realizou as fotografias.*

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LEIOMYOMA OF THE BLADDER

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ABSTRACT

Benign mesenchymal tumors of the bladder are rare and comprise less than 1% of the all bladder neoplasms. Leiomyoma is the most common type and comprises 35% of these tumors. These tumors may develop in submucosal (63%), intramural (7%) or subserosal (30%) layer, at any region of the bladder. The clinical presentation is varied and may include obstructive symptoms (50%), irritative symptoms (38%) and hematuria (11%). There are asymptomatic cases (19%), which make the diagnosis more difficult. Occurs more frequently in women than in men (3:1) and the majority of leiomyomas presented with a total extent of beyond 5 cm. The most common diagnosis exams are ultrasonography (US), intravenous urography and computed tomography scan. Recently, the transvaginal US and the magnetic resonance imaging (MRI) appear are useful imaging tools for diagnosis of leiomyoma of bladder.

A 38-year-old woman presented with lower abdominal pain and recurrent urinary tract infections during the last 4 years. Various examinations were performed in the last 6 months and none of them determined the diagnosis. We performed a transvaginal US, MRI and a cystoscopy with biopsy, confirming the diagnosis of leiomyoma. The surgical exploration revealed a well-circumscribed mass at the posterior bladder wall. The pathological examination revealed a leiomyoma of the bladder. The postoperative period was uneventful and the patient is doing well, without recurrence of the symptoms, during a 10-months follow-up.

Key words: bladder; neoplasms; benign tumor; leiomyoma**Braz J Urol, 27: 373-375, 2001****INTRODUÇÃO**

Os tumores mesenquimais benignos da bexiga são raros e correspondem a menos de 1% dos tumores vesicais. O leiomioma é o mais comum compreendendo 35% destes tumores (1). Apresentamos relato de um caso onde o diagnóstico foi feito somente 4 anos após o aparecimento do primeiro sintoma.

RELATO DE CASO

Paciente de 38 anos, sexo feminino, referidor em baixo ventre há 4 anos acompanhada de episódios recorrentes de infecção urinária adequa-

damente tratados. Há 6 meses apresentou intensificação do quadro doloroso. Antecedentes médicos incluíam uma drenagem percutânea de cisto de Gartner há 5 anos e cesárea há 15 anos. Exame físico sem alterações. Urina tipo I normal, ultra-sonografia (USG) demonstrou rins normais e bexiga com formação expansiva, hipoeocogênica, na parede pôsterior-mediana medindo 7.5 x 7.0 x 5.0 cm, dados estes comprovados pelo USG transvaginal (Figure-1). A urografia excretora mostrou boa excreção renal e falha de enchimento na bexiga. A ressonância nuclear magnética (RNM) revelou lesão em parede posterior de bexiga, medindo 7.0 x 6.0 cm, não invadindo estruturas adjacentes (Figure-2). A cistoscopia mostrou abaulamento em parede posterior

da bexiga. Esta massa foi biopsiada e o exame anáATOMO patológico foi sugestivo de tumor benigno composto por células musculares lisas.

Na exploração cirúrgica encontramos massa intramural na parede posterior da bexiga próximo à cúpula vesical, bem delimitada, medindo aproximadamente 7.0 x 6.5 cm. Foi realizada cistectomia parcial devido às proporções do tumor e à localização intramural. O anáATOMO-patológico revelou proliferação de células fusiformes sem atividade mitótica compatível com leiomioma vesical.

No seguimento de 10 meses houve resolução do quadro doloroso e dos episódios de infecção urinária.

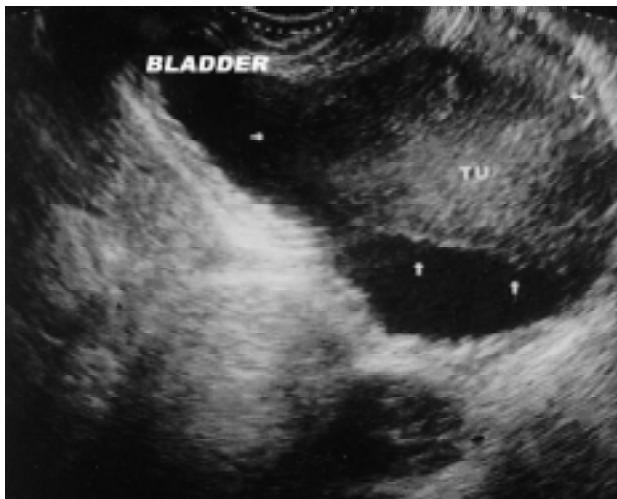


Figure 1 - Transvaginal ultrasound revealing an expansive, solid mass, located at the posterior wall, measuring 7.5 x 7.0 x 5.0 cm.

DISCUSSÃO

O diagnóstico diferencial dos tumores benignos da bexiga inclui os miomas (leiomiomas, e rabdomiomas), os fibromas, angiomas, mixomas e osteomas. Os leiomiomas compreendem 35% de todos estes tumores (1). Goluboff et al., revisou em 1994 os casos de leiomioma da literatura desde 1970 e relatou maior incidência em mulheres (3:1). Até 1997, encontravam-se descritos 230 casos de leiomioma vesical (2). Os sintomas freqüentes são os obstrutivos (50%), irritativos (38%) e hematúria (11%) (3). Os



Figure 2 - Magnetic resonance depicting a mass, circumscribed to the posterior bladder wall and preserving the adjacent tissues.

tumores assintomáticos correspondem a 19% dos casos e geralmente são de localização intramural ou extravesical.

Ressaltamos o emprego mais freqüente do USG transvaginal e da RNM para diagnóstico destes tumores. O USG é útil nas lesões de parede posterior (3) e a RNM pode diferenciar os tumores mesenquimais dos carcinomas de células transicionais da bexiga. Outros métodos diagnósticos têm sido relatados em literatura como a biópsia transretal guiada por ultra-som nos casos de tumores de parede posterior em pacientes do sexo masculino.

O tratamento depende do tamanho e da localização da lesão, optando-se pela enucleação ou cistectomia parcial, enquanto raros casos de massas endovesicais têm indicação de tratamento por RTU. A laparoscopia vem sendo empregada para auxílio diagnóstico e tratamento destas lesões.

CONCLUSÃO

Os tumores benignos da bexiga são raros, sendo de fundamental importância o diagnóstico prévio de leiomioma vesical, para que se estabeleça a adequada terapêutica. O ultra-som transvaginal e a RNM são ferramentas auxiliares modernas e de grande poder de resolução.

Os avanços da laparoscopia permitirão o diagnóstico mais preciso e a possibilidade de tratamento minimamente invasivo desta patologia raramente descrita.

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DOUBLE ONLAY PREPUTIAL FLAP FOR HYPOSPADIA REPAIR

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ABSTRACT

Objective: The conventional one stage hypospadias repair using island flaps has several disadvantages: Penile asymmetry resulting from rotation of the vascular pedicle around one side of the penile shaft and at times doubtful viability of the Byars flaps used for ventral skin coverage. We describe a technique that solves some of these problems: The double onlay preputial flap for hypospadias repair.

Surgical Technique: After circumcising incision is made, the urethral plate is outlined by 2 parallel incisions that extend to the glans. A total transverse preputial island flap is created and mobilized, ventral transposition is achieved by passing the penis through a bottom-hole created through the proximal third of the pedicle. The outer flap surface is then aligned with the urethral plate along its longitudinal axis. Suturing of the flap to the urethral plate is performed and the glans wings are re-approximated. The remaining preputial flap is used to cover the ventral skin defect.

Conclusion: The double onlay preputial flap technique for hypospadias repair offers good cosmetic and functional results.

Key words: hypospadias; congenital anomalies; surgical techniques
Braz J Urol, 27: 376-379, 2001

INTRODUÇÃO

O retalho ilhado prepucial tem sido utilizado para correção de hipospádias proximais em um estágio, com ou sem ressecção da placa uretral, com tubularização do retalho ou com colocação do retalho *onlay* (1,2). Este último apresenta os menores índices de complicações, além de nos casos de fistulas, estas são mais facilmente tratadas (2). Entretanto, este método de reparo tem a desvantagem de cobrir a porção ventral do pênis com um retalho do tipo Byars, que tem uma viabilidade duvidosa, já que pode não conter o suprimento sanguíneo arterial principal do prepúcio, aumentando, teoricamente, a chance de isquemia do retalho (3). Além disto, pode haver torção peniana devido à rotação do pedículo utilizado na reconstrução uretral (4,5). Nós descrevemos os passos

de uma técnica que resolve alguns desses problemas. Ela estaria indicada principalmente nos casos de hipospádia proximal ou médio-peniana, neste caso quando o diâmetro da placa é insuficiente para realização da cirurgia de Snodgrass.

TÉCNICA CIRÚRGICA

Figure 1- A)- Incisão circundando a placa uretral, circunscrevendo o meato uretral. Preservam-se 6 mm de largura da placa. A incisão é prolongada por toda a região subcoronal a 6 mm da glande, desnudando o pênis.

Figure 1- B)- Visão dorsal do pênis. Plicatura na linha média com fio inabsorvível para a correção da curvatura.

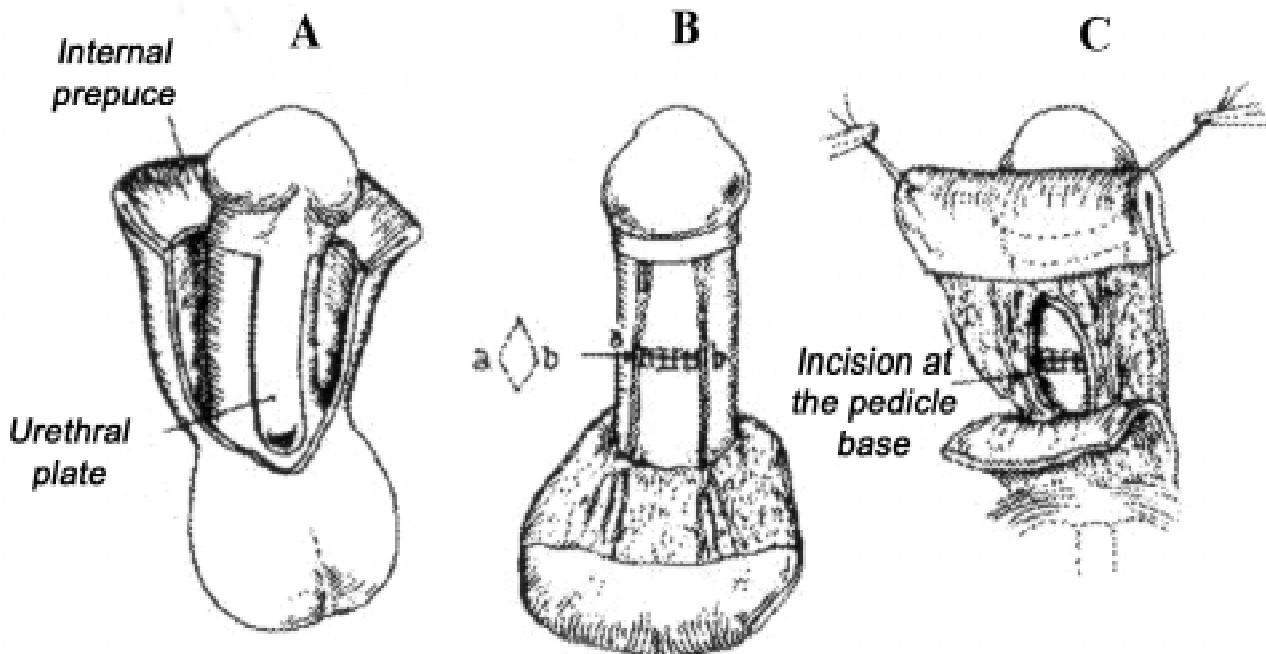


Figure 1 - A)- Incision delineating the urethral plate and circumferential to the urethral meatus. A 6 mm width of urethral plate is preserved. The incision is prolonged around the subcoronal region with penile degloving; B)- Dorsal view of the penis. Midline plication with non-absorbable suture for curvature correction; C)- Opening of a hole at the pedicle base. The flap is transferred to the ventral region through the glans.

Figure 1- C)- Abertura de um orifício na base do pedículo. O retalho é transferido para a porção ventral transpassando a glande.

Figure 2- A)- A glande é incisada bilateralmente e mobilizada conforme procedimento padrão para a correção das hipospádias. Notem que é o prepúcio externo que é utilizado para a reconstrução uretral.

Figure 2- B)- O prepúcio externo é rodado 90 graus e é suturado a um lado da placa uretral de forma contínua, com PDS 7-0. A sutura é extra-epitelial.

Figure 2- C)- O retalho é incisado 6 mm da borda suturada a placa, para perfazer um diâmetro uretral de 12 mm.

Figure 3- A)- A borda livre do retalho é suturada à borda da placa uretral, sobre um tubo de silicone multiperfurado 7F. Usa-se sutura contínua

com PDS 7-0, extra-epitelial. Uma nova camada de sutura utilizando-se tecido peri-uretral, é realizada.

Figure 3- B)- A glande é reaproximada na linha média com 2 camadas com PDS 5-0.

Figure 3- C)- O restante do retalho (porção interna) é utilizado para cobrir a porção ventral do prepúcio, após secção das bordas excedentes.

Após o procedimento procede-se bloqueio anestésico caudal para melhor controle da dor. O tubo de silicone é retirado após 5 a 7 dias da cirurgia.

