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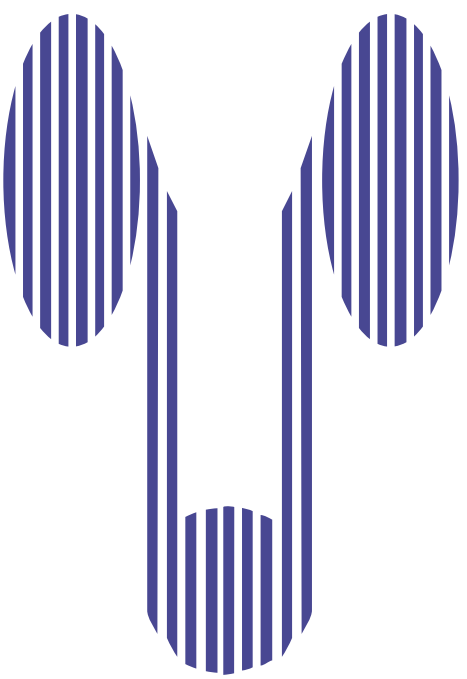

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EDITOR'S COMMENT

The July – August 2003 issue of the *International Braz J Urol* presents interesting contributions and the Editor will highlight some important papers.

Doctors Holzbeierlein and colleagues, from University of Kansas Medical Center, Kansas City and Medical College of Wisconsin, Milwaukee, USA, authored on page 291 a through presentation on case selection and outcome of radical perineal prostatectomy in localized prostate cancer. It was emphasized that proper patient selection is critical to the success of the procedure and the minimization of complications. The authors concluded that radical perineal prostatectomy has stood the test of time, with only a few technical modifications since its original description more than 100 years ago. The procedure offers outcomes similar to radical retropubic prostatectomy, the standard approach for the treatment of localized prostate cancer. Its advantages include decreased pain, blood loss, and convalescence, the same arguments currently being made in favor of laparoscopic prostatectomy.

Doctors Srougi and co-workers, from Federal University of São Paulo, Brazil, presented on page 336 a modification of the radical cystectomy technique with preservation of sexual function and urinary continence. The authors stated that the proposed maneuvers allow the performance of radical cystectomy with integral preservation of distal urethral sphincter and of cavernous neurovascular bundles, without jeopardizing the oncological principles. Doctor Mark S. Soloway, from University of Miami School of Medicine, Doctors John F. Ward and Horst Zincke, from Mayo Medical School, Rochester, and Doctor James E. Montie, from University of Michigan, Ann Arbor, USA, provided important editorial comments that emphasize critical points and give adequate balance on this proposed technique.

Doctors Der Horst and colleagues, from University Hospitals of Kiel and University of Mannheim, Germany, presented on page 332 a 2 institutions work on a slightly modified technique of the original Schroeder-Essed plication procedure for congenital penile deviation. The modification of the technique with inverted sutures described previously consisted of horizontal incisions in the tunica albuginea. The results indicated that this simple modification offered good functional and cosmetic results and most patients were satisfied with the penile angle correction outcomes. Doctor Drogo Montague, from The Cleveland Clinic Foundation, Ohio, USA, provided an editorial comment on this article, highlighting critical points.

EDITOR'S COMMENT - *continued*

Doctors Tobias-Machado and colleagues from ABC Medical School, São Paulo, Brazil, presented on page 313 a comparative randomized clinical assay between ciprofloxacin, norfloxacin and chloramphenicol as antibiotic prophylaxis in prostate biopsy. Two hundred and fifty-seven patients were randomized in 4 groups: 1) single dose of ciprofloxacin 2 hours before the procedure; 2) ciprofloxacin 3 days; 3) chloramphenicol 3 days; and 4) norfloxacin 3 days. The schemes using ciprofloxacin presented better results in prophylaxis previously to prostate biopsy. The single dose of ciprofloxacin is recommended due to its posologic ease and low cost, associated with a therapeutic response equivalent to a 3-day regimen.

Doctors Paschoalin and colleagues from Ribeirão Preto School of Medicine, São Paulo, Brazil, investigated on page 300 the prevalence of prostate carcinoma in a sample of volunteers known to have a large proportion of Bantu African ancestors, and the performance of total PSA (tPSA), PSA density (PSAD) and free-to-total PSA ratio (f/tPSA) on the diagnosis. The authors found that tumor prevalence was higher in Non-White than in White phenotype. Also, they proposed that the association of tPSA at a cut-off level of 2.5 ng/ml with a PSAD of 0.08 or a f/tPSA of 20% for biopsy indication deserves further investigations as an alternative to tPSA cut-off level of 4 ng/ml.

Doctor Barros and associates, from Federal University of Bahia, Brazil, analyzed on page 306 the prevalence of prostate adenocarcinoma according to race in an university hospital. The authors studied 580 patients with mean age of 60.7 ± 10.0 years, with 116 Whites (20.0%), 276 Mulattos (47.6%) and 188 Blacks (32.4%). Prostate adenocarcinoma was found in 16.6% of patients aged between 40 and 79 years. The authors did not find statistically significant influence of race in the population with prostate adenocarcinoma. Dr. Gustavo F. Carvalhal, from Catholic University, Rio Grande do Sul, Brazil, provided an interesting editorial comment on racial implications in prostate cancer

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

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CASE SELECTION AND OUTCOME OF RADICAL PERINEAL PROSTATECTOMY IN LOCALIZED PROSTATE CANCER

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ABSTRACT

Radical prostatectomy continues to play a central role in the management of localized prostate cancer. The majority of patients diagnosed with prostate cancer will undergo radical prostatectomy. A decrease in the morbidity of this surgical procedure has been accomplished through an improved understanding of pelvic anatomy and a greater understanding of the natural history of prostate cancer. Recently, minimally invasive techniques have been applied to radical prostatectomy (laparoscopic prostatectomy) in order to further decrease the morbidity of this operation. What remains to be determined is whether this approach confers the same long term surgical outcomes as the open approach. One method which offers known long term outcomes coupled with decreased morbidity is the radical perineal prostatectomy. The purpose of this paper is to review the criteria for patient selection as well as outcomes of the radical perineal prostatectomy.

Key words: prostatic neoplasms; prostatectomy; perineal; outcomes; surgical technique
Int Braz J Urol. 2003; 29: 291-9

INTRODUCTION

Perineal prostatectomy is the oldest means of prostate resection and has its origins from the perineal lithotomy which was first described in 400 BC (1). In 25 AD, Celsus developed a curved perineal incision which would eventually become the basis for the incision used in the perineal prostatectomy today (1). Covillard is credited with performing the first removal of a portion of the prostate during removal of a bladder stone through the perineum in 1639, although he and other surgeons, at the time, used a median incision in the perineum rather than the curved incision described by Celsus (2). Throughout the 18th and 19th centuries, several surgeons reported the removal of portions of the prostate similar to Covillard; however, the first planned prostate enucleation through a median perineal incision was performed by Guthrie in 1834 (2). This subsequently led to the use of the median perineal incision for the removal of prostatic carcinoma. In 1866, Kuchler was the first to suggest that the entire prostate could be removed using this approach, but it was Billroth, in 1867, who first described the perineal prostatectomy for the treatment of prostate cancer in a professional journal (3).

In 1901, Dr. Hugh Hampton Young employed the curved perineal incision to perform a prostatectomy for the removal of the entire prostate for benign prostatic hyperplasia (1). Dr. Young stressed the importance of performing all portions of the procedure under direct visualization and developed such tools as the Young retractor and the perineal table to facilitate visualization (Figures-1, 2 and 3). While removing the prostate for benign disease, Dr. Young noted that some of the prostates were involved with cancer. He then performed a series of autopsies in men with prostate carcinoma to identify the pattern of spread of the cancer. This led him to believe that prostate cancer spread along the ampullae of the vasa to the

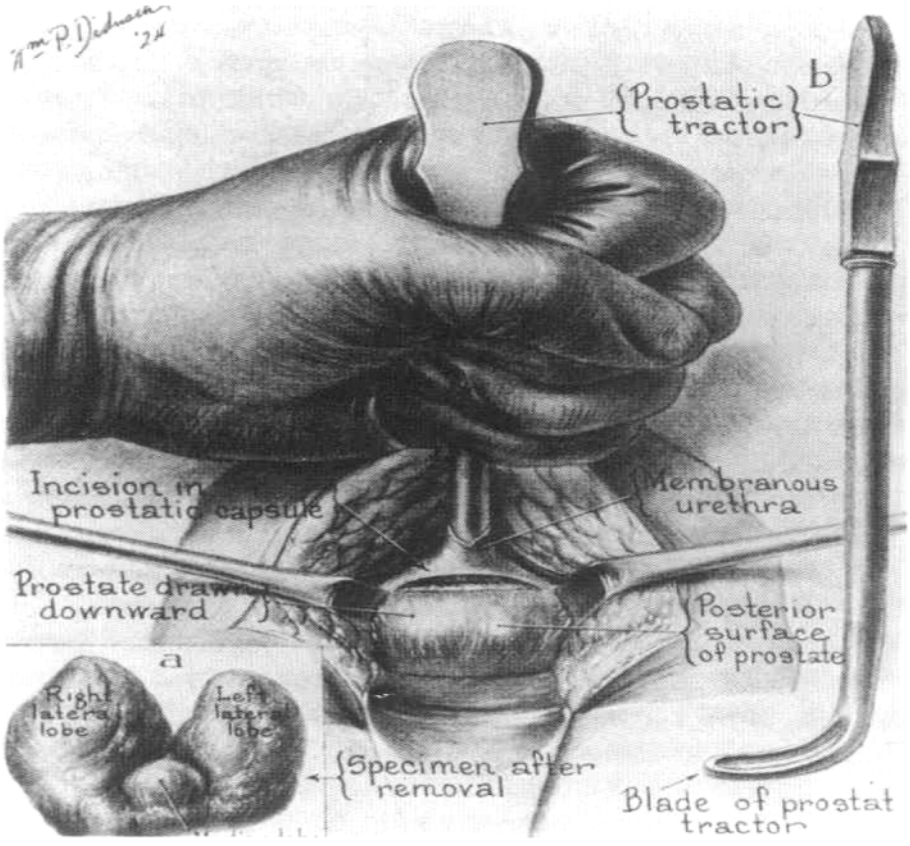

Figure 1 – *Dr. Young's original depiction of prostatic tractor used for enucelation of the hypertrophied lobes of the prostate*

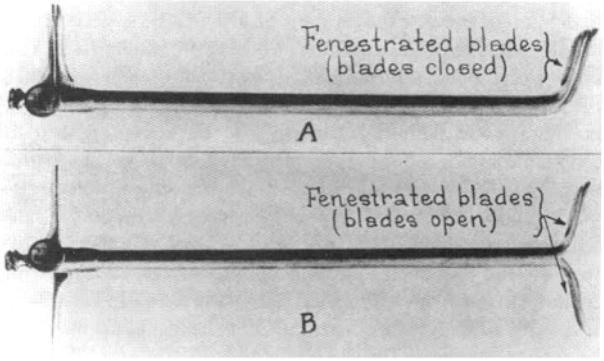

Figure 2 – *The Young retractor which is still used today for the perineal prostatectomy.*

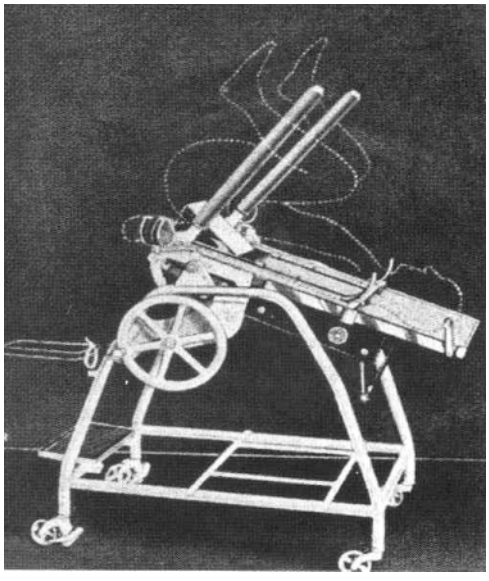

Figure 3 – *The Young perineal table*

seminal vesicles, and that the cancer was usually contained within Denovillier's fascia (4). During this same time period, Dr. Halsted was performing the radical mastectomy for the treatment of breast cancer. Together they developed a radical operation to remove the prostate, the fascia of Denovillier, the seminal vesicles, ampullae of the vasa, and the vesical neck with a portion of the trigone, and thus performed the first "radical" perineal prostatectomy in 1904 (5). This radical perineal prostatectomy has remained virtually unchanged in regards to technique since it was first described by Dr. Young.

Minor modifications of Young's original procedure have been made in order to reduce the morbidity of the operation. First, after the development of urinary calculi on the silk sutures used for the vesicourethral anastomosis, Dr. Young began using chromic catgut rather than silk (5). Next, Dr. Hans Wildbolz described a technique to preserve the tissue surrounding the external urinary sphincter to reduce the incidence of urinary incontinence (1). Also, prior to 1928, gauze pads were routinely packed into the perineal wound with a portion of the pad exposed for later removal. In 1928, Gibson recommended that these pads be omitted during closure. This modification significantly decreased wound problems as well as fistula formation (6). Another significant contribution was introduced by Dr. Elmer Belt in 1939. Dr. Belt described a new approach to the prostate through the perineum between the longitudinal fibers of the rectum and the circular fibers of the external anal sphincter (7). This approach dramatically decreased blood loss. However, Dr Belt also recommended leaving behind the apex of the prostate to achieve better urinary control, and opening the anterior layer of Denonvillier's fascia during the dissection. Dr. Young considered these last 2 changes in violation of the principals of cancer surgery and discouraged their use in radical perineal prostatectomy (RPP) (5).

In 1945, the development of the retropubic approach for the removal of the benign prostate would soon lead to the use of the radical retropubic prostatectomy for the treatment of prostate cancer (8,9). However, the procedure was soon abandoned due to the adoption of radiation therapy for prostate cancer, as it was thought to have less morbidity. Through the 1960's and early 1970's, literature began to accumulate on the morbidity associated with radiation, but it continued to play a significant role in the treatment of prostate cancer due to the significant morbidity, especially blood loss, associated with radical prostatectomy. Finally, in 1979 Reiner & Walsh reported early meticulous ligation of the dorsal vein during the radical retropubic approach which greatly decreased the blood loss associated with the procedure (10). In addition, Walsh et al., after performing detailed anatomical dissections in the male pelvis, published the first description of the nerve-sparing radical retropubic prostatectomy leading to wide acceptance of this procedure for the treatment of prostate cancer (11).

In recent years there has been renewed interest in the radical perineal prostatectomy technique for a number of reasons. First, the research of Weldon & Tavel in the late 1980's demonstrated that nerve-sparing techniques could be also be applied to the perineal approach (12). Second, with predictive models such as the Partin tables and the Kattan nomogram, patients at low risk for pelvic lymph node metastases can be identified, thus allowing for the safe exclusion of a pelvic lymph node dissection (13). Finally, with the advent of minimally invasive techniques and a focus on decreasing the morbidity of radical prostatectomy, perineal prostatectomy has had resurgence. In addition, as opposed to laparoscopy, the perineal prostatectomy has long-term data on outcomes available (14).

PATIENT SELECTION

Critical to performing a successful RPP is the proper selection of patients. The urologist who performs the RPP must have a clear understanding of which patients as well as what stages of disease are appropriate for RPP. One concern that has been raised regarding perineal prostatectomy is that it is a more difficult approach to learn. However, Mokulis & Thompson studied this in a group of chief residents. Using operative time, estimated blood loss, transfusion requirements, and postoperative stay as surrogate markers for ease of the operation they demonstrated that RPP was learned more quickly than the

retropubic approach (15). The only significant complication particular to learning the perineal approach was that of rectal injury. However, all of these rectal injuries were closed primarily at the time of RPP and resulted in no long term sequelae. This study contradicts the commonly held belief that the perineal approach is more difficult to teach and learn.

EXTENT OF DISEASE

Any form of prostatectomy, whether it is laparoscopic, radical retropubic, or radical perineal is curative only if all of the cancer can be removed during the procedure. In the RPP approach it is imperative that patients have organ confined disease in order for the procedure to be curative. This includes patients with clinical stages T1b, T1c, or T2 disease diagnosed by digital rectal examination. Furthermore, using predictive models such as the Kattan nomogram may help exclude patients who are at high risk for extra-capsular disease (13). For example, a patient who has a clinical stage T1c cancer, but a PSA of 12 and Gleason score of 9 has a high chance of extra-capsular disease and may be best served by an alternative form of treatment (13).

As patients who undergo RPP do not routinely have pelvic lymph nodes sampled, patients at high risk for nodal metastases are typically not candidates for this approach. Some surgeons have combined laparoscopic pelvic lymph node dissections with RPP for patients at greater risk for lymph node metastases. The drawback of this is of course the increased operative time as well as the expertise required to perform laparoscopic lymph node dissection. As mentioned previously, with the predictive models available, patients with a low probability of lymph node metastases can be selected (16). Furthermore with the stage migration that has been seen in prostate cancer since the introduction of PSA, patients can be accurately selected to undergo RPP with the exclusion of a pelvic lymph node dissection (17).

PATIENT CHARACTERISTICS

There are practical considerations in regards to the patients who may or may not be candidates for RPP. Patient size is one such consideration. Typically, obese patients have less subcutaneous fat on the perineum as compared to the lower abdominal area making RPP a better approach than the retropubic approach. However, if the patient is morbidly obese then the positioning required for RPP may pose a problem. Patients are placed in an exaggerated lithotomy position in order to place the perineum in a position which is essentially parallel to the floor (Figure-4). In morbidly obese patients this may increase the ventilatory pressures to > 40 cm of H_20 resulting in poor oxygenation and inability to perform the procedure. A simple office test that demonstrates the patient's ability to tolerate the exaggerated lithotomy position from a respiratory standpoint involves having the patient lie supine on the exam table and bring his knees to his chest. If the patient is able to tolerate this test, then he will likely tolerate the positioning required for RPP.

If the patient's body habitus is such that the base of the prostate gland is not palpable on digital rectal examination this may make dissection during RPP very difficult due to the depth of the wound. Also, if the patient has a narrow distance between his ischial tuberosities such that the prostate gland is wider than this distance then perineal removal of the prostate is very difficult. As a general rule, prostate glands greater than 100 g are difficult to remove through the perineal approach. If this approach is to be used in large prostates, one many consider downsizing of the prostate with an LH-RH agonist prior to prostatectomy. Other patient characteristics that may exclude them from the perineal approach are hip ankylosis, patients who have had lower extremity amputations, and patients with hip prostheses. These are relative contraindications and should be individualized to each patient.