COMENTÁRIOS

Barroso et al. recentemente publicaram a experiência com esta técnica (5). Identificou-se uma taxa de fístula de 17%, divertículo uretral em 9% e curvatura persistente em 4%. Esta taxa de complicações é baixa, considerando-se que 75% dos

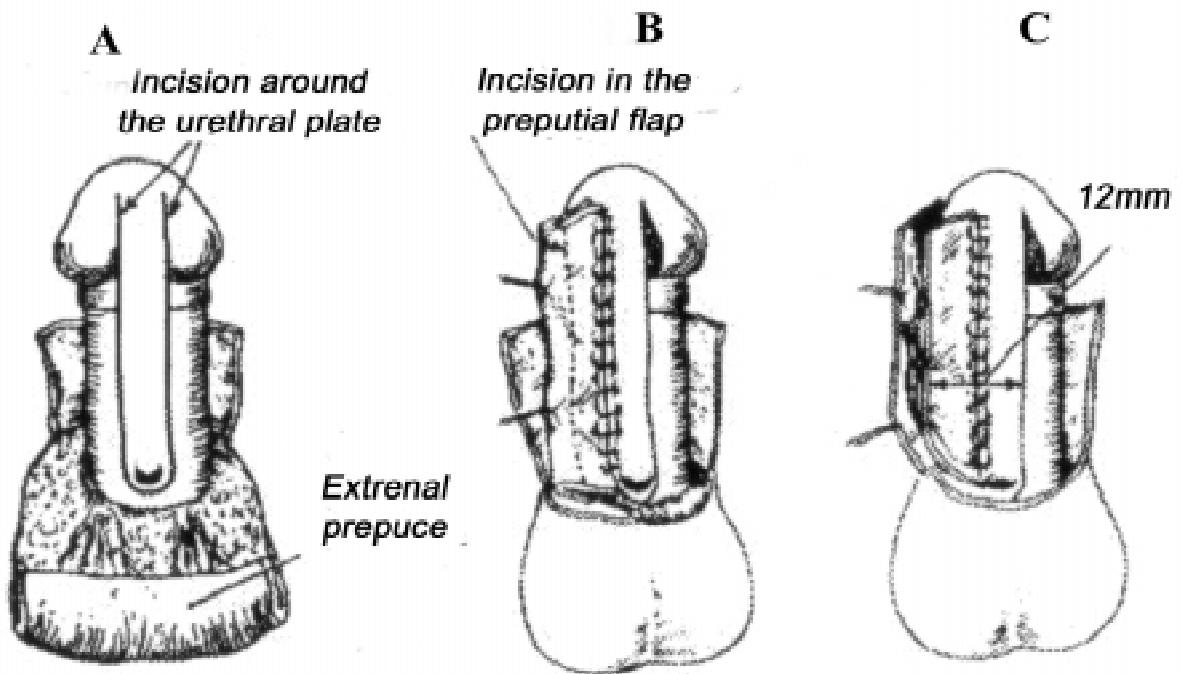


Figure 2 - A)-The glans is incised bilaterally and mobilized according to the standard procedure for hypospadias correction. Note that the external prepuce is used for the urethral reconstruction; **B)-** The external prepuce is rotated at 90-degrees and is running-sutured to one side of the urethral plate with PDS 7-0. The suture is extra-epithelial; **C)-** The flap is incised to 6 mm at the plate sutured margin, in order to create a urethral diameter of 12 mm.

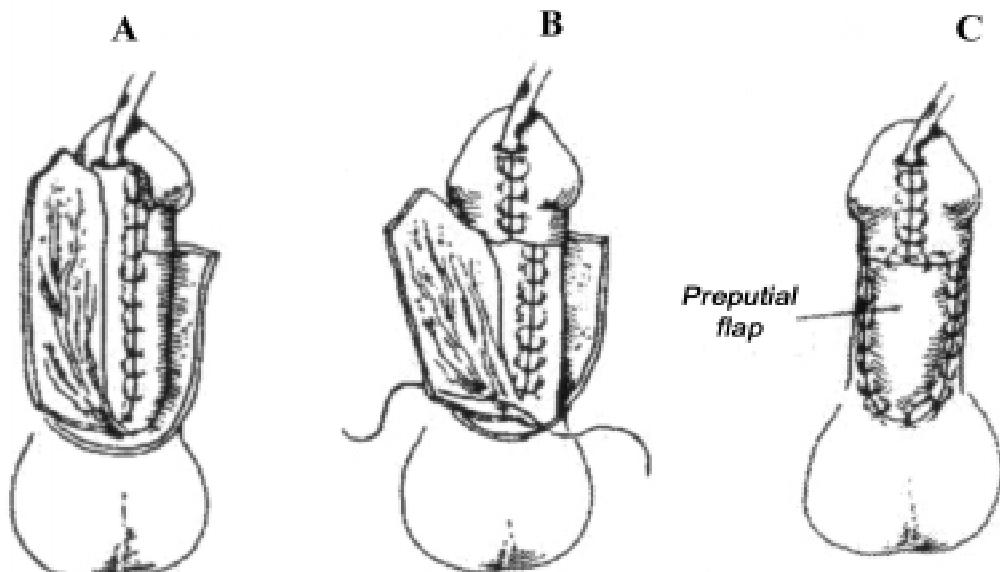


Figure 3 - A)- The free margin of the flap is extra-epithelial sutured to the margin of the urethral plate, over a 7F multi-perforated silicone catheter. Another layer is sutured with peri-urethral tissue; **B)-** The glans is re-approximated at the midline in 2 layers with PDS 5-0; **C)-** The rest of the flat (internal portion) is used to cover the ventral surface after excising the exceeding margins.

pacientes apresentavam hipospádias em região penoescrotal. Entre outras vantagens desta técnica incluem-se: não rotação peniana após a reconstrução, utilização de um retalho bem vascularizado tanto para a reconstrução da uretra como para a cobertura do defeito ventral. Este conceito de transposição ventral de retalho para cobrir o defeito ventral, pode também ser utilizado para correção de hipospádias distal por qualquer técnica.

A utilização de uma uretra de 12 mm permite um diâmetro satisfatório à passagem de urina, com menores riscos de divertículos. A correção da curvatura ventral quando necessária, é realizada com uma plicatura na linha média da porção dorsal do pênis. De acordo com Baskin et al. a inervação dorsal se dá lateralmente, portanto realizando-se a plicatura na linha média pode-se reduzir os riscos de lesão neural (2). Quando a plicatura dorsal não é suficiente para correção da curvatura, nós dissecamos a placa uretral, incisamos a albugínea e colocamos um enxerto de túnica vaginal.

Confecciona-se o orifício na base do pedículo do retalho, na região livre de vasos, que são facilmente visíveis por transparência. Um importante detalhe da técnica é a utilização do prepúcio externo para a construção uretral. Isto parece reduzir a possibilidade de divertículos pela maior resistência desta pele, comparada ao prepúcio interno. Além disto, a longo

prazo, o prepúcio interno utilizado para cobrir o defeito central queratiniza-se e adquire um aspecto normal.

É importante para a realização do procedimento utilizar lentes com lentes de no mínimo 2.5 vezes de aumento. Em conclusão, esta é uma técnica que oferece uma baixa taxa de complicações e excelente resultado cosmético.

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LAPAROSCOPIC EVALUATION AND TREATMENT OF THE IMPALPABLE TESTIS

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ABSTRACT

Objectives: To evaluate the laparoscopic technique as a diagnostic and therapeutic tool in the management of patients with impalpable testis.

Material and Methods: Fifty-nine patients with mean age of 6.3 years underwent laparoscopy to evaluate 85 impalpable testes that were classified as absent, canalicular and intra-abdominal. In the case of testicular absence, the procedure was terminated. In the case of canalicular testis, open inguinal exploration was performed. In intra-abdominal testis, either laparoscopic orchiopexy or orchietomy was performed. According to the length of the vascular pedicle, orchipexy was performed either with or without vascular ligature. Post-operatively, the treated testes were evaluated according to size and location in the scrotum.

Results: Seventeen (20%) of the 85 impalpable testes were diagnosed as absent, 21 (24.7%) as canalicular and 47 (55.3%) as intra-abdominal. Of the canalicular testes, 20 were explored by inguinotomy and one by laparoscopy. All the intra-abdominal testes were treated initially by laparoscopy, four being removed due to atrophy, 31 submitted to vascular ligation and 12 to primary orchipexy. Of those submitted to vascular ligation, 22 underwent a second stage orchipexy, of which 18 laparoscopically and 4 by inguinotomy. Of the 18 testes brought to the scrotum by staged laparoscopic orchipexy, 15 (83.3%) presented normal characteristics in the late follow-up, while of the 12 submitted to primary laparoscopic orchipexy, 8 (66.6%) were normal. There were no perioperative or late complications.

Conclusions: Laparoscopy is a minimally invasive procedure with low morbidity that enables precise diagnosis of the impalpable testes. When intra-abdominal testes are found, either immediate laparoscopic orchietomy, or primary and staged orchipexy are possible, with results equivalent to open procedures, with the advantage of smaller surgical incisions and shorter postoperative recovery.

Key words: testis; cryptorchidism; laparoscopy; diagnosis; treatment
Braz J Urol, 27: 380-385, 2001

INTRODUÇÃO

Em 1976 Cortesi descreveu a laparoscopia para avaliação de testículos impalpáveis, sendo esta técnica posteriormente incorporada à rotina diagnóstica em casos de criptorquidia (1,2). Em um trabalho pioneiro de grande repercussão internacional, Castilho apresentou o método no nosso meio, ressaltando sua acurácia e contribuindo para a sua divulgação (3). Em pouco tempo, a laparoscopia

deixou de ser exclusivamente diagnóstica, incorporando técnicas para o tratamento dos testículos intra-abdominais, que representam 10 a 20% dos casos de criptorquidia (4-7). Atualmente é um procedimento preconizado não apenas para avaliar os testículos impalpáveis, mas também para tratar, no mesmo ato, aqueles eventualmente localizados na cavidade abdominal. Na literatura nacional não existem relatos adicionais sobre o método, razão pela qual julgamos oportuna a apresentação de nossa experiência.

MATERIAL E MÉTODOS

A laparoscopia diagnóstica foi empregada em 59 pacientes com testículos impalpáveis, com idade variando entre 14 meses a 22 anos (média de 6.3 anos). Vinte e seis apresentavam criptorquidia bilateral, 21 unilateral esquerda e 12 unilateral direita, totalizando 85 testículos impalpáveis. No pré-operatório, todos foram avaliados por pelo menos 2 examinadores em ocasiões diferentes, inclusive por ocasião da anestesia, sendo critério de exclusão da casuística a palpação do testículo em qualquer ocasião.

Três pacientes referiam cirurgias prévias em outros serviços, exibindo cicatrizes de inguinotomia (bilateral em 1 caso), porém os testículos eram impalpáveis. Por falta de informações confiáveis sobre a primeira cirurgia, foram incluídos na investigação.

Em alguns casos com criptorquidia bilateral, foi feita avaliação laboratorial prévia, incluindo dosagens de testosterona antes e após estímulo com gonadotrofina coriônica, porém devido à inconsistência dos resultados, esse exame não interferiu na seleção dos pacientes, tendo sido abandonado. Em 11 foram realizados exames ultra-sonográficos, que identificaram testículos na região inguinal em apenas 3 pacientes, que mesmo assim foram incluídos na casuística, por não terem testículos palpáveis. Nenhum foi submetido à tomografia computadorizada ou ressonância magnética.

Não houve limitação etária para realização deste procedimento laparoscópico, sendo que o paciente mais jovem tinha 14 meses de idade. Não houve necessidade de cuidados pré-operatórios específicos. A anestesia foi geral com entubação endotraqueal e sondagem vesical e nasogástrica em todos os casos.

A técnica da laparoscopia exploradora e os critérios de identificação e caracterização do testículo foram detalhadamente descritos em publicações anteriores, não variando com a idade e tamanho do paciente (4-8). Baseado nesses critérios foram feitos os seguintes diagnósticos laparoscópicos: a)- ausência testicular, decorrente de agenesia testicular quando associada à ausência de deferente e vasos espermáticos ipsilaterais, ou de evanescência, quando

são visualizados os vasos espermáticos e o deferente terminando em fundo cego, podendo-se presumir a existência prévia da gônada, que desapareceu devido à torção durante a vida fetal b)- testículo canalicular, quando o testículo não é localizado, mas os vasos e o deferente são visualizados penetrando o anel inguinal interno, presumindo-se a existência de um testículo localizado no canal inguinal, de palpação dificultada por obesidade, atrofia ou evanescência c)- testículo intra-abdominal, localizados e visualizados desde o pólo inferior do rim até o orifício interno do canal inguinal, sendo caracterizados morfológicamente, por seu tamanho e características visuais, como normais ou atróficos. Eventualmente, na presença de uma hérnia inguinal, alguns se insinuam para o interior do saco herniário devido ao aumento da pressão intra-abdominal durante o procedimento, sendo visibilizados apenas ao se comprimir externamente a região inguinal, quando retornam para a cavidade abdominal. Nesta condição, são denominados testículos escondidos ou “peeping testes”.

As condutas e técnicas terapêuticas referentes a cada achado laparoscópico também foram descritas previamente (6-9). Resumidamente, no caso de ausência, o procedimento laparoscópico é encerrado, enquanto no caso de testículo canalicular está indicada a exploração inguinal, na qual eliminam-se os atróficos e relocam-se os preservados. No caso de testículo intra-abdominal atrófico, realiza-se a orquiectomia, porém se for morologicamente preservado, está indicada a orquiopexia. Ambas podem ser feitas com técnica laparoscópica, sendo a última realizada com ou sem secção do pedúculo vascular, de acordo com a posição inicial do testículo em relação ao orifício interno do canal inguinal e comprimento dos vasos espermáticos. No caso de secção vascular, a orquiopexia pode ser realizada no mesmo ato ou em etapa posterior, após 6 meses (9).

Após o tratamento cirúrgico definitivo, os pacientes foram seguidos ambulatorialmente por período que variou de 2 a 63 meses (média de 17.7 meses), sendo reavaliados pela incidência de complicações peri ou pós-operatórias, bem como pela localização, consistência e tamanho dos testículos intra-abdominais relocados para o escroto. Estes últimos dados foram obtidos por meio de palpação

seqüencial, pela qual os testículos foram classificados em normais, quando de tamanho e consistência preservadas e bem localizados no escroto, atróficos quando de tamanho ou consistência diminuídos e mal posicionados, quando de localização alta, mas de bom tamanho.

RESULTADOS

Os achados da laparoscopia diagnóstica estão apresentados na Table-1. Em 3 pacientes com criptorquidia bilateral, o diagnóstico dos testículos não foi coincidente, razão pela qual estão listados na coluna da esquerda. Nos 23 pacientes na coluna da direita, ambos os testículos tinham o mesmo diagnóstico.