ADVANTAGES OF RPP

Typically, patients who have undergone previous pelvic surgery are excellent candidates for RPP. In particular, patients who have had meshed hernia repairs, renal transplantation, and pelvic/abdominal vascular bypass grafts, are better candidates for the perineal approach than for the retropubic or

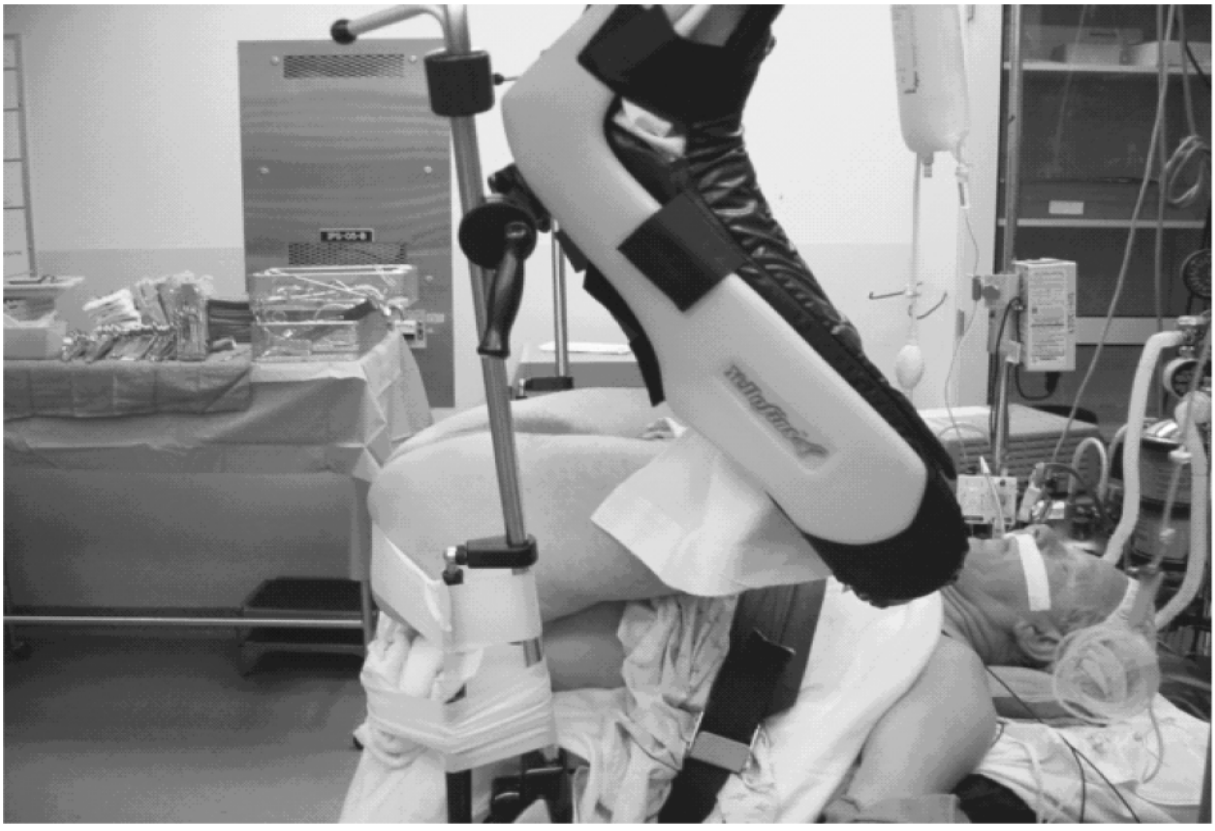

Figure 4 – *The exaggerated lithotomy position for radical perineal prostatectomy.*

laparoscopic approach, as the perineal dissection is through virgin tissue. Furthermore, in patients who have had prior pelvic irradiation for their prostate cancer and undergo prostatectomy (salvage prostatectomy) the perineal approach has tended to be technically advantageous as compared to the retropubic approach.

OUTCOMES

To date there has been no direct comparison of laparoscopic prostatectomy versus radical perineal prostatectomy. Most of the comparisons have been between perineal prostatectomy and the radical retropubic approach, although there are only a few studies which can be found directly comparing these approaches. One of the first published reports directly comparing retropubic versus perineal prostatectomy was from Boxer et al. in 1977 (18). In this study of 329 patients, Boxer et al. examined several variables including mortality due to the procedure, overall survival rates, incontinence, and long term complications. The authors found no significant differences between the two groups in the variables examined except for an increased blood loss of 700 ml in the retropubic group versus the perineal group. This study was a poor comparison for efficacy as many patients in the study had received estrogen therapy either pre or post operatively. In addition, only 20% of the patients had undergone pelvic lymphadenectomies leading to staging inaccuracies and difficulties in comparing the true cancer control rates of the 2 techniques.

A more contemporary series is that by Frazier et al. who compared 122 patients who underwent RPP versus 51 patients who underwent radical retropubic prostatectomy (RRP) (19). Variables examined were operative times, blood loss, hospital stay, short and long-term complications (including incontinence and

impotence), length of catheter drainage, weight of the specimen, and disease extent. For the purposes of operative time, only those patients who underwent a pelvic lymphadenectomy in conjunction with RPP were included. The authors concluded that there were no statistically significant differences between the 2 groups in terms of positive margin rates, short-term or long-term complications, and urethral or bladder neck involvement. Seventeen of the 22 patients (77.3%) in the RPP group who underwent nerve sparing procedures were potent after surgery. Unfortunately, no data on the potency rates in the RRP group were available making a direct comparison impossible in this study. Again, the only significant differences seen were in the estimated blood loss and transfusion requirements with both being significantly greater for the RRP group. Criticisms of the study include the lack of potency data in the RRP group, and the failure to match patients in the 2 groups by preoperative data. Furthermore, all RPP's were performed by 1 surgeon while 3 different surgeons performed the RRP's.

A smaller study by Haab et al. compared 71 patients who underwent either RRP (36 patients) or RPP (35 patients) for clinically localized cancer of the prostate (20). In this study, patients were matched by their preoperative data including PSA. Similar variables to the Frazier study were examined, including: operative time, number of blood transfusions, peri-operative complications, sexual and urinary function, positive margin rates, and specimen weights. The only significant differences noted were in the transfusion requirements (100% RRP vs. 54% RPP) and anastomotic strictures (2 RRP and 0 RPP). The incidence of rectal injuries and wound infections was the same between the groups as was the incidence of positive margins, biochemical recurrence rates, and continence. The conclusions were that the 2 procedures provide similar disease control outcomes but with significantly less blood loss in the RPP group. This study brings to light one of the major criticisms of any study comparing RRP with RPP, which is the lack of a pelvic lymph node dissection in the RPP patients making true disease control outcomes difficult to measure due to staging inaccuracies. However, with predictive nomograms patients can be accurately selected in which the risk of node positivity is minimal. Therefore, this criticism should not preclude a meaningful and accurate comparison of the 2 procedures such as was performed in this study.

These trials indicated that margin positivity and biochemical failure rates are equivalent between the 2 procedures. However, a more recent article by Boccon-Gibod et al. compared the incidence of positive surgical margins in patients undergoing RRP versus RPP (21). Ninety-four patients (48 RRP and 46 RPP) with clinically localized prostate cancer were retrospectively reviewed. The patients were stratified according to clinical stage, extra-capsular extension with and without positive margins, and iatrogenic positive margins (incision into the prostate). The authors reported a 56% incidence of positive margins in the perineal group versus 61% in the retropubic group. Biochemical recurrence rates at a mean follow-up of 25 months were the same for each group (33%). What was surprising in this study was the incidence of positive margin rates in patients with pT2 tumors which was significantly higher in the RPP group (43% versus 29%, $p < 0.05$). In addition, the incidence of iatrogenic margins was dramatically higher in the RPP group (90%) versus the RRP group (37%) ($p < 0.05$). Their conclusions were that RRP is a better approach for the treatment of prostate cancer, as it affords a lower likelihood of capsular incision. Problems with these conclusions are that despite the reported incidence of positive margins biochemical recurrence rates were the same. Furthermore, the RPP's in this study were not performed by surgeons experienced in this technique. In other studies utilizing data from surgeons with significant experience in the RPP technique, positive margin rates and iatrogenic positive margin rates are similar to those reported for RRP (20).

The largest comparison trial to date is that of the Uniformed Service Urology Research Group (22). This was a pooled analysis of data from 5 military institutions of 1,698 men who had undergone radical prostatectomies between 1988 and 1997. Of this group, 1,382 underwent RRP and 316 underwent RPP. Patients were retrospectively stratified according to race, clinical stage, Gleason sum, and preoperative PSA. The authors showed that there were no statisti-

cally significant differences between the groups for PSA failures, margin positivity, or organ confined rates. The only significant differences shown were a higher blood loss in the RRP group ($p < 0.001$) and a higher rectal injury rate in the RPP group ($p < 0.03$). There was no difference in the rates of incontinence, impotency, bladder neck contractures, or post-operative complications. All of the aforementioned studies are reviewed in Table-1.

COMPLICATIONS

Rectal injuries have been shown to occur more frequently in RPP than in RRP (22). Although, the experience of the surgeon plays a role in the frequency of rectal injuries with very low rectal injury rates being reported by surgeons experienced in RPP (14). In fact, at our institution we have seen no rectal injuries within the last 5 years. Rectal injuries usually occur as the rectourethralis is divided or as the plane of dissection changes from vertical to horizontal just before the apex of the prostate. Typically, these injuries are not exceedingly problematic if they are noted at the time of surgery, are repaired intraoperatively, and the patient received an adequate bowel preparation (23). The rectal injury is typically closed in 2 layers, with absorbable suture (we prefer 3-0 Vicryl™) for the first layer followed by 3-0 silk su-

***Table 1** – Comparison studies.*

Study	Patient Population	Significant Findings	Study Problems
Boxer et al. 1977	329 patients (265 RPP vs. 64 RRP)	Increased blood loss (average 700 ml) in RRP group	Patients received estrogen pre or post operatively Only 20% had pelvic lymphadenectomy
Frazier et al. 1992	173 patients (122 RPP vs. 59 RRP)	Increased blood loss (average for RPP = 565 ml vs. 2000 ml for RRP)	All RPP's performed by 1 surgeon vs. 3 surgeons for RRP Patients not matched on preoperative data
Haab et al. 1994	71 patients (35 RPP vs. 36 RRP)	Increased blood loss in RRP group vs. RPP group. Increased anastomotic strictures in RRP (2) vs. RPP (0).	Lack of pelvic lymph node dissections lead to staging inaccuracies
Boccon-Gibbod et al. 1998	94 patients (48 RPP vs. 46 RRP)	Increased incidence of positive surgical margins for patients with pT2 disease in RPP group. Increased capsular incision in RPP group.	Lack **r** experienced RPP surgeons Biochemical recurrence rates the same despite more positive margins
Uniformed Services Urology Research Group 2001	1,698 patients (316 RPP vs. 1,382 RRP)	Increased blood loss in RRP group. Increased incidence of rectal injuries in RPP group.	Retrospective

RPP – radical perineal prostatectomy; RRP – radical retropubic prostatectomy

tures in a Lembert fashion for the second layer. The surgical field is then copiously irrigated with 1 L of antibiotic irrigation and then two-finger anal dilation is performed to reduce sphincter tone. Broad spectrum antibiotics are given for 48 hours and a low residue diet encouraged for 5 days post-operatively.