A conduta terapêutica está apresentada na Table-2. Em 25.4% dos pacientes (20% dos testículos impalpáveis) com diagnóstico de ausência testicular (4 com agenesia e 11 com evanescência), interrompeu-se o procedimento laparoscópico, sendo os pacientes poupadados de exploração adicional desnecessária. Em 12 desses pacientes, já de maior idade, foi feita inserção de prótese testicular. Entre os 27.1% dos pacientes (24.7% dos testículos impalpáveis) nos quais diagnosticou-se testículo canalicular, em um foi possível realizar a orquiectomia por laparoscopia, dissecando-se o cordão espermático pelo anel

Table 1- Laparoscopic diagnosis of the impalpable testes.

Diagnosis	Unilateral	Bilateral
Absence	13	2
Canalicular	11*	5
Intra-abdominal	15	14
Total	39 testes (36 pts.)	42 testes (21 pts.)

*3 patients with bilateral cryptorchidism, but without coincident diagnoses: 2 with contralateral vanishing testis and 1 with contralateral intra-abdominal testis.

inguinal. Nos outros casos, encerrou-se a laparoscopia e realizou-se a inguinotomia exploradora. Em 5 destes pacientes foram detectados testículos viáveis, imediatamente relocados ao escroto. Em outros 3 pacientes foram encontradas gônadas atróficas, que foram removidas. Nos restantes, não se encontraram vestígios testiculares. Seis pacientes desse grupo foram submetidos a implante de prótese.

Em 47.5% dos pacientes (55.3% dos testículos impalpáveis) nos quais foram identificados testículos intra-abdominais, o tratamento variou de acordo com a morfologia e localização dos mesmos. Quatro testículos de 3 pacientes (bilateral em um caso) eram atróficos, sendo removidos laparoscopicamente no mesmo ato. Nos 43 restantes foi indicada a orquiopexia: em 31 testículos de 19 pacientes optou-

Table 2 - Laparoscopic and non-laparoscopic treatment of impalpable testes.

Diagnosis (No.)	Treatment (No.)			
	Laparoscopic	Non-laparoscopic		
	1 st . Stage*	2 nd . Stage	1 st . Stage	2 nd . Stage
Absence (17)			Test. prosthesis (12)	
Canalicular (21)	Orchiectomy (1)		Inguinotomy (20) with: Orchipexy (5) Orchiectomy (3) Test. prosthesis (6)	
Intra-abdominal (47)	Orchiectomy (4)			
	Vascular ligation (31) ⇒ Orchipexy (18)		⇒ Orchipexy (4)	
	Orchipexy Without vascular lig. (11)			
	With vascular lig. (1)			

*1st. stage corresponds to the diagnostic laparoscopy

se pela técnica estagiada, realizando-se a ligadura vascular no mesmo ato. Subseqüentemente, 22 destes testículos (de 15 pacientes) foram submetidos a orquiopexia em um segundo tempo, 6 ou mais meses mais tarde, dos quais 4 (de 3 pacientes) por cirurgia aberta e 18 (de 12 pacientes) por laparoscopia. Quatro pacientes com ligadura vascular de ambos testículos e outro com ligadura unilateral não se submeteram à orquiopexia, sendo 2 por abandono e 3 por não terem completado o período de espera para realização do segundo tempo. Os outros 12 testículos (de 11 pacientes) foram submetidos a orquiopexia primária laparoscópica, dos quais apenas um com secção vascular.

Na avaliação tardia dos testículos submetidos à orquiopexia, dos 22 levados ao escroto em 2 tempos, 16 (86.4%) estavam com tamanho preservado e localizados no escroto, e apenas 3, submetidos ao segundo tempo laparoscópico, evoluíram para atrofia. Quando se consideram apenas os tratados com segundo tempo também por via laparoscópica, a porcentagem cai para 83.3%. Entre os 12 testículos tratados por orquiopexia laparoscópica primária, 8 (66.7%) estavam tópicos e normais, enquanto 3 evoluíram para atrofia, incluindo o que foi submetido à ligadura do pedículo vascular, e um, de bom tamanho, não ficou adequadamente posicionado no escroto, por falha na fixação escrotal (Table-3).

Nenhum dos pacientes submetidos à laparoscopia diagnóstica e terapêutica apresentou

complicação intra-operatória, não tendo havido necessidade de conversão para cirurgia aberta ou transfusão sanguínea. A recuperação pós-operatória foi normal em todos os casos, com realimentação no mesmo dia. A alta hospitalar ocorreu em geral no primeiro dia de pós-operatório, retardando-se para o segundo no caso de orquiopexia. Os pacientes foram medicados rotineiramente com antibiótico, acrescentando-se analgésicos e antiinflamatórios apropriados para a idade, conforme necessidade. Em nenhum paciente foi observada complicação nas feridas operatórias, incluindo as dos trocares abdominais e escrotais. Tampouco foi observada hérnia inguinal ou incisional no pós-operatório tardio.

DISCUSSÃO

As justificativas do tratamento do testículo criotorquídico são bem conhecidas, estando relacionadas com o aspecto cosmético, a perda da capacidade germinativa e possibilidade de malignização. Esta última é particularmente importante no caso dos testículos impalpáveis, pela associação freqüente com displasia.

Atualmente recomenda-se que a identificação e tratamento dos testículos criotorquídicos seja feita antes dos 2 anos de idade (5). Entretanto, em nosso meio é freqüente a consulta inicial de pacientes criotorquídicos com mais idade, o que explica a idade média elevada de nossos pacientes.

Table 3 - Late results of orchipexy, regarding size and position of treated testis.

Treatment (No.)	Technique (No.)	Results
Staged orchipexy (22)*	Laparoscopic 2 nd . stage (18)	3 atrophic 12 normal
	Open 2 nd . stage (4)	4 normal
Primary orchipexy (12)**	With vascular ligature (1)	1 atrophic
	Without vascular ligature (11)	8 normal 2 atrophic 1 mal-positioned

*of 15 patients; ** of 12 patients

No caso dos testículos impalpáveis, inúmeros testes são empregados para diagnosticar a presença ou ausência dos testículos e permitir um adequado planejamento cirúrgico, e evitar cirurgias desnecessárias no caso de ausência dos mesmos. No caso de criptorquidia bilateral impalpável, o teste de estimulação com gonadotrofina coriônica pode ter utilidade. No entanto, seus resultados não são definitivos, pois a resposta positiva, com aumento dos níveis de testosterona sérica, embora confirme a existência de pelo menos uma gônada, não caracteriza seu número nem define o lado. Além disso, a resposta negativa, embora sugestiva de ausência, não elimina a possibilidade da presença de uma gônada displásica (6,10).

A ultra-sonografia tem sensibilidade de 90 a 95% nos testículos de posição intracanalicular ou pré-pubiana, porém nos intra-abdominais a sensibilidade é de 0 a 9%. Por outro lado, também ocorrem falsos positivos, pela presença de gânglios inguinais erroneamente interpretados como gônadas (6,9,10).

A tomografia computadorizada e a ressonância magnética têm melhor capacidade de identificação de testículos intra-abdominais, porém a frequência de falsos negativos com estes exames ainda é alta, particularmente em crianças menores, com pouca gordura retroperitoneal (9,10).

A angiografia por ressonância magnética com gadolínio, recém introduzida, apresenta resultados promissores, possibilitando a identificação do testículo pela caracterização dos vasos espermáticos. Apresenta sensibilidade de 96% e especificidade de 100% tanto para testículos intra-abdominais como canaliculares, porém é um exame que exige sedação, além de ser muito caro e não rotineiro em nosso meio (10).

A orquiopexia de testículos palpáveis é preferencialmente realizada através da inguinotomia. A rigor, este acesso também pode ser empregado para explorar e tratar testículos impalpáveis, porém a falta de informações pré-operatórias sobre a presença, localização e características do testículo pode levar a incisões e dissecções extensas, eventualmente desnecessárias, particularmente no caso de bilateralidade.

A laparoscopia é um procedimento diagnóstico, que embora seja invasivo, tem caráter de mínima agressividade, fornecendo o diagnóstico preciso da presença ou não do testículo, sua localização e morfologia. No caso de bilateralidade, ambos testículos podem ser avaliados sem necessidade de punções adicionais.

Em 25.4% dos nossos pacientes, com diagnóstico de ausência de testículo por agenesia ou evanescência, a laparoscopia foi exclusivamente diagnóstica, pouparando-os de inguinotomia desnecessária. Em outros 27.1%, com diagnóstico de testículos canaliculares, a laparoscopia orientou para a exploração inguinal mínima no mesmo ato, que foi ampliada apenas quando se identificou testículo viável, para realizar a sua pexia.

A grande vantagem da laparoscopia foi evidenciada no restante dos pacientes, nos quais não apenas foi feita a identificação dos testículos intra-abdominais, como também iniciado, no mesmo ato, o tratamento dos mesmos pela orquiectomia, ligadura vascular ou orquiopexia, com isso abreviando o tratamento.

Nas orquiopexias realizadas exclusivamente por técnicas laparoscópicas, além do aspecto cosmético, evidentemente favorável à laparoscopia, também se ressalta o retorno mais precoce às atividades físicas do que em cirurgia aberta. Embora seja difícil avaliar de modo objetivo a intensidade da dor pós-operatória em crianças menores, existem evidências clínicas sólidas comprovando a vantagem da laparoscopia sobre a cirurgia aberta em adultos, tanto em urologia como outras especialidades (11). Mesmo que estes aspectos não sejam muito relevantes na faixa etária pediátrica, deve-se considerar que a menor necessidade de cuidados pós-operatórios em cirurgia laparoscópica permite que os pais sejam liberados mais precocemente destas tarefas, para reassumir suas atividades rotineiras.

Quanto ao resultado tardio das orquiopexias realizadas exclusivamente por laparoscopia, obtivemos 83.3% de testículos tróficos e bem posicionados com a técnica em 2 tempos e 66.7% com a técnica em um tempo. Estes valores são equivalentes aos da orquiopexia aberta para testículos

intra-abdominais, ao redor de 70.1% em crianças até 6 anos e 64.5% em pacientes de mais de 6 anos (12). Alguns trabalhos recentes demonstram sucesso de 90% com orquiopexia laparoscópica, porém em grupos etários significativamente mais jovens que o nosso (13,14).

Em uma análise retrospectiva, é provável que, por falta de experiência no início de nossa casuística, tenhamos feito a secção vascular desnecessariamente em alguns casos. Nesta fase, a orquiopexia foi realizada em 2 tempos, sendo o segundo aberto. Com maior experiência, passamos a realizar o segundo tempo também por via laparoscópica, incluindo testículos cada vez mais altos. Finalmente, eliminamos o segundo tempo cirúrgico, passando a realizar a orquiopexia laparoscópica primária, preferencialmente sem ligadura vascular. Atualmente, esta é feita previamente apenas nos testículos muito altos, com limitação importante no comprimento do pedículo vascular.

Em nosso serviço, consideramos atualmente a laparoscopia imprescindível, suficiente e segura na avaliação de testículos impalpáveis, tendo dispensado a avaliação pré-operatória por imagem. Em mais da metade de nossos pacientes, a laparoscopia foi exclusivamente diagnóstica, tendo demonstrado com segurança a inexistência de testículos na cavidade abdominal. Nos restantes, além da identificação precisa das gônadas, foi possível a complementação terapêutica parcial ou total por técnica laparoscópica, com sucesso equivalente à cirurgia aberta, porém com evidentes vantagens no aspecto cosmético e de recuperação pós-operatória.

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VAGINAL WALL TRANSVERSE FLAP SLING FOR REPAIR OF SEVERE CYSTOCELE AND CYSTOURETHROCELE WITH ASSOCIATED STRESS INCONTINENCE

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ABSTRACT

Objective: Surgical treatment of severe anterior vaginal wall prolapse and associated stress incontinence is controversial. We present our experience with a modification of the vaginal sling combined with anterior colporraphy for severe cystocele and cystourethrocele.

Patients and Methods: Since 1992 we used this technique in 41 consecutive patients suffering stress incontinence and anterior vaginal wall prolapse, with a minimum postoperative follow-up of 1 year. Vaginal wall prolapse was severe in all cases: 19 (46%) grade III and 22 (54%) grade IV cystocele. Stress incontinence was evidenced in all cases, originally consulted in 29 (71%) and revealed by a positive vaginal pack test in the rest (29%). Anterior colporraphy was accomplished by percutaneous suspension of a large vaginal wall transverse flap that was rotated to support the bladder neck and was sutured to the rectus fascia. Vaginal hysterectomy and posterior colporraphy were performed in 14 (34%) and 25 (62%), respectively.

Results: At a mean follow-up of 42 months success rate was 93% (38/41) for cystocele repair and 88% (36/41) for treatment of associated stress incontinence. Significant postoperative detrusor instability was present in 9 (22%), and "de novo" developed in 3 of them. Intermittent catheterization was needed in 22 (54%) and time to resume postoperative voiding was 3.6 weeks, range 1-14. No patient developed permanent urinary retention. No sexually active patient suffered dyspareunia six months after surgery. Mean hospital stay was 3.1 days, including cases with hysterectomy.

Conclusions: Anterior colporraphy with buttressed support of the bladder through a vaginal wall transverse flap sling is a safe method for repair of severe cystocele or cystourethrocele and treatment of associated stress incontinence that achieves satisfactory results at a reasonable follow-up. This approach prevents development of stress incontinence after surgery of cystocele in cases with a positive vaginal pack test. Besides, the peculiar orientation of the vaginal mucosa harvested for the sling avoids the potential problems of foreshortening the vaginal vault.

Key words: urinary incontinence; stress; bladder; surgery; cystocele
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INTRODUCTION

Based on novel concepts, the selection of the proper approach to treat stress urinary incontinence must consider both the degree of anterior vaginal wall prolapse and the anatomical origin of incontinence:

hypermotility or intrinsic sphincteric deficiency. Anterior vaginal wall prolapse can be graded according to the level of descend of the bladder in relation to vaginal introitus. Most often the bladder base produces the cystocele; but the bladder neck and urethra are often involved, especially when prolapse

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is severe. Urethral hypermobility and occult sphincteric deficiency are generally present with moderate and severe cystocele (1).