Fecal soilage after radical prostatectomy is a particular complication that was not reported until relatively recently. In 1998, Bishoff et al. reported a significant rate of fecal incontinence in patients after prostatectomy (24). Patients were mailed a questionnaire asking about both fecal and urinary incontinence. From these questionnaires, 3, 9, 3, and 16 percent reported daily, weekly, monthly, or less than monthly fecal incontinence respectively after RPP. This was less although still present in the RRP group who reported rates of 2, 5, 3, and 8 percent, daily, weekly, monthly, or less than monthly fecal incontinence. This experience is different from the authors' experience as well as the experience of other experienced surgeons employing radical perineal prostatectomy. Also, this study did not employ a validated quality of life questionnaire for prostate cancer, once again calling in to question the validity of the data. We are currently reviewing data from a nationwide database to determine the incidence of bowel bother and bowel dysfunction after RRP and RPP.

A unique morbidity to RPP is lower extremity neuropraxia. The etiology is presumed to be to undue pressure on the sural nerve due to positioning. Price et al. reported that 43 of 111 patients (38.7%) undergoing RPP experienced some degree of lower extremity neuropraxia (25).

Figure 5 – *Yellowfins™ stirrups.*

Fortunately, these cases of neuropraxia were of short duration (2-3 days) and resolved in all cases. We also experienced this problem at our institution until recently when we began using the Yellofins Stirrups™ (Figure-5) and subsequently we have not seen this complication again. This is due to the fact that the stirrups support the entire leg from the calf down to the foot in a boot like support. This minimizes any pressure on the fibular head and ankle which prevents the neuropraxia.

CONCLUSION

Radical perineal prostatectomy is an example of a surgical technique which has stood the test of time. With only a few technical modifications since its original description, it offers outcomes similar to radical retropubic prostatectomy, the standard approach for the treatment of localized prostate cancer. Its advantages include decreased pain, blood loss, and convalescence, the same arguments currently being made in favor of laparoscopic prostatectomy. In addition, it is the optimal approach for obese patients, patients with prior pelvic surgery, or patients with prior pelvic radiation. As shown in this paper, proper patient selection is critical to the success of the procedure and the minimization of complications. Furthermore, a detailed understanding of the perineal anatomy combined with surgeon experience make RPP is necessary for success, but for the experienced surgeon RPP is an attractive option for the selected patient with localized prostate cancer.

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RACIAL INFLUENCE ON THE PREVALENCE OF PROSTATE CARCINOMA IN BRAZILIAN VOLUNTEERS

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ABSTRACT

Purpose: To investigate the prevalence of prostate carcinoma in a sample of volunteers known to have a large proportion of Bantu African ancestors, and the performance of total PSA (tPSA), PSA density (PSAD) and free-to-total PSA ratio (f/tPSA) on the diagnosis.

Materials and Methods: A total of 473 volunteers (range: 40 - 79 years) were screened for prostate carcinoma. Those with tPSA >2 ng/ml and/or abnormal digital rectal examination were submitted to a transrectal ultrasound-directed biopsy (10 cores). The volunteers were classified as White, Mulatto or Black according to physical characteristics and to ancestors race reference. The following variable number of tandem repeats (VNTR) were analyzed in the blood of 120 volunteers without cancer and in 27 patients with prostate cancer: D4S43, PAH, F13A1, APOB and vW-1.

Results: The biopsies performed in 121 volunteers revealed cancer in 27 (5.7% of 473). The proportions of cancer in White, Mulatto and Black were respectively: 0.6% (1/148), 6.7% (6/90) and 8.5% (20/235) (p = 0.006). The VNTRs analysis revealed heterogeneity in White, Mulatto and Black anthropologic phenotypes with the following admixture of Caucasian, African and Amerindian gene lineages: 67.5 ± 8%, 20.8 ± 8%, 11.7 ± 7%; 54.8 ± 9%, 36.3 ± 5%, 8.9 ± 7%; and, 45.3 ± 3%, 45.9 ± 4%, 8.8 ± 7%. Such a mixture was 50.5 ± 9%, 49 ± 8% and 0.5 ± 4% in volunteers bearing cancer, and 59.1 ± 7%, 31.7 ± 8% and 9.2 ± 5% in those without cancer. The sensitivity and specificity of tPSA at cut-off levels of 2, 2.5 and 4 ng/ml for volunteers with tPSA ≤ 10 ng/ml were respectively: 100% and 6,6%, 100% and 36,6%, 69,2% and 62,2%. PSAD at a cut-off level of 0.08 or 0.10, and f/tPSA at a cut-off level of 20% were able to increase significantly tPSA specificity without loss on sensitivity.

Conclusions: The tumor prevalence was higher in Non-White than in White phenotype. The association of tPSA at a cut-off level of 2.5 ng/ml with a PSAD of 0.08 or a f/tPSA of 20% for biopsy indication deserves further investigations as an alternative to tPSA cut-off level of 4 ng/ml.

Key words: prostatic neoplasms; prevalence; race; prostate-specific antigen
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INTRODUCTION

The prevalence of prostate adenocarcinoma is 50% higher in North-American Afro-American than in Caucasians, and it can be 3 or 4 times higher when compared to Chinese and Japanese (1). At the moment of diagnosis in Afro-Americans, the stage is more advanced, and for this reason the earlier beginning of screening has been advocated in Afro-American men (2).

The definition for the normality range of the prostate specific antigen (PSA), published in 1986 by Myrtle et al. (3), is largely accepted. This group from Hybritech, using Tanden-R assay, established the interval between 0 and 4 ng/ml as the normality range. One among 3 men with a level superior to that will show carcinoma in prostate biopsy (4).

However, there are reports proposing changes in this range, which could vary according to race and age (1).

Gann et al. (5) showed that men with total PSA (tPSA) between 2 and 4 ng/ml are 12-fold more likely to develop prostate cancer compared to others with tPSA below 1 ng/ml, when followed during 10 years. There are studies showing that in the tPSA range between 2.5 and 4 ng/ml the prevalence of cancer reaches 24%, and that is why many centers started to recommend this cut-off level for indication of biopsy (6).

In Brazil, studies on screening for prostate adenocarcinoma are scarce. The existing data present similarity in sensitivity and specificity of tPSA in a cut-off of 4 ng/ml, for Southeastern population, as observed in North American population, but there are no reports of investigation using lower cut-off levels. On the other hand, 3 studies with Southeastern population involving 5,313 volunteers were not able to convincingly demonstrate a higher prevalence of prostate cancer in Afro-Brazilians than in Caucasians (7-9). It must be stressed that about 70% of Brazilian black population originate from Angola, Congo and Mozambique where the Bantu haplotype is predominant (10). The study of hemoglobin β genes confirms that in Brazil 73% of the haplotypes are Bantu type, with Senegal haplotype being practically inexistent (11). These data reveal that Afro-Brazilian are genetically distinct from North American black population, where the haplotype Benin predominates (59%) with equivalent frequencies of Bantu and Senegal haplotypes (12). Additionally, studies based in polymorphism of nuclear and mitochondrial DNA stress the role of the intense process of miscegenation undergone by Afro-Brazilian population (urban or isolated – remainders of the quilombos) (13). The African component in black populations can range from 46 to 67% in "rural" areas, but these data do not have universal validity for urban populations (14). Obviously, the ethnic admixture is not restricted to Afro-Brazilian descendants, but it is extended to Caucasians. Such data warrant the performance of screenings in our environment aimed to racial prevalence of prostate tumor and a better characterization of PSA.

MATERIALS AND METHODS

The target population for screening consisted of 473 volunteers with ages ranging from 40 to 79 years from the city of Ipirá, Bahia. All of them underwent a digital rectal examination, blood collection for dosage of tPSA and free PSA (DPC – Immulite test)® and DNA extraction for genetic race analysis. Volunteers with tPSA equal or superior to 2 ng/ml or digital rectal examination suspected of prostate cancer underwent transrectal ultrasound-directed prostate biopsy (at which time the prostate volume was measured) collecting 10 fragments from the peripheral zone (15). These fragments were conserved in 10% formalin solution until their processing for histological examination following hematoxylin-eosin staining.

Volunteers were classified in White, Mulatto or Black according to anthropological criteria that considered not only the skin color aspect, but the ancestors' racial reference up to 3rd degree (great-grandparents).

Racial genetic diversity was studied through variable number of tandem repeats (VNTR) in the DNA of 40 volunteers randomly chosen from each of the 3 racial groups defined by the anthropological criteria, as well as all bearers of neoplasia. DNA extraction was performed by a standardized technique, and its amplification (PCR) was made with 35 cycles in "Perkin-Elmer-Cetus®" thermocycler employing the following starters: APO B, vW-I Factor, D4S43, PAH and 13A1 Factor (13). The different alleles were recognized through electrophoretic migration in 4% polycrilamide gel after marking PCR products with flurochrome. Differences in molecular weight (or number of bases) were determined by comparison with migration of the "Gene Scan 2500 ROX® Kit" standard using the equipment's "ABIPrism 377®" software. The organization of the database with frequency of alleles for comparison between groups was done by the GDA software (16). That computerized VNTR database was employed as a reference, with data on descendants with European origin (Portuguese, Spanish, Italian and German – urban region of Ribeirão Preto), Africans from Congo and Cameroons (origin: Lubumbashi and Yaoundé) and Amerindian

from isolated tribes of Pará (Arara, Wayana-Apalai, Wayampi, Yanoman and Kayapo) (13). The estimate of ethnic admixture was calculated by the ADMIX 3 software (17).

The variables related to cancer prevalence, PSA test and other characteristics of the sample were performed by the Graph Prism® software version 3.0. Classificatory attributes were analyzed by Fisher's exact test or χ^2. Continuous variables of normal distribution were compared by unpaired bi-caudal "t" test or variance analysis, and those which did not pass the normality test were assessed by non parametric test. The significance level was fixed in 5%.