The classical approach to cystocele was based on the approximation of lax pubocervical fascia and narrowing of the bladder neck (Kelly plication), but failure rate in terms of correcting or preventing incontinence is well-known (2). The abdominal approach of Burch colposuspension successfully achieves continence in many cases but only treats mild-to-moderate cystocele and needs a laparotomy (3). Its recent laparoscopic modification diminishes both morbidity and hospital stay but is still inappropriate to cope with a severe cystocele. In the search of a rational repair of severe cystocele that allows improvement of results and decrease of morbidity, the transvaginal route with

combined bladder neck suspension and repair of the defect in the pubocervical fascia was promoted (4,5). In this sense, some authors have described the use of a vaginal tube fixed in the bladder neck or suspended subcutaneously, similarly to the technique of Pereyra (6). Recently, pubovaginal sling (7-9) and even transvaginal placement of a hammock of nonabsorbable mesh (10) have been promoted as first choice therapy for anterior vaginal wall prolapse and associated stress incontinence of any kind.

We report our experience with a modification of Raz procedure for the treatment of severe anterior vaginal wall prolapse that uses the combination of both anterior colporraphy and a transverse long vaginal flap sling to support the bladder neck and effectively treat stress incontinence.

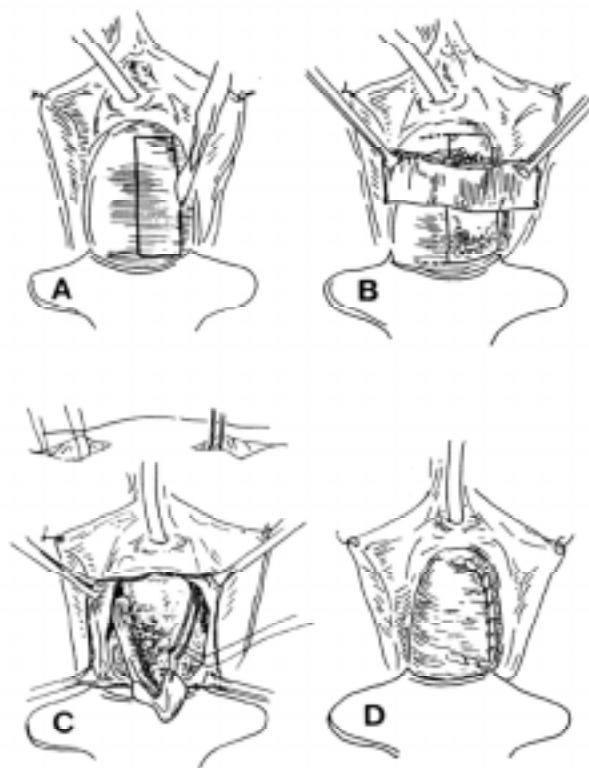


Figure 1 - A)- The vertical midline incision in the anterior vaginal wall is extended laterally to create a rectangular flap; **B)-** This vascularized island is transversely rotated to act as a sling; **C)-** The retropubic space is entered after dissection of the perirethral fascia and urethropelvic ligament, and the vaginal transverse flap sling is passed up to the rectus fascia as in Raz's technique; **D)-** A second lateral vaginal wall flap is advanced to restore the vagina after anterior colporraphy is performed.

PATIENTS AND METHODS

Surgical Technique

The patient is placed in the lithotomy position with access to the suprapubic area and a 18F Foley catheter is inserted through the urethra and the bladder emptied. Perioperative intravenous ampicillin and gentamicin are administered, and will be continued until hospital discharge. The vagina is exposed and a vertical midline incision is made in the anterior vaginal wall, from the area of the mid urethra to the posterior edge of the cystocele, and extended laterally to create a rectangular flap measuring 8 to 10 cm long and 3 to 4 cm wide (Figures-1A and B). This island of anterior vaginal wall is dissected with the help of Allis clamps but great care is taken to preserve the vascular supply of the vaginal wall. For this purpose the periurethral fascia is included in the flap. This flap will be transversely rotated to act as a sling and the contralateral side of the vagina is incised and undermined to create a second advance flap that will cover the island at a later step (Figures-1B and D). Lateral dissection is performed along the periurethral fascia to the pubic bone. The urethropelvic ligament is identified and bluntly dissected to perforate the endopelvic fascia and enter the retropubic space. The bladder neck and urethra are easily mobilized. At the level of the bladder base the pubocervical fascia and the edge of levators are dissected from the bladder

on each side and separated from the herniated bladder that will be later introduced.

The vaginal transverse flap sling is prepared. No. 1 polypropylene sutures that incorporate the entire vaginal wall and periurethral fascia anchor the four corners of the rectangle and are transferred individually using a double-pronged ligature carrier from the vagina to the suprapubic region up to the rectus fascia as designed by Raz et al. (11) (Figure-1C). The sling is carefully placed at the level of the bladder neck and proximal urethra. The edges of the pubocervical fascia are approximated by 2-0 polyglactin sutures from the bladder neck to the cardinal ligaments. Endoscopic examination is helpful at this point to prevent unnoticed penetration of bladder or urethra. Vaginal hysterectomy and/or posterior colporraphy can be performed at this time if needed. The lateral vaginal wall flap is advanced to restore the integrity of the vagina using a running 2-0 polyglactin suture (Figure-1D). Only after closure of the vaginal wall the 4 sutures are tied independently by the assistant at the small suprapubic incision on each side. Not much tension is needed but urethral motility must no longer be felt by tugging on the Foley catheter while the knot is tied down. The small suprapubic incisions are closed. A vaginal pack is not considered necessary unless significant bleeding persists, and we do not use suprapubic tube either. The Foley catheter is removed on postoperative day 2 and post-void residual is recorded. If patient is

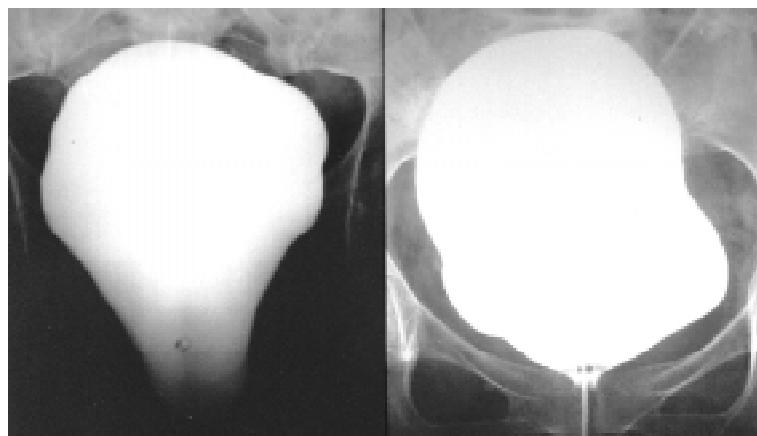


Figure 2 - Preoperative (left) frontal view of grade IV cystocele (bladder base below hymeneal ring at rest) and postoperative (right) orthostatic frontal view during Valsalva maneuver.

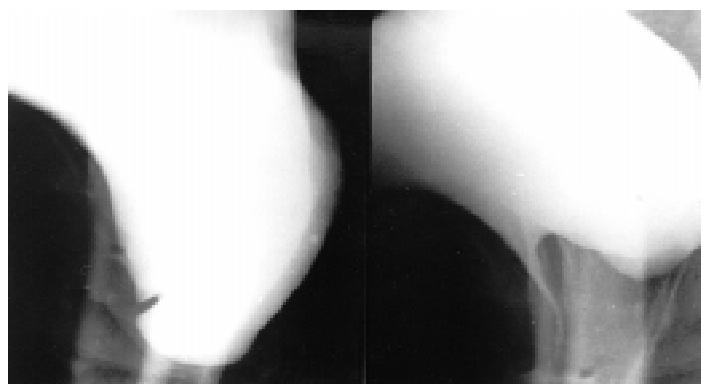


Figure 3 - Lateral preoperative (left) and postoperative (right) voiding cystourethrogram in the same patient, of Figure 2.

unable to void, or residual volume is greater than 100 cc, intermittent self-catheterization is started. The patient is taught and supervised in the office, thus allowing early discharge. Intermittent catheterization is continued until residual urine is consistently less than 100 cc. All patients were examined, operated, and controlled by the same surgeon (JCA). To reduce potential examiner bias, a blinded third party (ME) reevaluated all patients postoperatively, independently from surgeon assessment. Follow-up was closed at the time outcome measurements, based on physical examination and physician's interview, were performed. Presence of a significant cystocele, continence status, persistent and de novo urge incontinence, duration of self-catheterization, and the possibility of dyspareunia were recorded.

Patients

Since 1992 we have used this technique in 41 consecutive patients suffering severe cystocele, with a minimum follow-up of at least one year. Inclusion criteria were large (grade III and IV) cystocele (Figure-2), positive vaginal pack test, and absence of previous surgical procedures to correct incontinence. Mean age was 65.4 years (C.I. 62.8-67.9, range 49-76). In 19 patients (46%) the bladder base appeared outside introitus with strain (grade III cystocele) and in 22 (54%) the bladder base was below the hymeneal ring at rest (grade IV cystocele or cystourethrocele). The degree of the cystocele was also documented under fluoroscopic monitoring with the patient in standing position (Figure-3). Vaginal

pack test demonstrated stress incontinence in all cases ($n = 41$). Without insertion of the vaginal pack, stress urinary incontinence was evidenced on physical examination in 29 cases (71%) and the vaginal pack test demonstrated occult incontinence in the remaining 12 (29%). Patients with a large cystocele that remained continent after vaginal pack insertion are not the object of this communication as they received cystocele repair alone without the vaginal sling. Incontinent patients, either at initial examination or after the pack test, were treated as described above by anterior colporraphy and vaginal wall transverse flap sling. Multichannel cystometry was performed before surgery in 22 patients (54%) and approximately 30-60 days after surgery in 8 (20%). Indications for preoperative urodynamic study were associated urgency incontinence and previous surgical procedure (vaginal hysterectomy and failed cystocele repair). Urodynamic study was performed postoperatively when results were unsatisfactory, either due to persistent stress incontinence or de novo urge incontinence. A number of added procedures were needed to complete perineal repair. Vaginal hysterectomy was performed in 14 cases (34%), posterior colporraphy in 25 (62%), and enterocoele repair and vaginal vault prolapse in 1 (2.4%) each. Hysterectomy was indicated either for medical reasons (e.g., fibroids, bleeding) or because of the presence of significant uterine prolapse associated with pelvic discomfort and dyspareunia. This procedure had been previously performed in 7 cases (17%), 4 of them with associated failed

colpopereineorraphy. Patients were periodically followed until June 1999, and outcome was assessed from June 1999 to September 1999.

RESULTS

At a mean follow-up of 42 months (C.I. 31.3-52.8, range 12 to 83) 36 of the 41 patients were completely continent for a success rate of 88%. Continence is defined as absent or very rare stress incontinence, without need of pads or any social limitations. Among the cases that were incontinent after surgery, 2 patients worn 2 pads or less a day and 3 patients used at least 3 pads. Abdominal leak point pressure was under 60 cm water in 4 of 5 cases with failure, thus suggesting intrinsic sphincter deficiency. In one case incontinence was demonstrated before surgery only by a positive vaginal pack test, but it was clinically overt after surgery. Therefore, we were able to correct stress incontinence in 25 of 29 patients (86%) with severe cystocele and associated stress incontinence and were able to prevent development of incontinence in 11 of 12 patients (92%) in which incontinence was only revealed by a positive vaginal pack test.

Preoperative Valsalva leak point pressure ranged from 15 to 180 cm H₂O (mean 61.3, SE 8.6) in the patients studied. Stress incontinence was accompanied by urgency incontinence at diagnosis in 16 patients (39%) and urodynamic testing demonstrated instability in 13. Postoperative significant detrusor instability (i.e. frequency, urgency and/or urge incontinence in the absence of a positive urine culture) was complained in 9 cases (22%). It appeared de novo in 3 patients (7%) and persisted despite surgery in 6 (15%). In all cases it was effectively controlled with anticholinergic therapy and no patient suffered urge incontinence. Therefore, with the use of this surgical procedure, bladder instability disappeared after cystocele repair in a significant number of cases (10 of 16 patients), and was easily managed medically in the rest.

The success rate for anatomical cystocele repair with the vaginal wall transverse flap sling and colporraphy was 93%. Cured cystocele, considered

so when an excellent anterior vaginal wall support or a mild asymptomatic cystocele in the standing position is documented, was achieved in all cases but three. Persistent cystocele was mild but symptomatic, and 2 of them coexisted with stress incontinence. There were no intraoperative complications, such as need for blood transfusion, bladder perforation or fistula formation. Postoperative complications include already mentioned de novo detrusor instability (3 cases); wound infection with formation of a suprapubic abscess (1 case), and enterocele formation (1 case). No patient suffered permanent retention but 22 (54%) suffered it transiently, i.e. needed intermittent catheterization, a week or more. Among them, the mean time to resume voiding with postvoid residual under 100 cc was 3.6 weeks (range 1 to 14 weeks, C.I. 1.8-5.4). No patient complained dyspareunia postoperatively. Mean hospital stay was 3.1 days (C.I. 2.5-3.7, median 3 days), and that included cases with hysterectomy. Mean stay of 27 cases treated with anterior colporraphy and vaginal wall transverse flap sling without hysterectomy was 2.2 days (C.I. 1.6-2.8).

DISCUSSION

We present a simple and secure vaginal procedure for the correction of severe cystocele or cystourethrocele and associated incontinence, either evident or occult. This technique incorporates anterior colporraphy with buttressed support of the bladder neck through a vaginal sling. The peculiar transversely rotated quadrangular flap we describe, later covered by a second contralateral advance flap, allows a very satisfying reconstruction of redundant anterior vaginal wall and is particularly appropriate to repair a large cystocele. The main advantage over the conventional inverted U vaginal flap described by Raz et al. (11) is that no vaginal shortening is to be expected but a reconstructive narrowing is performed instead. Dyspareunia has been investigated and proved absent in every case.