RESULTS

Of the 473 volunteers, 148 (31.3%) were White, 90 (19%) Mulatto and 235 (49.7%) Black according to the anthropological criteria. Respective mean age in these groups was: 56.8 ± 9.5 years, 54.7 ± 10.7 years and 57.9 ± 9.5 years. Simultaneous comparison between the groups by variance analysis showed p = 0.03. Tukey test showed similarity between White and Black, as well as between White and Mulatto groups, but not between Mulatto and Black groups. The comparison of mean age of Whites and non-Whites by the t-test showed no difference (p = 0.8).

Biopsies were indicated and performed in 121 volunteers. The prevalence of prostate adenocarcinoma for a tPSA cut-off level of 2 or 2.5 ng/ml was 5.7%, or 27/473 men, with ages ranging from 40 to 79 years, and 7.9% or 27/341 volunteers with ages between 50 and 79 years. If a tPSA cut-off level of 4 ng/ml was considered the prevalence would be 23/473 (4.8%) between 40 and 79 years, and 23/341 (6.7%) from 50 to 79 years.

Tumor occurred in 1 White, 6 Mulattos and 20 Blacks. Simultaneous comparison of cancer prevalence in the 3 groups, according to the anthropological criteria, showed a high significance (p = 0.005). The comparison between groups showed the following results: White versus Black: p = 0.008, White versus Mulatto: p = 0.01, White versus non-White: p = 0.009 and Mulatto versus Black: p = 0.65.

The mean values of admixture rate of African, Caucasian and Amerindian genes, in the samples classified by anthropological criteria as White, Mulatto or Black are exposed in Table-1. The gene admixture in volunteers with or without cancer regardless of anthropological phenotype is presented in this Table as well.

Tumor ratios in tPSA ranges from 2.1 to 4 ng/ml, from 2.5 to 4 ng/ml, from 4 to 10 ng/ml and >10 ng/ml were respectively: 6/62 (9.6%), 6/43 (13.9%), 7/35 (20%) and 14/30 (77.7%). The performance of the tPSA test in 3 cut-off levels in volunteers with tPSA ≤ 10 ng/ml is exposed in Table-2.

Table-3 shows the performance of digital rectal examination as well as a simulation of influence, on the performance of tPSA, of free/total PSA ratio and of PSA density in cases they were used. For simulation, the selection of cut-off levels of free/total PSA ratio and PSA density was made in such a way to maintain the sensitivity of total PSA according to the cut-off level.

Table 1 - *Analysis of gene admixture in "Whites", "Mulattos" and "Blacks" from Ipirá, Bahia, Brazil, as classified under an anthropological perspective.*

		Residents in Ipirá			
Alleles	**Whites**	**Mulattos %**	**Blacks %**	**With Cancer %**	**Without Cancer %**
Caucasians	67.5 ± 8	54.8 ± 9	45.3 ± 3	50.5 ± 9	59.1 ± 7
Africans	20.8 ± 8	36.3 ± 5	45.9 ± 4	49.0 ± 8	31.7 ± 8
Amerindians	11.7 ± 7	8.9 ± 7	8.8 ± 4	0.5 ± 4	9.2 ± 5
Total	100.0	100.0	100.0	100.0	100.0

Table 2 - *Performance of total PSA test in different cut-off levels for all volunteers with PSA < 10.1 ng/ml.*

Cut-off Level	Ss %	Sp %	PPV %	NPV %	Accuracy
2.0 ng/ml	100	6.6	13.4	100	18.4
2.5 ng/ml	100	36.6	18.0	100	42.7
4.0 ng/ml	69.2	62.2	20.9	93.3	63.1

Ss – sensitivity; Sp – specificity; PPV – positive predictive value; NPV – negative predictive value.

DISCUSSION

The prevalence of prostate cancer in volunteers from Bahia community (Northeastern) under study seems equivalent to those found in the State of São Paulo since those ranged from 1.3% to 3.2% (7-9,18). It must be stressed that in Northeastern volunteers the prevalence would be 4.8% if a tPSA cut-off level 4 ng/ml was employed, and that the performance of biopsies with collection of 10 peripheral fragments can lead to a 35% addition in cancer diagnosis compared to the sextant biopsy (15). In developed countries, the prevalence of prostate cancer in screenings has ranged from 1% to 6% in the age range from 50 to 75 years (1,4,6), which appears to indicate a similarity with our population.

Tumor prevalence in Blacks and Mulattos, alone or jointly, was statistically superior to that found in Whites from Ipirá. However the prevalence in Blacks and Mulattos was similar.

The difference in racial prevalence observed in this work cannot be explained based on age composition of groups, but it could be casual (despite significant), mainly due to the low prevalence observed in the White sample (1/148 - 0.7%).

When confronting the anthropological classification with the genetic composition, a marked process of ethnic admixture is observed in that region. What strongly suggests that Bantu ancestry is associated to a higher prevalence of prostate cancer is that in tumor bearers the proportion of African alleles was 49% whereas in those without cancer it was 31.7% (Table-1). However, it is remarkable that the proportion of Amerindian alleles in volunteers without cancer was approximately 18 times higher (9.2%) than the one observed in neoplasia bearers (0.5%). Could it be that the Amerindian (Asiatic) genes were counterbalancing the role of African genes in a higher predisposition to cancer?

Table 3 - *Some performance parameters of methods for indication of prostate biopsies, alone or associated, for the volunteers set with total PSA from 0 to 10 ng/ml.*

Method	Ss %	Sp %	Biopsies		Missed Tumors	Nº of Biopsies per Diagnosed Tumor
			Done	Avoided		
Digital rectal examination	15.3	83.3	17	86	11/13	8.5
tPSA 2 ng/ml	100	6.6	97	6	0/13	7.4
tPSA 2.5 ng/ml	100	36.6	72	31	0/13	5.5
tPSA 4 ng/ml	69.2	62.2	43	60	4/13	4.7
tPSA 2.5 ng/ml + F/T PSA 20%	100	52.2	56	47	0/13	4.3
tPSA 4 ng/ml + F/T PSA 20%	69.2	80.0	27	76	4/13	3.0
tPSA 2.5 ng/ml + PSAD 0.08	100	51.1	57	46	0/13	4.3
tPSA 4 ng/ml + PSAD 0.10	69.9	70.0	36	67	4/13	4.0

tPSA – total PSA; F/T PSA – free/total PSA; PSAD – PSA density; Ss – sensitivity; Sp – Specificity.

The explanation for the difficulty in demonstrating a higher prevalence of tumor in Southeastern Blacks is not simple with data published up to now. One study about miscegenation in a Southeastern region using the same criteria for anthropological (considering also the ancestry) and genetic (VNTR) classification, as it can be seen on Table-4 (13), seems to show some ethnic differences between Southeastern and Northeastern samples. The sample studied in the Northeast suggests a markedly lower crossing proportion between Caucasian and Indians since the percentage of Amerindian alleles in Whites was approximately 2.5 times lower (4.6%) than in the Northeastern sample (11.7%). That means that the proportion of Amerindian alleles in the Northeastern Whites sample is 154% higher than the Southeastern one, which would allow us to speculate if this would be the factor responsible for the low prevalence of tumor in Whites of that city. Other differences are less significant, even though it can be stressed that in the Southeast the proportion of African alleles in Whites was 14.9% higher, of Amerindian alleles in Blacks was 23.8% higher and of African alleles in Blacks was 14.3% higher than those found in the Northeastern. Thus, it is possible that the difference in prevalence among regions can be explained by ethnic diversity. Another explanation could be the lower longevity of Blacks pointed out in one of the Southeastern studies (7). However, maybe the main reason is the difference in criteria for anthropological classification, or even the difficulty or limitations for its application in a mixed population, because it is not clear if in other screenings the racial antecedent was considered.

Table 4 – *Ethnic admixture in residents from the urban region of Ribeirão Preto classified in Whites, Mulattos and Blacks according to anthropological criteria (13).*

	Residents in Ribeirão Preto		
Alleles	**Whites %**	**Mulattos %**	**Blacks %**
Caucasians	71.4 ± 5	49.5 ± 8	36.4 ± 3
Africans	23.9 ± 6	40.1 ± 4	52.5 ± 4
Amerindians	4.6 ± 4	10.3 ± 6	10.9 ± 4
Total	100.0	100.0	100.0

Our study also suggests that the sensitivity of tPSA, cut-off of 4 ng/ml, in the group of volunteers with tPSA below or equal to 10 ng/ml, is unsatisfactory. Of the 13 tumors found in this range, 6 were associated to tPSA < 4 ng/ml, and 4 (30.7%) of them would not have been diagnosed because the digital rectal examination did not suggest a tumor. On the other hand, the cut-off of 2 ng/ml presented a very low specificity, which meant a large proportion of unnecessary biopsies. The combination of tPSA cut-off in 2.5 ng/ml associated to additional criteria for indication of biopsy, such as free/total PSA ratio in 20% or PSAD in 0.08, seemed to represent a better option than employing only tPSA in all other cut-off levels. In the literature, results are controversial and there is no agreement about the best cut-off level for tPSA, as well as about the benefits gained with the associated use of the free/total PSA ratio and tPSA density, but one can note a tendency towards recommending a reduction in the cut-off level of tPSA and applying associated parameters in order to improve the test specificity (4,6). Maybe the most convincing recent multiracial study about the subject involving the screening and the follow-up of 12,902 men, of whom 7,541 were considered without prostate disease, showed that 95% of the sample without disease had tPSA ≤ 2.45 ng/ml, and this is the reason why this value was proposed as the upper limit for normality (19). Nevertheless, it must be stressed that the cut-off level of the free/total PSA coefficient that is able to maintain the tPSA sensitivity above 90%, in the same sample of patients, varies considerably with the brand of reagent that is used (20).

CONCLUSION

The prevalence of prostate cancer in Ipirá, Bahia, Brazil, was 5.7%, being higher in Blacks and Mulattos than in Whites. In cancer bearers the mean proportion of African alleles was 49%, whereas in those without cancer it was 31.7%. In volunteers with tPSA ≤ 10 ng/ml, the use of a cut-off level for tPSA in 2.5 ng/ml, the free/total PSA fraction of 20% and tPSA density of 0.08, represented a better option for indication of biopsies than the isolated use of tPSA in a cut-off level of 4 ng/ml.