Many patients with severe genital prolapse have underlying incontinence uncovered during urodynamic testing (13). We consider this technique

is specially indicated when severe cystocele is accompanied by a positive vaginal pack test. Under this circumstance a high percentage of patients demonstrates internal sphincteric deficiency and the rest suffer urethral hypermotility (1). Once type III incontinence is identified pubovaginal or vaginal sling, in addition to pelvic floor repair, is recommended (14-16). Results of vaginal and pubovaginal slings appear equally satisfactory on the long-term (17). Besides, increasing evidence exists to expand the indication of sling procedures for treatment of type II stress incontinence, based on its high success rate and affordable low number and severity of complications related to the procedure (i.e., long-term obstruction and *de novo* detrusor instability). Sling procedures can therefore be the ideal overall treatment for stress incontinence regardless of type, and be indicated as first line treatment for both urethral hypermotility and intrinsic sphincteric deficiency (16,18-20).

We report 93% cure rate for cystocele and 88% cure rate for incontinence with the use of anterior colporraphy with vaginal wall transverse flap sling, at a mean follow-up of more than 3 years. The fact that the vaginal pack test was positive in all cases means a high proportion of patients with complicated type III stress incontinence has been selected and, even though, outcome is encouragingly good. Anterior colporraphy with buttressed support of the bladder through a vaginal wall transverse flap sling, is a safe method to prevent development of iatrogenic incontinence after repair of severe cystocele. It is a minimally invasive vaginal procedure that can easily be combined with vaginal hysterectomy and/or posterior colporraphy. It obviates the morbidity associated with an abdominal procedure and allows early hospital discharge.

Herniation of the bladder outside the introitus, either with strain (grade III cystocele) or at rest (grade IV), implies severe weakness of vesicopelvic fascia both in its lateral aspect (lateral defect) and in the midline (central defect). According to Raz et al., the lateral defect can be repaired by a four corner bladder neck suspension that supports the bladder base anchoring the pubocervical fascia, cardinal ligaments and vaginal wall; and the central

defect is repaired by re-approximation of the pubocervical fascia and cardinal ligaments in the midline (2,5). The Burch operation both corrects urethral hypermotility and repairs the cystocele by suspending the vaginal wall and secondarily the urethra and bladder to Cooper's ligament, without urethral obstruction (12). A vaginal wall sling has the advantage to provide both compression and support for the urethra and also resuspend the bladder neck (21). It has proved an excellent option for the treatment of both genuine incontinence and intrinsic sphincteric deficiency (16,22). Therefore, vaginal sling combined with central defect repair by re-approximation of the pubocervical fascia and cardinal ligaments is a logical option for repair of anterior vaginal wall prolapse. The technique we describe is a variation of the pubovaginal sling that uses a flap of anterior vaginal wall, and could behave more like a pubovaginal sling than the vaginal sling described by Raz et al. In this sense, the results we present could be better than those reported for other techniques to treat large cystoceles; however, prospective comparative trials evaluated with validated questionnaires are needed. Other authors have already proposed the association of a sling and formal cystocele repair as a good option within the therapeutic arsenal of large volume cystocele (7-10,23).

The degree of cystocele formation is not totally related to the degree of incontinence. A large cystocele may serve as a pressure-relief system that protects a poor urethral continence mechanism and prevents leakage with exercise. The vaginal pack test is a simple maneuver to identify patients at risk for stress urinary incontinence after repair of a cystocele. If urethral hypermotility or intrinsic sphincteric deficiency is not detected and, therefore, cystocele repair is not completed with any form of urethral support, *de novo* stress incontinence is very likely to develop. Surgical techniques that do not face the possibility of sphincteric deficiency are at increased risk of failure. Anterior colporraphy with buttressed support of the bladder through a vaginal wall transverse flap sling is a safe method for repair of severe cystocele or cystourethrocele and treatment of associated stress incontinence or prevention of the

novo stress incontinence after a positive vaginal pack test. Anterior colporraphy alone may be effective enough, however, to cure a cystocele with a negative pack test during evaluation. We share the opinion that vaginal pack test makes sophisticated videourodynamics equipment unnecessary for evaluation of large cystourethrocele (24). Abdominal leak point pressure is not valid in the presence of a cystocele and cannot be taken as an accurate indicator to classify type II or III incontinence under this circumstance, neither can it define the appropriate operation. Based on increasingly acceptance of sling procedures for type II incontinence, we have abandoned Raz bladder neck or Burch abdominal suspensions to treat grade III and IV cystocele with a positive vaginal pack test and currently perform a vaginal wall sling in the fashion we describe. It not only suspends the bladder neck, but also elevates the whole trigone centrally and laterally, and reinforces paraurethral and paravesical fascia with a resistant and totally biocompatible tissue. We hope that same as its close relative, fascial pubovaginal sling, this technique withstands the test of time.

In conclusion, we consider vaginal wall transverse flap sling in combination with anterior colporraphy is a reconstructive technique of choice for severe cystocele or cystourethrocele with a positive vaginal pack test. This simple and minimally invasive technique can be easily combined with vaginal hysterectomy or posterior colporraphy. Morbidity is minimal and laparotomy is avoided. Transitory retention requiring intermittent catheterization is frequent but we have not observed permanent retention. De novo detrusor instability develops in a small percentage but can be managed with anticholinergics. Mean hospital stay is short, even when hysterectomy or other associated procedures are performed.

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COMPOSITION CHANGES OF GLYCOSAMINOGLYCANs IN THE URETHRAL STRICTURE DISEASE

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ABSTRACT

Purpose: Glycosaminoglycans (GAGs) are components of the extracellular matrix and play key roles in the normal physiology and pathology of several tissues. Recently, we have described the composition of GAGs in the several segments of the normal male urethra. There is no data, however, on GAGs composition in the urethral stricture disease.

Material and Methods: Urethral stricture samples were obtained from 7 patients submitted to end-to-end anastomosis of bulbar urethroplasties. The patients mean age was 48.0 years (range 18 to 62 years). GAGs in defatted, dry tissue samples were extracted by papain digestion and cetylpyridinium chloride/ethanol precipitation. The concentration of total GAGs was assessed by a hexuronic acid assay and expressed as microgram hexuronic acid per milligram dry tissue, while the proportions of sulfated GAGs were determined by agarose gel electrophoresis. The concentration of hyaluronic acid was determined by ion-exchange chromatography. The control group consisted of 10 bulbar urethra samples obtained from fresh, macroscopically normal cadavers aged 16 to 38 years (mean 25.6 years).

Results: The mean value of total GAG concentration in stricture of the bulbar urethra was 1.097 ± 0.186 and was significantly lower than the control group ($p < 0.05$). While the most predominant GAG in the normal urethra was hyaluronic acid ($40.7\% \pm 5.0$), dermatan sulfate predominated in the urethral stricture ($39.5\% \pm 3.1$). There were no significant changes in the relative concentration of heparan sulfate and chondroitin sulfate between normal and strictured urethras. Hyaluronic acid relative concentration decreased 45.2% and dermatan sulfate increased 47.4%.

Conclusion: Dermatan sulfate is mostly associated with fibrillar collagen, and the increased concentration of this GAG in the urethral stricture disease, together with a decrease of total GAGs, imply excessive collagen accumulation. These alterations, including a decrease in hyaluronic acid content, may change the urethral compliance and would lead to functional changes.

Key words: urethra; stricture; glycosaminoglycans; proteoglycans; extracellular matrix
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INTRODUÇÃO

A matriz extracelular desempenha um papel fundamental na fisiologia e na biomecânica dos tecidos. Nela existe uma atividade constante devido à degradação e síntese de seus componentes. A regulação do depósito de matriz extracelular é um evento importante em muitas condições, tanto normais quanto patológicas (1). É fundamental para uma cicatrização normal, onde as moléculas da matriz necessitam ser rapidamente sintetizadas durante a formação do tecido de granulação, na reposição final por tecido conjuntivo e no remodelamento tardio (2). Portanto, um balanço adequado entre síntese e degradação é necessário para um funcionamento normal do tecido. Um balanço inadequado, tanto

quantitativo quanto qualitativo, pode produzir uma diminuição na complacência do tecido lesado, causando alterações funcionais e consequentemente problemas clínicos (1). A característica fundamental da estenose de uretra é a fibrose (ou espongofibrose) que pode obstruir seu lumen causando sintomas urinários obstrutivos.

Glicosaminoglicanos (GAGs) são heteropolissacáideos complexos que possuem quantidades diversas de grupamentos carboxila e sulfato, existindo em forma nativa como glicoconjungados denominados proteoglicanos (3). Proteoglicanos são componentes importantes da superfície celular e da matriz extracelular, podendo interagir especificamente com vários outros componentes matriciais, tais como colágeno, laminina, fibronectina e citocinas (4). Estas interações são responsáveis pela organização estrutural da matriz extracelular e regulação da interação célula-célula e célula-matriz. Com isso, os GAGs têm um papel fundamental no fenômeno de cicatrização (5).

Embora a identificação dos GAGs em tecidos em processo de cicatrização é conhecido desde décadas passadas (6), suas funções ainda não estão completamente elucidadas. Além disso, apenas recentemente foi descrita a composição de GAGs na uretra masculina normal (7) e não existem dados sobre a composição deste componente da matriz extracelular em processos patológicos envolvendo a uretra. No presente trabalho determinamos as alterações na concentração e composição bioquímica de GAGs em estenoses da uretra bulbar.

MATERIAL E MÉTODOS

O presente estudo foi aprovado pelo Comitê local de Ética em Pesquisa envolvendo seres humanos. Amostras de estenose foram obtidas de 7 pacientes submetidos a uretroplastia término-terminal da uretra bulbar. A média de idade dos pacientes foi de 48 anos, variando entre 18 e 62 anos. A causa das estenoses foi traumática ($n = 4$) e infecciosa ($n = 2$), e em um caso não foi possível estabelecer a etiologia. O grupo controle consistiu de 10 amostras de uretra bulbar obtidas de cadáveres frescos e sem alterações

relacionadas ao trato urogenital. A idade média deste grupo foi de 25.6 anos, variando de 16 a 38 anos. Todas as amostras foram imediatamente fixadas em acetona e clivadas em fragmentos de aproximadamente 3 x 3 mm. Depois foram delipidadas por meio de duas trocas de clorofórmio: metanol (2:1, v/v), e secas a 60°C.

A extração de GAGs seguiu um protocolo previamente descrito (8). Resumidamente, cerca de 35 a 155 mg de tecido delipidado e seco foram incubados em papaína bicristalizada (Sigma, St. Louis, USA) em tampão acetato 100 mM, pH 5.0, contendo cisteína 5mM e EDTA 5 mM, por 24 horas a 60°C. Após centrifugação, cloreto de cetilpiridínio (CPC) foi adicionado ao sobrenadante para precipitar os GAGs. As amostras foram centrifugadas e o complexo CPC-GAG no pellet foi dissociado com NaCl 2M. Os GAGs foram por fim precipitados ao se adicionar 2 volumes de etanol absoluto às amostras, que foram então mantidas a 4°C por 24 horas. Após uma série de centrifugações e lavagens do pellet com etanol, obteve-se a preparação final de GAGs totais, a qual foi utilizada nas análises subsequentes.

A quantificação dos GAGs totais foi feita por meio da dosagem de ácido hexurônico, utilizando o método do carbazol (9), no qual as amostras purificadas de GAGs são primeiramente tratadas com ácido sulfúrico a 100°C. A concentração de GAGs na uretra foi expressa em microgramas de ácido hexurônico por miligrama de tecido delipidado e seco.

A quantidade relativa dos GAGs sulfatados (condroitin sulfato, dermatan sulfato e heparan sulfato) foi determinada por eletroforese em gel de agarose a 0.5 % em tampão de 1,3-diaminopropano 50 mM, pH 9.0 (10). Após corrida a 80 V, o gel foi fixado em brometo de N-Cetil-N,N,N-trimetilamônio 0.1%, corado em azul de toluidina 0.1%, e a proporção dos GAGs foi determinada por densitometria das bandas seguida de integração dos picos usando o programa Scion Image (Scion Corporation, USA). A identificação das bandas na placa de agarose foi feita com base na comparação com a migração de padrões de GAGs comerciais (Sigma, USA).

GAGs totais foram fracionados por cromatografia de troca iônica em colunas de DEAE-Sephadex eluídas com um gradiente linear de 0.1 ®

0.9M NaCl. Três picos foram obtidos, os quais já foram previamente identificados (8). O primeiro pico corresponde ao ácido hialurônico e foi usado para a determinação de sua concentração relativa.

A diferença dos dados obtidos entre os grupos foi analisada pelo teste para duas amostras de Wilcoxon. As diferenças foram consideradas estatisticamente significativas quando $p < 0.05$. Os dados são apresentados como médias \pm um desvio padrão.

RESULTADOS

A concentração de GAGs totais no segmento bulbar estenosado foi de 1.097 ± 0.186 e foi significativamente ($p < 0.05$) menor que no grupo controle. O ácido hialurônico ($40.7\% \pm 5.0$) foi o GAG predominante na uretra bulbar normal, enquanto que o dermatan sulfato ($39.5\% \pm 3.1$) foi o GAG predominante na uretra estenosada (Table). Houve uma diminuição significativa ($p < 0.01$) de 45.2% da concentração de ácido hialurônico nas uretras com estenose. Também foi significativo ($p < 0.05$) o aumento de 47.4% na concentração de dermatan sulfato. Apesar do condroitin sulfato ter apresentado um pequeno aumento de 18.9% na sua concentração, este aumento não foi significativo ($p > 0.05$). A concentração de heparan sulfato manteve-se estável ($p > 0.10$).

DISCUSSÃO

Os tratamentos atuais da estenose da uretra masculina proporcionam resultados variáveis e às

vezes frustrantes para o cirurgião, fazendo com que a morbidade para o paciente seja alta. Apesar de existirem alguns estudos sobre a estrutura da estenose da uretra (11-14), sabe-se pouco sobre as alterações moleculares que ocorrem na matriz extracelular. Em relação aos GAGs, apenas recentemente foi descrito a sua composição no tecido esponjoso normal (7). Como nossos resultados prévios mostraram que a concentração e a composição de GAGs varia nos diversos segmentos da uretra esponjosa, no presente trabalho nós decidimos estudar as alterações que ocorrem na estenose apenas do segmento bulbar, pois além de permitir uma comparação mais precisa também é o lugar de maior incidência de estenoses, incluindo as de origem idiopáticas.

A cicatrização é um fenômeno que envolve principalmente a matriz extracelular e uma série de moléculas (citocinas), algumas ainda não completamente elucidadas. O heparan sulfato, um GAG de membrana basal, tem uma distribuição irregular na uretra, chamando a atenção sua alta concentração na uretra bulbar (7). A heterogeneidade nas cadeias de GAGs associados a diferentes tipos de proteoglicanos pode providenciar lugares para a interação de fatores de crescimento com componentes da matriz extracelular. De fato, domínios estruturais específicos no heparan sulfato vascular têm demonstrado atividade antiproliferativa para músculo liso (15). As estenoses da uretra masculina, sobretudo as que comprometem o segmento bulbar, se caracterizam por um denso tecido rico em colágeno, pouco vascularizado, e com ausência de músculo liso uretral. Tudo isso está de acordo com as funções de proteoglicanos de heparan sulfato envolvidos em processos de cicatrização e fibrose (16,17).

Table - Relative concentration of glycosaminoglycans (GAGs) in normal and strictured bulbar urethras.
Values are expressed as percentage of total GAGs.

	Normal	Stricture	
Hyaluronic acid	40.7 ± 5.0	22.3 ± 4.8	$p < 0.01$
Heparan sulfate	7.2 ± 2.9	8.0 ± 3.1	$p > 0.10$
Dermatan sulfate	26.8 ± 5.2	39.5 ± 3.1	$p < 0.05$
Chondroitin sulfate	25.0 ± 2.8	29.7 ± 4.0	$p > 0.05$

Em virtude da bem conhecida interação dos GAGs com o colágeno e outros componentes da matriz extracelular (18), pode-se inferir que eles têm participação importante nas propriedades de complacência uretral, embora tal fato não tenha sido ainda apropriadamente estudado. Em processos fibróticos ocorre uma diminuição da complacência do tecido (1), que é a principal característica da estenose da uretra. As características da complacência resultantes do processo de cicatrização vão determinar a clínica do paciente e toda a repercussão urodinâmica proximal à estenose (19). Decorina e biglican são pequenos proteoglicanos ricos em dermatan sulfato, enquanto o versican, um proteoglicano de cadeia longa, apresenta grande quantidade de condroitin sulfato (4). Estes dois GAGs, que têm uma distribuição predominantemente intersticial, são os mais comumente encontrados na estenose da uretra bulbar, como evidenciado por nosso estudo. Além disso, a grande diminuição na concentração de ácido hialurônico bem como a de GAGs totais nas amostras com estenose, também podem estar implicadas com a perda da complacência uretral. Logicamente que outros componentes da matriz extracelular, que não foram analisados no presente estudo, também podem estar implicados na característica final da estenose (13,14).

Maiores concentrações de ácido hialurônico são encontradas no início do processo de cicatrização, sendo substituído progressivamente por GAGs sulfatados (5,20). Portanto, as maiores concentrações de GAGs sulfatados e menores de ácido hialurônico na uretra estenosada sugerem que as estenoses analisadas em nosso estudo se encontravam em uma fase mais avançada do processo de cicatrização.

Desde que o controle farmacológico de cicatrizes indesejadas é teoricamente possível, é imperativo que sejam realizados estudos enfocando as alterações moleculares da matriz em resposta à lesão em vários tecidos. Assim, uma vez descrita essas alterações, pode-se conhecer melhor os eventos moleculares que ocorrem durante o processo de reparação especificamente em um determinado tecido, para poder intervir da forma mais apropriada.

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UROLOGICAL SURVEY

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ENDOUROLOGY AND LAPAROSCOPY

Impact of lower pole renal anatomy on stone clearance after shock wave lithotripsy: fact or fiction?

K Madbouly, KZ Sheir, E Elsobky

J Urol, 165: 1415-1418, 2001

O impacto da anatomia do cálice inferior na eliminação do cálculo após litotripsia por ondas de choque: fato ou ficção?

Objetivo: Determinar se há relação significativa entre a anatomia espacial do cálice inferior, analisada por urografia excretora prévia, e o sucesso na eliminação do cálculo tratado por litotripsia extracorpórea por ondas de choque (LEOC).

Material e Métodos: dentre 258 casos com cálculo calicinal inferior, 108 preencheram os critérios e constituem o material de estudo. A ausência de cálculos foi avaliada pela tomografia computadorizada e /ou ultra-sonografia renal. O índice de ausência de cálculos aos 3 meses pós LEOC foi correlacionado com o comprimento do infundíbulo, a largura do mesmo em milímetros e o ângulo infundíbulo-pélvico, medido em graus.

A LEOC foi realizada com 3 equipamentos: Dornier MFL 5000, Toshiba Echolith e Dornier Lithotripter S.

Resultados: Três meses após a litotripsia, 79 pacientes (73.1%) estavam sem cálculos, com taxa de re-tratamento de 1.84 ± 0.96 . O número de sessões variou de 1 a 5. Todos os casos cujo cálculo era maior de 2 cm necessitaram mais de uma sessão de tratamento.

O tamanho médio dos cálculos foi de 14.42 ± 5.11 mm. (igual/maior 2 cm).

O comprimento médio do infundíbulo variou de 20.9 ± 6.55 mm, 45.4% acima de 3 cm e 54.6% menor ou igual a 3 cm. O comprimento do infundíbulo foi discretamente mais longo nos casos nos quais persistiram fragmentos de cálculos, porém a diferença não foi estatisticamente significante ($p = 0.1768$).

A largura média do infundíbulo foi de 5.65 ± 2.34 mm. A largura do infundíbulo > 5 mm. foi encontrada em 41.7% e igual/maior 5 mm em 58.3%. Também aqui, não houve diferença estatística da largura com a presença de cálculos residuais ($p = 0.6608$).

A variação do ângulo infundíbulo-pélvico foi de $48.33 \pm 14.84^\circ$ (de 19 a 90°). Não foi encontrado ângulo infundíbulo-pélvico obtuso.

Foi observado comportamento semelhante tanto no grupo de pacientes com ângulo menor ou igual a 45° como naqueles que apresentavam ângulo maior que 45° .

Nenhum dos 3 fatores anatômicos teve importante impacto na taxa livre de cálculo em 3 meses.

A taxa de eliminação não sofreu qualquer interferência. Quando os cálculos tinham comprimento igual/maior de 2 cm.

A morfologia renal foi o único fator realmente relevante na taxa livre de cálculo, visto que a eliminação dos cálculos foi substancialmente menor nos rins acometidos por pielonefrite ($p = 0.0009$).

Conclusão: As diferenças anatômicas do cálice inferior não apresentaram importância significativa na eliminação dos cálculos após LEOC.

Comentário Editorial

Em 1992, Sampaio & Aragão descreveram, em moldes anatômicos, algumas características do sistema coletor do pólo inferior do rim humano. Analisaram as condições espaciais dos cálices do pólo inferior, e determinaram o comprimento e a largura do infundíbulo, o ângulo entre o infundíbulo calicinal inferior e a

pelve renal. Verificaram nos moldes anatômicos que, em 74% dos rins de não formadores de cálculo o ângulo era maior de 90 graus (1). Em 1998, Clayman et al. aplicaram esses conceitos anatômicos, na prática clínica. Concluíram que as medidas anatômicas poderiam ser facilmente determinadas em urografias excretoras (UIV) com o auxílio de uma régua e um transferidor. Entretanto, Bagley et al. (3) mediram o ângulo infundibulopélvico na UIV usando o eixo ureteral e o infundíbulo calicinal inferior. Nenhum de seus pacientes, portadores de cálculo calicinal inferior, tinham ângulo maior de 90 graus.

Os resultados de Clayman et al., baseados nos estudos de Sampaio & Aragão, diferem da população estudada no presente artigo. Eles não incluíram cálculos acima de 15 mm, o grau de hidronefrose máximo foi grau II e o litotritor usado foi Dornier HM3, que é mais potente que os aqui utilizados. Nos pacientes cujos dados anatômicos eram favoráveis (ângulo maior de 90 graus, comprimento menor de 3 cm e diâmetro do infundíbulo > 5 mm) todos eliminaram os cálculos pós LEOC.

A impressão deixada é que não houve exata reprodução dos estudos anatomo-clínicos sendo diferente a amostra estudada e, portanto, os resultados não podem ser comparados. Sugerimos a realização de estudos rigidamente restritos aos parâmetros estudados por Clayman no sentido de serem reproduzidos seus resultados.

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**Dr. Marcelo Travassos
Dr. Nelson R. Netto Jr.**

TC for the evaluation of flank pain

KR Anderson, RC Smith

J Endourol, 15: 5-23, 2001

CT para avaliação de dor lombar

Objetivo: Demonstrar o valor do CT helicoidal no diagnóstico de cólica renal, permitindo rápida e acurada avaliação da presença de cálculo em algum ponto do trato urinário. Na interpretação deste exame existe uma curva de aprendizado, tanto para o radiologista quanto para o urologista, porém com a experiência, o reconhecimento de um número de sinais, confere alto valor preditivo no diagnóstico do cálculo urinário. A CT helicoidal deve ser sempre acompanhada por “scoutgram” para se ter uma idéia de como o cálculo se parece. O exame não requer contraste e demora de 5 a 10 minutos para que sejam tomadas as imagens, tornando o seu custo efetivo. Os urologistas e radiologistas devem se familiarizar com as técnicas de interpretação destes exames.

Pacientes e Métodos: Os autores examinaram 813 pacientes com dor lombar através de TC helicoidal, entre janeiro de 1994 e fevereiro 1996. Para o diagnóstico de dor lombar 417 pacientes tiveram o diagnóstico confirmado por outros estudos de imagem e seguimento clínico.

Resultados: A TC helicoidal demonstrou 95% de sensibilidade, 98% de especificidade, e 98% de acurácia, que é superior à acurácia demonstrada pela urografia excretora.

O diagnóstico de doenças não relacionadas com cálculo foi estabelecido em 65 pacientes dos 417 incluídos no estudo.

Conclusões: A TC helicoidal consegue diagnosticar todos cálculos urinários, mesmo os radiotransparentes, se compararmos com o “scout film” e RX simples de abdome, o qual é feito no mesmo momento. Também pode dar as medidas do cálculo através reconstituição da imagem.

Comentário Editorial

Em uma época em que tratamentos estão se tornando minimamente invasivos também os exames estão ficando cada vez mais rápidos, precisos e práticos. Embora atualmente, preço da TC helicoidal seja superior ao da urografia, provavelmente será o método de eleição na rotina dos grandes serviços, para avaliação de cólica renal e dor lombar, em função de sua simplicidade, rapidez e abrangência.

As principais vantagens da TC são: avaliação de dor lombar de forma rápida (5 a 10 minutos); grande acurácia (98%); permitir o diagnóstico de dor lombar de origem não calculosa; não necessitar contraste, com suas conhecidas implicações tais como alergia; diagnosticar cálculos muito pequenos (1 mm); diagnosticar cálculos de ácido úrico, que são visíveis por este método (as imagens correspondentes não são visíveis ao RX simples e o diagnóstico de que se trata de cálculo de ácido úrico é inferido)

As maiores desvantagens são: dificuldade de avaliar o grau de obstrução urinária, sendo extremamente sensível, pequenas calcificações renais tais como placas Randal podem ser interpretadas como cálculos; maior custo que a urografia excretora, especialmente no nosso meio, embora seja um método mais simples e rápido.

O diagnóstico e o grau da obstrução urinária, não fornecidos pelo TC helicoidal, poderia ser feita complementada através da determinação do índice de resistividade pelo Doppler USG (> 0.04) com uma sensibilidade de 90% (1).

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Dr. Pedro P. de Sá Earp

Laparoscopic radical cystectomy with continent urinary diversion (rectal sigmoid pouch) performed completely intracorporeally: the initial 5 cases

Türk I, Deger S, Winkelmann B, Schönberger B, Loening SA

J Urol, 165: 1863-1866, 2001

Cistectomia radical laparoscópica com derivação urinária contínente (bolsa reto-sigmoidea) realizada de modo completamente intracorpóreo: 5 casos iniciais

Objetivos: Relatar a experiência com os 5 primeiros pacientes submetidos à cistectomia radical com linfadenectomia bilateral e derivação urinária contínente (bolsa reto-sigmoidea) realizadas com técnica laparoscópica intracorpórea.

Material e Métodos: Três homens e 2 mulheres entre 59 e 65 anos de idade com carcinoma de células transicionais, invasivo da bexiga, porém confinado ao órgão, foram operados. O procedimento incluiu linfadenectomia pélvica, cistectomia radical com prostatectomia ou pan-histerectomia, confecção de uma bolsa reto-sigmoidea e reimplantar ureteral-intestinal bilateral, com técnica anti-refluxo. A técnica de sutura utilizada foi inteiramente intracorpórea. Os espécimes cirúrgicos foram ensacados e removidos pelo reto ou pela vagina, sem laparotomia.

Resultados: O tempo cirúrgico variou de 6.9 a 7.9 horas (mediana 7.4) e a perda de sangue foi de 190 a 300 ml (mediana 245). Nenhum dos 5 pacientes necessitou de transfusão sanguínea. A ingestão oral foi iniciada no 3º. PO, os cateteres ureterais foram retirados no 8º. PO e o cateter da bolsa foram retirados no 9º. PO. A permanência hospitalar foi de 10 dias em todos os casos. O exame anatomo-patológico das peças cirúrgicas revelou carcinoma urotelial estádio pT1G3 no caso 1, pT2bG2 nos casos 2 e 3, pT3aG2 no caso 4 e pT3aG3 no caso 5. Os linfonodos e as margens de ressecção estavam livres de tumor. Nenhuma complicação intra ou pós-operatória foi observada.