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PREVALENCE OF PROSTATE ADENOCARCINOMA ACCORDING TO RACE IN AN UNIVERSITY HOSPITAL

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ABSTRACT

Objectives: To determine the prevalence of prostate cancer and to assess potential associations between race and prostate adenocarcinoma according to age in patients followed in an outpatient service of general urology in an university hospital.

Materials and Methods: Retrospective study of men aged from 40 to 79 years, followed during the period from 1999 to 2001. Patients were classified according to race in White, Mulatto and Black. Those with abnormal digital rectal examination and/or serum level of prostate specific antigen (PSA) > 4.0 ng/ml, underwent a transrectal prostate biopsy.

Results: 580 patients with mean age of 60.7 ± 10.0 years were studied, with 116 Whites (20.0%), 276 Mulattos (47.6%) and 188 Blacks (32.4%). There was no significant difference regarding the mean age (p = 0.62), serum level of PSA (p = 0.65) and prevalence of prostate adenocarcinoma between Whites, Mulattos and Blacks (p = 0.36). While studying the association between race classified in 2 groups (Whites versus Mulattos and Blacks) and prostate adenocarcinoma according to age, no association was found when the total group was assessed, neither among those with age above 60 years old. In the group between 40 and 60 years, even though without statistical significance, the estimate of prevalence ratio was 2.2 (CI 95%: 0.52 to 9.0; p = 0.38).

Conclusion: Prostate adenocarcinoma was found in 16.6% of the patients aged between 40 and 79 years. We did not find a racial influence in our population.

Key words: prostatic neoplasms; prevalence; race; prostate-specific antigen
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INTRODUCTION

Prostate cancer is becoming a major public health problem in the world, being one of the most frequent causes of malignant neoplasia in men (1). Estimates of incidence and mortality due to prostate cancer in Brazil for the year 2002 were 29.7 and 9.1 per 100,000 inhabitants, respectively, according to the Cancer National Institute - INCA (2). Studies developed in other countries have demonstrated a higher prevalence of prostate adenocarcinoma in Blacks than in Whites in several centers (3,4). However, other studies have not found any statistically significant difference when comparing prostate adenocarcinoma in Whites and in Blacks (5). Similarly, in Brazil the majority of screening studies did not demonstrate a higher prevalence of this tumor in Blacks than in Whites (6-8).

The objective of this study was to determinate the prevalence of prostate cancer and to assess potential associations between race, age and prostate adenocarcinoma in patients followed in the general urology outpatient service within a college hospital.

MATERIALS AND METHODS

We retrospectively studied men aged from 40 to 79 years, attended and followed in the gen-

eral urology outpatient service, in an university hospital in the period from 1999 to 2001.

Besides careful anamnesis and physical examination, all patients underwent a digital rectal examination, performed by urologists. Patients were classified according to race in Whites, Mulattos and Blacks, being considered as Mulatto the skin color between white and black. All patients underwent a determination of prostate specific antigen (PSA) by chemoluminescence technique (Immulite) and abdominal ultrasonographic evaluation for estimating the volume and the presence of hypoechoic nodules in the prostate. In cases where the serum level of PSA was higher than 4.0 ng/ml and/or prostate abnormalities were found on digital rectal examination, patients underwent transrectal biopsy, with fragments being collected by sextant sampling and submitted to pathological analysis. Diagnosis of prostate adenocarcinoma was based in histological findings and defined by Gleason score.

Continuous variables were described through mean ± standard deviation and by median and categorical through their percentages. For comparison of continuous variables, the "t" test or ANOVA was performed, when indicated. The χ^2 test or Fisher's exact test was performed for comparison of categorical variables. The frequency of prostate adenocarcinoma was compared with races, classified in 2 groups (Whites versus Mulattos or Blacks), and the prevalence ratio (PR) was calculated. This approach aimed to assess an association between race and prostate adenocarcinoma, considering a group with the total of patients and other group with those submitted to prostate biopsy. Additionally, aiming to assess a potential influence of age on the association between race and prostate adenocarcinoma, this approach was performed, separating patients with ages under or above 60.7 years. It was considered significant when the "p" value (bi-caudal) was lower than 5%. The variation in the sample was estimated by means of the confidence interval (CI) of 95%. Analyses were performed using the Statistical Package for the Social Sciences (SPSS) software for Windows, version 10.0.

RESULTS

Main demographic and clinical data of 580 patients studied with ages between 40 and 79 years, are presented on Table-1.

No significant difference was found between racial groups as for the studied variables (Table-2). There was no significant difference regarding mean age, presence of symptoms, assessment by prostate ultrasound and mean serum level of PSA in the racial groups. As for the prostate consistency alterations on digital rectal examination, there was a higher prevalence among Blacks (22.3%) when compared with Mulattos (14.9%) and Whites (12,9%), even though without statistical significance (p = 0.48). Diagnosis of prostate adenocarcinoma was made in 16 White (13.8%), 40 Mulatto (14.5%) and 37 Black patients (19.7%), and the difference was not statistically significant (p = 0.25).

Table-3 shows the results of pathological examinations of 162 patients submitted to prostate biopsy, according to race. Prostate adenocarcinoma was the most frequent diagnosis among the 3 racial groups followed by benign prostatic hyperplasia (BPH) and prostatitis. Figure-1 shows the degree of malignancy

Table 1 – *Demographic and clinical data of 580 patients followed in the urology outpatient service.*

Age (years)	
Mean ± SD	60.7 ± 10.0
Median	61
Race	
White	116 (20.0%)
Mulatto	276 (47.6%)
Black	188 (32.4%)
Digital rectal examination (abnormal)	98 (16.8%)
PSA > 4.0 ng/mL	176 (30.3%)
PSA (ng/ml)	
Mean ± SD	6.6 ± 12.9
Median	2.0
Biopsied	162 (27.9%)

PSA – prostate specific antigen.

Table 2 – *Some clinical-pathological characteristics of 580 patients according to race.*

	White	Mulatto	Black	p value
Nº of patients	116 (20.0%)	276 (47.6%)	188 (32.4%)	-
Age (years)	62.3 ± 9.8	60.6 ± 10.0	59.8 ± 10.1	0.1
Symptoms	55 (47.4%)	144 (52.2%)	86 (45.7%)	0.36
Ultrasound (prostate)*	37.1 ± 22.7	38.1 ± 23.9	39.6 ± 26.8	0.65
PSA	7.1 ± 16.3	6.0 ± 11.5	7.1 ± 12.6	0.57
Biopsy	30 (25.9%)	75 (27.2%)	57 (30.3%)	0.65
Adenocarcinoma	16 (13.8%)	40 (14.5%)	37 (19.7%)	0.25

*PSA – prostate specific antigen; * - volume in ml.*

of prostate adenocarcinoma by the Gleason score distributed among the racial groups. The histological grade of intermediary prostate adenocarcinoma (Gleason 5 - 7) was the most frequent in the 3 groups.

Analyzing the distribution of race in the 162 patients submitted to prostate biopsy (Table-4), there was no significant difference concerning age (p = 0.62), PSA level (p = 0.65) and diagnosis of prostate adenocarcinoma (p = 0.36).

When evaluating the association between prostate adenocarcinoma and race classified in 2 groups (Whites versus Mulattos and Blacks) in the total of patients, after excluding those who refused prostate biopsy, it was found in 16 of the 112 White (14.3%) and 77 of the 448 Mulatto and Black men (17.2%). In patients aged from 40 to 60 years, 2 of 51 Whites (3.9%) and 19 of the 217 Mulattos and Blacks (8.7%) had the diagnosis of prostate adenocarcinoma. In those with age above 60 years (Table-5), 14 of the 61 Whites (22.9%) and 58 of the 231 Mulattos and Blacks (25.1%) were found to have prostate adenocarcinoma.

Table 3 – *Histological diagnosis of 162 patients submitted to prostatic biopsy.*

	White	Mulatto	Black	Total
Nº of patients	30 (18.5%)	75 (46.3%)	57 (35.2%)	162 (100.0%)
Adenocarcinoma	16 (53.3%)	40 (53.3%)	37 (64.9%)	93 (57.4%)
BPH	12 (40.0%)	22 (29.3%)	13 (22.8%)	47 (29.0%)
Prostatitis + BPH	2 (6.7%)	11 (14.7%)	4 (7.0%)	17 (10.5%)
Prostatitis	0	2 (2.7%)	3 (5.3%)	5 (3.1%)

BPH – benign prostatic hyperplasia.

Table 4 – *Pathological data and age range of 162 patients submitted to prostatic biopsy according to race.*

	White	Mulatto	NBlack	p value
Nº of patients	30 (18.5%)	75 (46.3%)	57 (35.2%)	-
Age (years)	68.6 ± 7.0	67.3 ± 7.6	67.0 ± 17.1	0.65
PSA (ng/dl)	22.0 ± 27.3	18.1 ± 16.8	19.3 ± 17.1	0.65
Adenocarcinoma	16 (53.3%)	40 (53.3%)	37 (64.9%)	0.36

PSA – prostate specific antigen.

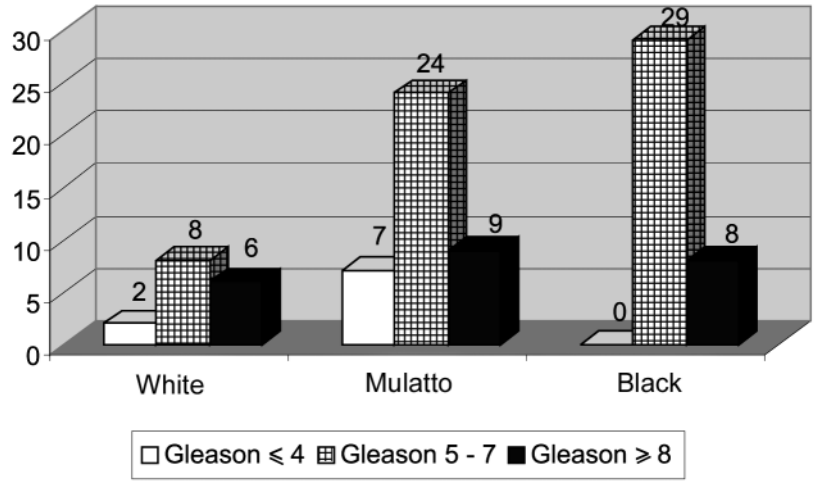

Figure 1 – *Gleason score in 93 patients with prostate cancer.*

Assessing only the group of 162 patients biopsied (Table-6), we did not find statistically significant differences as well: we found prostate adenocarcinoma in 16 of the 30 Whites (53.3%), 77 of the 132 Mulattos and Blacks (58.3%). Among patients aged between 40 and 60 years, 2 of the 4 were White (50%) and 19 of the 27 were Mulatto and Black (70.4%). In patients over 60 years old we found prostate adenocarcinoma in 14 of the 26 White (53.8%) and 58 of the 105 Mulatto and Black patients (55.2%).

DISCUSSION

In the present study, of the 162 patients (27.9%) who underwent transrectal prostatic biopsy, the pathological study revealed prostate adenocarcinoma in 93 of them, representing 16.6% of men followed in the general urology outpatient service, excluding those who refused the biopsy, which was not surprising because it was a group of high risk patients for prostate adenocarcinoma.

Table 5 – *Association between race and diagnosis of prostate adenocarcinoma according to age.*

Age Range	White	Mulatto / Black	PR (CI 95%)	p value
Total group	16/112 (14.3%)	77/448 (17.2%)	1.2 (0.73 - 1.98)	0.46
40 to 60 years	2/51 (3.9%)	19/217 (8.7%)	2.2 (0.54 - 9.28)	0.25
> 60 years	14/61 (22.9%)	58/231 (25.1%)	1.1 (0.66 - 1.82)	0.73

PR = prevalence ratio; CI = confidence interval.

Table 6 – *Association between race and diagnosis of prostate adenocarcinoma according to age (biopsied).*

Age Range	White %	Mulatto / Black %	PR (CI 95%)	p value
Biopsied	16/30 (53.3%)	77/132 (58.3%)	1.1 (0.76 - 1.57)	0.6
40 to 60 years	2/4 (50.0%)	19/27 (70.4%)	1.4 (0.51 - 3.8)	0.58
> 60 years	14/26 (53.8%)	58/105 (55.2%)	1.0 (0.7 - 1.52)	0.9

RP = razão de prevalência; IC = intervalo de confiança.

Additionally, in the analyzed material, no significant difference was found between the 3 racial groups concerning age, presence of urinary symptoms and prostate volume. As for the serum level of PSA, no significant difference was found between the 3 groups as well, differing from Henderson et al. (9) who, in a retrospective study, found higher serum levels of PSA in Black men, when compared to White man of a similar age group, though it did not involve men with evidence of prostate adenocarcinoma. The reasons for this discrepancy are not apparent and were not a matter of this study.

Literature has called the attention to several risks for developing prostate cancer, with race being one of them (10,11). Studies conducted in North-American population showed a high incidence of prostate cancer in Blacks, with a low incidence in Whites (12-14).

Though the number of White men with diagnosis of prostate adenocarcinoma was lower than that of Mulatto and Black men, there was no difference relative to the proportion of patients with prostate adenocarcinoma in each racial group, in our population. Even when Mulattos and Blacks were jointly considered, no association was found between race and diagnosis of prostate adenocarcinoma neither in the group of all patients assessed nor in those who underwent prostatic biopsy. When stratified by age, the lack of association remained both for the total group (prevalence ratio - PR = 1.1) and among the biopsied patients (PR = 1.0) aged above 60 years old. Among those aged under 60 years, as well, there was no association between the analyzed groups. However, it is important to observe that in the total group the frequency of prostate adenocarcinoma was 2 times higher among Mulattos and Blacks than among Whites. Studies with larger groups of participants could determine if such result is incidental or if, really, Mulatto and Black men have a higher risk of prostate adenocarcinoma in lower age ranges.

Our data are in accordance to others in the literature. Antonopoulos et al. (7) and Cotter et al. (5) did not find a significant difference in the prevalence of prostate adenocarcinoma between Whites and Blacks as well. However, Cotter et al. (5) demonstrated that American Black men have a familial history of prostate cancer more often and are younger at the time of diagnosis than White men. In a subsequent publication, however, Antonopoulos et al. (15) reported a higher prevalence of neoplasia in Negroid than in White patients. The reasons for the difference between the 2 series were nor assessed, but it is known that genetic, environmental, dietetic, educational, and socio-economic factors, related to the diagnosis of prostate adenocarcinoma, also vary in different Brazilian regions.

We must call to attention that racial distribution in the studied population is similar to that in the metropolitan region of Salvador - Bahia, according to the demographic census conducted by the Brazilian Institute of Geography and Statistics (IBGE) in the year of 2000 (16), which suggests that, in a certain way, it represents the prevalence behavior of prostate pathology in the population.

We must pay attention to the fact that Brazilian population and, mainly the one from Bahia, has a high miscegenation index. It is important to stress that the classification of race using skin color as a parameter is inaccurate, especially in countries like ours, and it was discussed by Azevedo (17). However, the importance of phenotypic characteristics in biomedical studies and even in clinical practice is acknowledged, as evaluated by Burchard et al. (18). A better investigation of genetic and environmental differences between Black and White men can be helpful for clarifying the mechanisms of prostate carcinogenesis (19).

CONCLUSION

Prostate adenocarcinoma was found in 16.6% of patients aged between 40 and 79 years. We found no influence of race in our population with prostate adenocarcinoma though the punctual estimate had indicated a frequency 2 times higher among Mulattos and Blacks (PR = 2.2) than in Whites in the age range between 40 and 60 years, even if it was not statistically significant.

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EDITORIAL COMMENT

This paper addresses a controversial and much discussed subject in international literature – the association of racial factors with the prevalence of prostate cancer in the population submitted to screening for early detection of this pathology. Studies on detection of prostate cancer coordinated by Catalona observed that black race men present an increased risk for this disease, which can also appear earlier in these individuals (1,2). Such data have generated much discussion, since they imply in differentiated politics for health programs based on race, which is often seen as a discriminatory factor by some people. In the Brazilian population, little is known about racial differences concerning the diagnosis of prostate cancer. In this aspect, the present work brings relevant information, and stresses that there was no statistically significant difference between the racial groups under study, despite the prevalence ratio was 2.2 times higher among younger Black men, in the age range between 40 and 60 years. Maybe, with a larger number of patients, this difference could reach a significance, which would corroborate North-American data. In Brazil, though, racial differentiation is not an easy task to be done due to the strong miscegenation that occurred since colonial times between European, Indian and African populations (and the latter one with different origins as well). It is also interesting to note the high positive predictive value of prostate biopsy in the population studied in this paper, higher than the one internationally reported. Could it be that our patients are being diagnosed with neoplasias in more advanced stages or that biopsy techniques have evolved?

Racial implications in prostate cancer gain importance because they go beyond a mere diagnosis. Black race has also been questioned as a factor associated to adverse pathology or inferior responses to treatments such as radical surgery or external radiotherapy (1-3). More recently, however, these results have been doubted, stressing that in populations with identical access to health, racial factor cannot be an independent factor of pathology or of therapeutic outcome (4,5). Moreover, it can be stressed that co-factors indirectly related to race, and not always studied, e.g., a higher tendency to obesity, have been suggested as the actual responsible for the racial differences in the behavior of prostate neoplasia (6).

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ANTIBIOTIC PROPHYLAXIS IN PROSTATE BIOPSY. A COMPARATIVE RANDOMIZED CLINICAL ASSAY BETWEEN CIPROFLOXACIN, NORFLOXACIN AND CHLORAMPHENICOL

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ABSTRACT

Objective: To compare, prospectively, 4 different schemes of antibiotic prophylaxis previously to transrectal prostate biopsy.

Materials and Methods: 257 patients were randomized in 4 groups: Group I: single dose of ciprofloxacin 2 hours before the procedure; Group II: ciprofloxacin 3 days; Group III: chloramphenicol 3 days; and Group IV: norfloxacin 3 days. The complication rate was assessed in a blind way on the third and on the thirtieth days through a questionnaire. Groups were compared by the qui-square method and, in small samples, by the Fisher method, with statistical significance of 95%.

Results: Complications index throughout the sample differed between the 4 groups of patients under study, being 3.1% for group I, 2.1% for group II, 18.3% for group III and 10.5% for group IV. Schemes employing ciprofloxacin were statistically superior to those that used norfloxacin or chloramphenicol ($p < 0.05$). There was no difference between a single dose and 3 days of ciprofloxacin ($p > 0.05$).

Conclusion: Schemes using ciprofloxacin presented better results in prophylaxis previously to prostate biopsy. We recommend using a single dose of ciprofloxacin due to its posologic ease and low cost, associated with a therapeutic response equivalent to 3-day regimens.

Key words: prostate; biopsy; needle; ultrasonography; antibiotic prophylaxis
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INTRODUCTION

Transrectal prostate biopsy (TPB) is simple and fundamental in the diagnosis of prostate adenocarcinoma (1). However, it is reported that TPB can be accompanied by infectious events in 3% to 37% of the cases (2-6). Urinary tract infections, transitory bacteremia and fever episodes are complications that can occur following transrectal prostate biopsy (3,4).

The majority of works points to the need of antibiotic prophylaxis previously to TPB (6-19). However, there is a lot of controversy and diversity of therapeutic schemes in the literature concerning the ideal drug to be used and the time employed for infectious prophylaxis (20).

The objective of this study was to assess 4 different schemes of antimicrobial prophylaxis, previously to TPB, aiming to identify potential infectious complications following prostate biopsy. Our results will be discussed and compared to the literature, in order to enable one to conclude which is the best prophylactic schemes tested in our patient population.

MATERIALS AND METHODS

From April 2001 to April 2002, 285 patients underwent TPB, with 257 patients being randomly selected and sequentially included in this study. Were excluded from the protocol those patients with ind-

welling urethral catheter, positive urine culture, presence of cardiac valve prosthesis, diabetes mellitus, rectal stenosis and patients using antimicrobials in the 7 days prior to biopsy.