Conclusões: Pelo que se conhece, esta é a primeira série de cistectomia radical laparoscópica com derivação urinária interna (bolsa reto-sigmoidea) e os resultados são promissores. Com maior experiência e aperfeiçoamento da técnica cirúrgica, a cistectomia radical laparoscópica, com derivação contínente, pode tornar-se uma alternativa para o tratamento de pacientes selecionados, com câncer invasivo da bexiga.

Comentário Editorial

Em 1991 foi publicado o primeiro caso de nefrectomia, realizada urologista norte-americano Ralph Clayman, com técnica inteiramente laparoscópica. A partir daí, os procedimentos laparoscópicos ablativos dominaram as publicações dos anos 90. Desde o final da década passada surgiram relatos de procedimentos laparoscópicos complexos, com técnicas de reconstrução mais elaboradas, como a prostatectomia radical, a substituição ureteral com íleo, a ampliação vesical com íleo, a cirurgia de Mitrofanoff e, agora, a cistectomia radical com derivação interna. Com o auxílio da robótica e da telecirurgia, ainda incipientes, mas já comercialmente disponíveis, as técnicas reconstrutivas dominarão o cenário da cirurgia urológica laparoscópica nesta década. Parece que a laparoscopia ainda vai demorar um pouco para encontrar os seus limites.

Dr. Lísias N. Castilho

IMAGING

Brachytherapy for prostate cancer: endorectal MR imaging of local treatment-related changes

Coakley FV, Hricak H, Wefer AE, Speight JL, Kurhanewicz J, Roach III M
Radiology, 219: 817-821, 2001

Braquiterapia no câncer da próstata: aspectos da ressonância magnética endorectal nas alterações locais relacionadas ao tratamento

Objetivos: Determinar os achados da ressonância magnética endorectal (RMN-ER), nas alterações locais relacionadas à braquiterapia no câncer da próstata.

Casuística e Métodos: RMN-ER foi realizada em 35 pacientes consecutivos durante um intervalo médio de 12 meses (1 a 31 meses) após braquiterapia para câncer da próstata. As seqüências utilizadas foram: imagens ponderadas em T1 (cortes axiais) e imagens ponderadas em T2 de alta-resolução (cortes axiais e coronais). Dois observadores revisaram a qualidade das imagens e os achados, sendo as discrepâncias resolvidas por consenso. Os sintomas urinários pós-tratamento, observados em 24 pacientes, foram documentados pela revisão dos prontuários médicos.

Resultados: Todos os estudos apresentaram qualidade diagnóstica. Nas imagens ponderadas em T2, os achados prostáticos consistiram em hipointensidade difusa ($n = 35$) e anatomia zonal indistinta ($n = 34$). A localização das sementes intra e extra-prostática pode ser distinguida. O local extra-prostático mais comum de implantação da semente foi na região dos feixes neurovasculares ($n = 35$, bilateral em 32). O achado tecidual extra-prostático mais comum foi um hiper-sinal nas imagens ponderadas em T2 na região do músculo elevador do ânus ($n = 34$) e no diafragma genitourinário ($n = 28$). Os sintomas urinários pós braquiterapia não mostraram correlação com a implantação da semente peri-uretral ou com a implantação da semente ou alteração do sinal no diafragma genitourinário.

Conclusão: A RMN-ER pode ser usada para avaliar a distribuição das sementes e demonstrar as alterações relacionadas ao tratamento com braquiterapia no câncer da próstata.

Comentário Editorial

A braquiterapia no tratamento do câncer da próstata (implantação transperineal de sementes radioativas intersticiais guiada por ultra-som transretal) tem ganhado recentemente maior popularidade devido a publicações que conferem ao método alta eficiência, relativa baixa morbidade, e um alto índice de preservação da potência. Evidentemente, esta técnica não está indicada para todos os pacientes, sendo sua indicação entre outros fatores dependente do volume prostático. Como se sabe as técnicas atuais de braquiterapia são elaboradas com o intuito de se reduzir a dose de radiação na uretra e para se evitar os sintomas urinários agudos (noctúria, disúria e freqüência). Outros sintomas tais como os sintomas ano-retais, podem ocorrer (urgêncnia, sangramento ou ulceração). Neste estudo, os cortes coronais da RMN-ER foram muito úteis para demonstrar o alinhamento linear das sementes, achado encontrado em quase todos os pacientes estudados. Esse fato, segundo os autores, praticamente anula a hipótese de que a migração das mesmas é um fator na distribuição sub-ótima das sementes. Do mesmo modo, os autores não encontraram relação entre a morbidade urinária e a distribuição peri-uretral das sementes. Especulam que os sintomas urinários devam ser relacionados ao aumento do volume glandular ao invés da lesão uretral mecânica ou da uretrite actínica. Outro dado interessante encontrado é o de que as alterações inflamatórias demonstradas pela RMN-ER no músculo elevador do ânus, possam juntamente com as

alterações da retite actínica explicar os sintomas ano-retais. Do mesmo modo, interrogam sobre uma eventual associação entre disfunção erétil pós-braquiterapia e o achado de sementes nos feixes neurovasculares e diafragma geniturinário. Ressaltam, todavia, que novos estudos devam ser realizados com especial ênfase na elucidação desta questão que não pôde ser respondida por este estudo inicial.

Dr. Adilson Prando

Local recurrence after radical prostatectomy: correlation of US features with prostatic fossa biopsy findings

Leventis AK, Shariat SF, Slawin KM

Radiology, 219: 432-439, 2001

Recorrência local após prostatectomia radical: correlação das características sonográficas com os achados de biópsia da fossa prostática

Objetivos: Avaliar a acurácia da US transretal na detecção da recorrência local após prostatectomia radical.

Material e Métodos: Noventa e nove pacientes com recorrência bioquímica após prostatectomia radical foram avaliados com US transretal e biópsia da fossa prostática. A localização da recorrência suspeitada pelo US e as características clínicas como níveis de PSA e achados do toque digital, foram correlacionados com resultados de biópsia.

Resultados: 41 (41%) dos 99 casos de recorrência local foram detectados. As porcentagens de locais de lesão identificados e das correspondentes biópsias positivas foram: área anastomótica uretrovesical 56% e 61%, colo vesical 26% e 54%, espaço retrovesical 4% e 100%, mais de um local 14% e 71%. Comparando US e toque digital as sensibilidades foram 76% e 44%, enquanto a especificidade 67% e 91%. Aumento de biópsias positivas com aumento de PSA foi observado.

Conclusões: US transretal é um exame mais sensível, mas menos específico que o toque digital na detecção da recorrência local. Achados de biópsia em mais da metade das lesões suspeitas da área anastomótica e do colo vesical foram positivos. Lesões do espaço retrovesical, embora menos freqüentemente encontradas apresentavam uma alta possibilidade de representar recorrência neoplásica.

Comentário Editorial

Este estudo ressalta a importância clínica de se distinguir pacientes com doença localmente recorrente, somente na fossa prostática, daqueles com doença metastática oculta, pois os primeiros podem se beneficiar da radioterapia local, curativa em cerca da metade dos pacientes apropriadamente selecionados.

A validade da biópsia e demais aspectos já foram abordados na literatura, mas o presente trabalho é interessante por integrar os achados de imagem da fossa prostática com os resultados da biópsia, bem como a correlação com o toque digital.

Além dos resultados deste trabalho, acrescentamos 3 comentários, que na nossa opinião têm relevância. A biópsia sistemática guiada por US deve ser realizada independentemente dos achados sonográficos, sempre incluindo a zona de anastomose. Cerca de 33% dos casos de recorrência do câncer prostático são demonstrados apenas pela repetição da biópsia transretal. A ressonância magnética pode aumentar a acurácia nos exames de pacientes com biópsia transretal negativa, otimizando os resultados de uma segunda biópsia da fossa prostática, mostrando áreas de difícil acesso à sonografia ou adenopatias.

Dr. Nelson M.G. Caserta

ONCOLOGY

Lack of retroperitoneal lymphadenopathy predicts survival of patients with metastatic renal cell carcinoma

Vasselli JR, Yang JC, Linehan WM, White DE, Rosenberg SA, Walther MM

J Urol, 166: 68-72, 2001

Ausência de linfadenomegalia retroperitoneal prediz sobrevida de pacientes com carcinoma renal metastático

Objetivos: Avaliar quais pacientes com tumores metastáticos do rim se beneficiariam de combinação de nefrectomia e imunoterapia com interleucina-2 (IL-2), antes de se iniciar qualquer tratamento.

Material e Métodos: Análise retrospectiva de pacientes tratados entre 1985 e 1996 no NIH (EUA), que se apresentavam com carcinoma renal metastático, e nos quais se realizou nefrectomia radical com linfadenectomia retroperitoneal (LR) total ou parcial, e também ressecção de lesões extrarenais (cirurgias complexas). Comparou-se a sobrevida de grupos de pacientes que apresentavam ou não linfadenomegalia, que realizaram a LR total ou parcial e/ou ressecção de outras lesões, e também de pacientes que realizaram imunoterapia com IL-2 posteriormente.

Resultados: O total de 154 pacientes forma analisados, 82 com tumores metastáticos e sem linfadenomegalia retroperitoneal, tiveram maior sobrevida (14.7 meses) que 72 pacientes com linfadenomegalia (85 meses, $p = 0.0004$). Pacientes com ressecção incompleta, irresssecáveis ou volume ressecado indeterminado tiveram pior sobrevida do que aqueles sem doença retroperitoneal. De 82 pacientes sem linfadenomegalia, 11 (13%) tiveram sobrevida maior que 5 anos, e das 6 respostas completas com IL-2, 5 ocorreram nesse grupo. Apenas 1 paciente com LR incompleta viveu mais que 5 anos. Não houve diferença significativa de sobrevida entre pacientes que fizeram ou não cirurgias complexas para ressecção de lesões extrarenais.

Conclusões: Pacientes que se apresentam com câncer renal metastático e linfadenomegalia retroperitoneal têm menor sobrevida do que aqueles sem doença retroperitoneal. Deve-se continuar realizando cirurgias complexas se necessário, durante a nefrectomia radical, uma vez que não se notou diferença na resposta à IL-2 ou na sobrevida média destes pacientes, comparados ao grupo no qual se realizou apenas a nefrectomia radical sem a retirada das lesões metastáticas.

Comentário Editorial

Quinze a 20% de resposta é observada na imunoterapia com IL-2. Cirurgia citoreductora freqüentemente é realizada antes da utilização da IL-2, para se reduzir o volume tumoral e minimizar problemas associados com o tumor primário, como dor, sangramento, infecção ou desnutrição. Outra alternativa pode ser a de se realizar antes um ciclo de IL-2, reservando-se a nefrectomia para aqueles pacientes que responderam ao tratamento inicial. Este estudo visa identificar o subgrupo de pacientes com tumores renais metastáticos que se beneficiariam de um tratamento mais agressivo, e parece que aqueles sem linfadenomegalia, ou que tiveram uma ressecção completa da doença retroperitoneal, seriam este grupo.

É interessante notar que na última reunião anual da AUA, em Junho de 2001, encontram-se 4 trabalhos (abstratos 761, 763, 764 e 769) sobre cirurgia citoreductora em câncer de rim, um deles é deste grupo do NIH, e os outros são dos grupos da UCLA, MD Anderson e de Hannover. Todos mostram a propriedade de se realizar cirurgias complexas nesses pacientes, antes de se proceder à imunoterapia com IL-2, embora não tenham feito referência à linfadenopatia retroperitoneal como fator prognóstico em casos de tumores metastáticos.

Dr. Francisco F.H. Bretas

Apoptosis and its relevance to urologists

Jefferson KP, Persad RA, Holly JMP

BJU International, 86: 598-606, 2000

Apoptose e sua relevância para os urologistas

A apoptose, ou seja, a morte eucariótica da célula, programada geneticamente, é fundamental para o desenvolvimento humano normal, homeostase tissular, eliminação de células infectadas por vírus e resposta imunológica adequada. Vários defeitos que levam à inativação dos mecanismos de apoptose têm sido ligados ao aparecimento de várias doenças, tais como anormalidades de crescimento, distúrbios autoimunes e câncer. Por outro lado, a ativação dos mecanismos da apoptose podem levar a neuropatias degenerativas e doenças musculares. A apoptose é encontrada e pode contribuir no processo da disfunção erétil, na incontinência urinária no idoso, causando o enfraquecimento do esfínter uretral. Na insuficiência renal crônica, encontra-se apoptose difusa, com perda da massa renal. Da mesma forma, a nefropatia obstrutiva causa a supressão dos fatores de crescimento das células tubulares, com consequente apoptose. A seqüência morfológica da apoptose é a seguinte: encolhimento celular, perda da aderência celular, picnose nuclear, degradação das organelas, compartimentalização da célula numa membrana cercada de vesículas, para que ocorra a fagocitose pelas células vizinhas. Essa seqüência consome energia (ATP), ocorre de forma organizada e não ocasiona uma reação inflamatória. A ativação irreversível da apoptose pode ocorrer dentro de segundos após um estímulo adequado, e a morte celular pode ocorrer em horas. Assim, a apoptose é uma maneira organizada de eliminação celular, de forma ordenada, em contraste com a necrose, que envolve aumento do volume celular, dissolução nuclear e ruptura da membrana plasmática, dando origem à reação inflamatória. O índice de apoptose no carcinoma de células renais é um importante fator prognóstico. Pacientes portadores de carcinoma renal apresentam níveis elevados de uma proteína (sFas) que inibe a apoptose nas células renais. Verificou-se que os níveis dessa proteína se normalizaram após a nefrectomia. É possível que mecanismos que impedem a apoptose contribuam na grande resistência do carcinoma de células renais à radio e quimioterapia.

Outra proteína, o gene p53 pode induzir a apoptose. É interessante lembrar que as células neoplásicas são hipersensivas aos estímulos para apoptose num período de transformação maligna, o que pode estar correlacionado com aumento dos níveis de p53. Após esse período, as mutações genéticas se acumulam. Essa verificação fortalece a hipótese de um tratamento radical não-invasivo para tumores precocemente diagnosticados, levando a cura pela completa apoptose das células tumorais.

Comentário Editorial

Apesar do conhecimento adquirido no campo das ondas de choque de alta energia, até o momento, nenhum estudo avaliou seu potencial efeito na morte celular programada, a apoptose.

As implicações de uma fonte não-invasiva e segura de energia extracorpórea, potencialmente, causar apoptose são evidentes e muito atraentes.

Atualmente, em relação ao carcinoma de células renais, não se observou queda na mortalidade e nem no diagnóstico de casos com metástases à distância. Por isso, os métodos diagnósticos e de tratamento devem melhorar sua acurácia e eficácia.

Em particular, a terapia do tumor renal deve evoluir para métodos menos invasivos, como a laparoscopia. Contudo, a nefrectomia parcial é de difícil realização e a ablação tumoral ainda não é segura.

Assim, formas de tratamento ainda menos invasivas devem ser pesquisadas, como a radiofreqüência por agulha (guiada por ressonância magnética) ou o ultra-som de alta energia, que causa uma destruição por necrose, a alta temperatura do tumor. Por outro lado, houve um grande aumento no diagnóstico dos incidentalomas, com

tamanho muito pequeno. Essas lesões muito pequenas são de difícil localização e remoção durante a cirurgia. Assim, no futuro, não veremos cirurgias tradicionais ou laparoscópicas, mas sim cirurgias moleculares.

Haverá lugar, nesse futuro, para uma fonte de ondas de choque de alta energia (a exemplo do litotritor atual) capaz de destruir, por apoptose, as células do carcinoma renal?

Dr. Joaquim de A. Claro

Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer protocol No. 30924

CN Sternberg, PHM de Mulder, JH Schornagel, C The'odore, SD Fossa, AT van Oosterom, F Witjes, M Spina, CJ van Groeningen, C de Balincourt, L Collette for the European Organization for Research and Treatment of Cancer Genitourinary Tract Cancer Cooperative Group

J Clin Oncol, 19: 2638-2646, 2001

Estudo fase III, randomizado de metotrexate, vinblastina, doxorrubicina e cisplatina (MVAC) em altas doses e intensificado com uso de fator estimulador de colônias de granulócitos recombinante humano versus MVAC clássico em câncer avançado do trato urotelial: European Organization for Research and Treatment of Cancer protocolo No. 30924

Objetivos: Avaliar a atividade antitumoral e sobrevida associada com MVAC em altas doses (AD) versus MVAC comum.

Material e Métodos: Estudo randomizado incluindo 263 pacientes com carcinoma de células transicionais do urotélio metastático ou avançado (CCT) sem quimioterapia prévia. Método de randomização não citado, mascaramento da seqüência de randomização não citado, mascaramento da avaliação de resposta não realizado, descrição de perdas não existente. Tratamento com MVAC-AD realizado a cada 14 dias com o uso de fator estimulador de colônias. End point primário: sobrevida. Estudo desenhado para detectar 50% de diferença na sobrevida.

Resultados: 129 pacientes randomizados para MVAC e 134 para MVAC-AD; os grupos eram semelhantes e comparáveis. Após seguimento mediano de 38 meses, a análise por intenção de tratamento mostrou que não houve diferenças significativas na sobrevida global ou no tempo de progressão. Houve uma diferença marginal na sobrevida livre de progressão favorecendo o braço MVAC-AD ($p = 0.037$; hazard ratio 0.75; intervalo de confiança 0.58 a 0.98). O índice de resposta global não foi diferente, enquanto que as respostas completas foram significativamente melhores no braço MVAC-AD.

Conclusão: Apesar de com o regime MVAC-AD ser possível infundir duas vezes mais a dose de cisplatina e doxorrubicina em metade do tempo, a diferença de 50% pré-programada não foi detectada.

Comentário Editorial

A publicação deste estudo era aguardado com expectativa na esperança que uma melhor sobrevida pudesse ser detectada, o que infelizmente não ocorreu. Os ganhos marginais vistos na sobrevida livre de progressão ou no índice de resposta completa, de maneira nenhuma justificam a adoção deste tratamento na rotina clínica. Nem o efeito é significativo do ponto de vista clínico nem houve mascaramento da avaliação das respostas, o que pode ter seriamente interferido nestes resultados. Nível II de evidências contra o uso de MVAC-AD em CCT avançado.

Dr. Otávio Clark

PATHOLOGY

Prognostic factors in prostate cancer. College of American Pathologists consensus statement

Bostwick DG, et al.

Arch Pathol Lab Med, 124: 995-1000, 2000

Fatores prognósticos no câncer da próstata. Reunião de consenso do Colégio Americano de Patologistas

Objetivos: Os 14 autores deste artigo apresentam as conclusões de consenso do Colégio Americano de Patologistas realizada em junho de 1999 em Chicago sobre os fatores prognósticos no câncer da próstata.

Material e Métodos: Os fatores prognósticos foram agrupados em 3 categorias: *categoria I*, fatores comprovadamente de importância prognóstica e úteis na conduta clínica dos pacientes; *categoria II*, fatores exaustivamente estudados clínica e laboratorialmente, mas cuja importância precisa ser confirmada em estudos com análise estatística forte; e, *categoria III*, fatores não suficientemente estudados para demonstração do seu valor prognóstico.

Resultados e Conclusões: Na *categoria I*, os autores incluiram o valor do PSA pré-operatório, estadiamento pelo sistema TNM de 1997, graduação histológica pelo sistema Gleason e margens cirúrgicas na peça de prostatectomia radical; na *categoria II*, incluiram o volume tumoral (nas biópsias de agulha e na prostatectomia radical), tipo histológico e ploidia de DNA; e, na *categoria III*, invasão perineural, diferenciação neuroendócrina, densidade microvascular, formato e textura cromatínica nucleares, outros fatores cariométricos (formato e volume nucleolar, número de nucléolos e área nuclear), marcadores de proliferação (PCNA, Ki-67 e MIB-1) e fatores vários (oncogenes, genes de supressão tumoral e genes relacionados à apoptose).

Comentário Editorial

A estratificação dos fatores prognósticos nas três categorias propostas pelo grupo de consenso é da máxima importância. É um indicador objetivo do que é importante na abordagem do paciente portador de câncer da próstata, inclusive de natureza econômica, dispensando exames cuja validade ainda não está suficientemente comprovada como fator prognóstico. Chamamos a atenção para os fatores prognósticos da *categoria I* que dependem de informações do exame anatomapatológico: grau histológico e margens cirúrgicas nas peças de prostatectomia radical. A recomendação no que se refere à graduação histológica é o uso do sistema Gleason sempre indicando no laudo o grau histológico principal, o secundário e a contagem final. Em caso de um único grau histológico repete-se o número (Exemplos: 3 + 4 = 7, 3 + 3 = 6, etc). Eventual comprometimento das margens cirúrgicas na prostatectomia radical foi considerado da máxima importância e incluído na *categoria I*. O estadiamento recomendado é o sistema TNM proposto em 1997. Há grande variação nos métodos para avaliação do volume tumoral tanto em biópsias de agulha como nas prostatectomias radicais. Apesar de ser altamente recomendável esta avaliação foi incluída na *categoria II*. Por ser mais prático e acessível a todos, foi recomendado que a avaliação do volume tumoral pode ser relatado como o percentual da área ocupada pela neoplasia na biópsia ou na prostatectomia radical. Notar que os oncogenes, nos quais está incluído o p53, estão na *categoria III*.

Dr. Athanase Billis

PEDIATRIC UROLOGY

Synchronous bladder reconstruction and antegrade continence enema

A Wedderburn, RS Lee, A Denny, HA Steinbrecher, MA Koyle, PS Malone

J Urol, 165: 2392-2393, 2001

Reconstrução vesical e enema anterógrado para continência simultâneos

Objetivo: Avaliar os resultados de longo prazo com a reconstrução vesical e enema anterógrado de continência simultâneos numa grande série de pacientes.

Material e Métodos: Foram revisados retrospectivamente os prontuários de 50 pacientes consecutivos, tratados em dois centros: Southampton & Denver.

Resultados: O total de 46 pacientes foi avaliado, sendo 24 de Southampton e 22 de Denver. A idade média dos pacientes ocasião da cirurgia foi de 12 anos (4 a 30anos), com média de seguimento de 44 meses (7 a 100), sendo que 80% dos pacientes tinha neuropatia ou mal formação ano-retal. Uma variedade de procedimentos de reconstrução vesical foram realizados e 58% foram tratados pelo princípio de Mitrofanoff. A continência fecal e urinária foi atingida em 76% dos casos, mas a taxa de revisão cirúrgica foi alta, sendo que a estenose da ostomia foi a principal (17%). Os procedimentos secundários consistiram de reconstrução da uretra, fechamento do colo vesical, ampliação vesical e revisão do conduto.

Conclusões: Atualmente é possível produzir continência total em alguns pacientes com cirurgia combinada simultânea, o que não era possível sem uma colostomia, antes da descrição do princípio de Malone. Entretanto, a cirurgia é complexa e pode exigir elevados índices de revisão cirúrgica e assim deve ser indicada apenas em pacientes muito motivados e com grau de inteligência e destreza razoáveis. Esta seleção criteriosa é confirmada pelo fato de que a cirurgia foi realizada em dois a três pacientes por ano em cada instituição. A cirurgia deve ser feita apenas em instituições que permitam seguimento de longo prazo.

Comentário Editorial

O avanço das técnicas de reconstrução urinária possibilitou que pacientes com risco de deterioração do trato urinário superior e incontinência urinária por diferentes causas, entre elas a bexiga neurogênica por mielomeningocele, a bexiga da válvula de uretra posterior e a extrofia de bexiga passassem a ter ganho significativo na sua qualidade de vida. Muitos pacientes, no entanto, passavam a ser continentes da parte urinária, mas não dispensavam o uso de fraldas por causa de perdas fecais.

Com a descrição do procedimento de Malone, o apêndice cecal passou a ser utilizado como acesso contínuo para aplicação de enemas anterógrados que limpavam o cólon desde o ceco até o reto e assim garantia algumas horas de ausência de perdas para estes pacientes. Com isso melhorava-se muito a qualidade de vida. Por outro lado, o apêndice passou a ser utilizado para o princípio de Malone, mas, por outro lado, exigia outro conduto para o princípio de Mitrofanoff. Com a introdução da técnica de Monti, um segundo segmento intestinal tubularizado transversalmente passou a representar importante alternativa para a apendicovesicostomia (1). Mais recentemente, Macedo & Srougi propuseram técnica em que tanto a ampliação vesical quanto o canal eferente são produzidos a partir de um único segmento ileal o que simplifica a estratégia atualmente empregada baseada em dois eventos (2).

Mouriquand et al. passaram a investigar o uso do cólon esquerdo para a realização dos enemas (3). Os autores construíam um tubo de Monti que era implantado no cólon esquerdo.

Visando diminuir a morbidade desta abordagem, Macedo et al. recentemente apresentaram um conduto contínuo feito da parede do cólon esquerdo, análogo ao princípio do reservatório ileal cutâneo contínuo, que permitia o acesso ao cólon esquerdo sem a necessidade de criar um conduto ileal e anastomosá-lo ao cólon (4). Esta técnica é de simples execução e encontra-se em investigação clínica inicial.

No trabalho revisado, os autores concluem que a realização simultânea da reconstrução urinária e do enema é factível, mas deve ser feita em pacientes motivados e em centros de referência.

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Dr. Antônio Macedo Jr.

UROLOGICAL NEUROLOGY

Long-term followup of newborns with myelodysplasia and normal urodynamic findings: is followup necessary?

Tarcan T, Bauer S, Olmedo E, Koshbin S, Kelly M, Darbey M
J Urol, 165: 564-567, 2001

Seguimento a longo prazo de recém-nascidos com mielodisplasia e urodinâmica normal: é necessário seguimento?

Objetivo: Avaliar a longo prazo crianças com mielodisplasia e sem disfunção vesical para determinar a necessidade de acompanhamento urológico destas crianças.

Material e Métodos: Retrospectivamente, foram analisados 25 de 204 recém-nascidos onde a avaliação neurourológica foi normal após o fechamento do defeito espinal. A avaliação inicial incluiu estudo urodinâmico completo, ultra-som renal, urina I e cultura de urina. Os pacientes foram reavaliados após 3 meses, de 6 em 6 meses até 6 anos de idade e anualmente depois. O seguimento mais longo foi de 18.6 anos.

Resultados: Das 25 crianças, 22 tinham mielomeningocele e 3 mielocele. Oito apresentaram deterioração neurológica com seguimento médio de 9.1 anos. Esses pacientes foram submetidos à ressonância nuclear magnética que demonstrou síndrome da cauda equina. Após a correção cirúrgica, 2 recuperaram micção normal, enquanto que 6 mantiveram disfunção miccional leve ou moderada. Após 6 anos de vida, não houve alteração neurourodinâmica em nenhum paciente.

Conclusões: Crianças com mielodisplasia e avaliação neurourodinâmica normal estão em risco de deterioração nos 6 primeiros anos de vida, secundariamente à síndrome da cauda equina. Nesse período é preciso um seguimento rigoroso para prevenir seqüelas.

Comentário Editorial

Este estudo preenche uma lacuna na literatura sobre como evoluem e como devemos seguir pacientes que, apesar do defeito de fechamento do tubo neural, não apresentaram alterações neuroourológicas na avaliação inicial. Os autores estão corretos quanto à necessidade de seguimento rigoroso dessas crianças. Quanto à síndrome da cauda equina, este mesmo grupo já havia demonstrado que o primeiro evento envolve alguma piora neuroourológica, muitas vezes sutil, mas o suficiente para ser detectada pela eletromiografia com agulha no esfíncter externo. Neste estudo ocorreram 3 boas informações: 17 pacientes nunca apresentaram comprometimento neuroourológico; melhora em 2 e estabilização em 6 dos 8 pacientes que foram submetidos ao desencarceramento; e ausência de evolução após 6 anos de idade. Entretanto, o seguimento médio foi de 9 anos, e certamente resultados com seguimento mais longo serão necessários para consolidar estes (bons) achados.

Dr. Aderivaldo C. Dias Filho