After explanation and obtaining the informed consent, patients were divided into 4 groups: 1) Group I: 64 individuals (24.9%) receive a single oral dose of ciprofloxacin, 500 mg, 2 hours before the procedure; 2) Group II: 46 individuals (17.9%) received ciprofloxacin 500 mg, orally, during 3 days, being instructed to take a dose of the medication 12 hours before the examination, other dose 1 hour before biopsy, maintaining treatment for 2 additional days, each 12 hours; 3) Group III: 71 patients (27.62%) received chloramphenicol 500 mg, orally, with posologic instructions similar to group II; 4) Group IV, with 76 patients (29.57%), received norfloxacin 400 mg, orally, with a similar posology to groups II and III.

Blood cultures for aerobes and anaerobes were collected in patients from group I 1 hour and 3 hours after the procedure. All patients had urine cultures before and 3 days after TPB, with a growth equal or superior to 10^5 UFC/ml being considered as presence of urinary infection. Rectal preparation with enema was not used before the biopsy. Twelve fragments were taken from the prostate in each patient.

Patients had their axillary temperature measured each 8 hours during the first 2 days and were assessed, by a questionnaire applied by another clinician that did not participate in the study, on the third and on the thirtieth days.

We considered as minor infectious complication the presence of fever alone or the presence of mild urinary symptoms, that resolved with the use of antipyretic and/or antibiotic therapy, with no need of hospitalization. We classified as major infectious complication the presence of fever associated with intense urinary symptoms, sepsis, bacteremia or need of hospitalization and intravenous antibiotic therapy.

The comparative statistical analysis was assessed by the qui-square method and, in small samples, by the Fisher method, with a level of statistical significance of 95%, calculated by the EPI INFO 6.0 software.

RESULTS

All patients used the medication and performed the biopsy according to the protocol. Patients' mean age was 68.77 (± 8.37) years, mean PSA was 15.19 (± 14) ng/mL and prostate volume as assessed by transrectal ultrasound was 35.67 (± 18.2) grams, without statistical difference in this parameters between the 4 groups studied ($p > 0.05$). (Table-1).

Table-2 shows the frequency of minor and major complications in patients for each group of antibiotic prophylaxis.

In patients from group I (ciprofloxacin single dose), 2 minor complications occurred (3.1%), corresponding to an episode of temperature equal to 38°C in the first day post-biopsy, with sodic dipyrone being administered in both cases with clinical improvement. There were no major complications in this group of patients, and there was no evidence of bacterial growth in the respective urine cultures as well. In relation to the blood cultures, only 1 of the patients included in group I presented a positive result for *Staphylococcus epidermidis*. We also observed

Table 1 – *Comparison of mean and standard deviation for age, serum PSA level and prostate volume between the 4 groups of patients who underwent transrectal prostate biopsy, evidencing the homogeneity between the 4 groups under study.*

Patients	Group I	Group II	Group III	Group IV
Age (years)*	66.5 ± 8.5	68.0 ± 9.0	69.1 ± 8.2	68.7 ± 9.5
PSA (ng/ml)*	13.5 ± 12.2	14.2 ± 11.5	16.0 ± 13.2	15.2 ± 12.1
Prostate volume (g)*	37.2 ± 23.2	35.8 ± 15.8	38.5 ± 18.3	36.5 ± 17.2

** $p > 0.05$ for all studied parameters.*

Table 2 – *Relation and frequency of infectious complications obtained in the 257 patients who underwent transrectal prostate biopsy according to the groups of patients under study.*

Variables	Group I	Group II	Group III	Group IV	Total
Number of patients	64	46	71	76	250
Minor Complication					
Self-limited fever	2	0	3	4	9 (3.5%)
Prostatitis not requiring hospitalization	0	0	4	2	6 (2.3%)
Urinary tract infection	0	0	2	2	4 (1.5%)
Orchiepididymitis	0	0	3	0	3 (1.5%)
Fever and acute urinary retention	0	1	0	0	1 (0.4%)
Major Complications					
Prostatitis with bacteremia and hospitalization	0	0	1	0	1 (0.4%)
Total	2 (3.1%)	1 (2.1%)	13 (18.3%)	8 (10.5%)	24 (9.6%)

that this patient did not present fever or any voiding symptom following transrectal prostate biopsy.

The only complication (2.7%) that occurred among patients from group II (ciprofloxacin during 3 days) corresponded to an episode of fever and acute urinary retention, requiring antibiotic therapy for 7 days. Upon treatment, the patient presented no complaints, no fever and had his voiding reestablished. There was no need for hospital admission or major complications.

Among patients in group III (chloramphenicol), 13 (18.3%) presented complications following transrectal prostate biopsy (Table-2). Among them, there was a major infectious complication corresponding to acute prostatitis with bacteremia due to *Escherichia coli*, with need of hospitalization for treatment and intravenous antibiotic therapy.

As for the 76 patients from group IV (norfloxacin), 8 (10.5%) presented minor complications following TPB (Table-2). There were no major complications in this group of patients.

In the late follow-up visit after 30 days, none of the patients reported fever or other symptom due to infectious process. In relation to global comparative results, there was a statistically significant difference between groups (Tables-3, 4 e 5).

When we compared groups I and II (ciprofloxacin) we did not observe significant difference (Fisher monocaudal $p = 0.6$) (Table-3). Aiming to compare the schemes using ciprofloxacin (groups I and II) with the other groups, we performed the sample gathering between groups I and II.

A statistical difference was observed concerning the infection index between patients who received ciprofloxacin both when compared to chloramphenicol ($x^2 = 13.0$ and $p = 0.0003$) (Table-4) and when compared to norfloxacin (Fisher monocaudal $p = 0.03$) (Table-5).

We did not observe statistically significant differences when we compared the complication general indexes between chloramphenicol and norfloxacin ($p > 0.05$).

DISCUSSION

Programs for early detection of prostate cancer have surprisingly increased the number of pros-

Table 3 – *Occurrence of infectious complications, comparing the groups of patients who received ciprofloxacin single dose (Group I) and ciprofloxacin for 3 days (Group II).*

Prophylactic Scheme	Infectious Complications		p value
	Yes	No	
Group I	2	62	0.6
Group II	1	45	

Table 4 – *Occurrence of infectious complications, comparing the group of patients who received ciprofloxacin (Groups I and II) with the group who received chloramphenicol (Group III).*

Prophylactic Scheme	Infectious Complications		p value
	Yes	No	
Groups I e II	3	107	0.0003
Group III	13	58	

Table 5 - *Occurrence of infectious complications, comparing the group of patients who received ciprofloxacin (Groups I and II) with the group who received norfloxacin (Group VI).*

Prophylactic Scheme	Infectious Complications		p value
	Yes	No	
Groups I e II	3	107	0.03
Group IV	8	68	

tate biopsies (7,8). More recent series show that infectious complications can occur between 0.8% and 17% of the cases, with spontaneously resolving fever, probably due to transitory bacteremia, being the most frequent symptom. Urinary tract infection, prostate abscess with urinary retention, sepsis and death have also been described (9-19).

The main microbial agents responsible for symptoms are Gram-negative germs, which normally colonize the rectum, in particular *Escherichia coli.* Patients with some degree of immunologic depression can develop infection due to anaerobes.

A comparative analysis with randomized studies in the literature tends to show a superiority of schemes using antibiotics in relation to placebo, with the use of quinolones being preferred, presenting the lowest infection indexes (6,10,12,14-17,20). However, there are few randomized prospective studies aimed to assess which antibiotic is more effective, its ideal dose, as well as the administration route, duration and cost of treatment for prophylaxis in transrectal prostate biopsy (11,20). In Table-6 we present the results obtained by several authors according to the antibiotic regimen employed.

In our patient population we could observe that the prophylactic effectiveness of schemes using ciprofloxacin was similar between them and significantly superior to the others. We also had a concern to document the possibility of bacteremia when the ciprofloxacin was administered in a single dose, since we did not find this information available in the literature.

Aron et al. observed that the use of ciprofloxacin in a single dose was similar to the 3-day scheme (16), an impression that was confirmed by our results.

Our results, compared to the experience of other authors (12,13,20), testify that norfloxacin is a feasible option with a low index of infectious complications.

Results with the use of chloramphenicol were discouraging. We observed a high index of minor complications, including orchiepididymitis, which is rarely reported with other schemes, in addition to significant complication requiring hospitalization. Its wide range of action, low cost and lack of previous report in literature concerning antibiotic prophylaxis previously to TPB motivated its utilization in this study. Thus, we believe that its use is not recommended for such purpose.

We could also observe that initiating the antibiotic therapy before the biopsy has an important impact when compared to schemes initiated after the biopsy (12,13). Such data suggest that higher probability of infection occurs during the procedure. If this hypothesis is correct, therapeutic schemes with single dose and longer half-life should present infection indexes similar to more prolonged schemes.

Coverage for anaerobes, little studied up to now, however, seems to have little impact on the infection index (9,16,18). In our selected sample of 257 patients, we did not isolate in culture any case of anaerobes, reinforcing this hypothesis.

Table 6 – *Incidence of infectious events in randomized comparative studies using several schemes of antibiotic prophylaxis following TPB.*

Ref.	N	Antibiotic Regimen	Infection	P
(3)	117	Netilmicin, 1.5 mg/kg, IV + metronidazole, 500 mg, oral, 60 min before biopsy	17%	0.01
		Trimethoprim, 320 mg + sulfamethoxazole, 1600 mg, oral, 60 min before biopsy	2%	
(6)	55	Ciprofloxacin, 500 mg, oral, 12 h before biopsy and 12 h after the first dose	7%	0.0032
		Gentamicin, 1.5 mg/kg, IV, 2 h before biopsy + 80 mg , IV, 8 h after biopsy	37%	
(8)	537	Ciprofloxacin, 500 mg, oral, single dose, 30-120 min before biopsy	3%	0.009
		Placebo	8%	
(12)	347	Norfloxacin 400 mg, oral, immediately after biopsy, with an additional dose on the same day	6.5%	< 0.05
		Norfloxacin 400 mg, oral, 60 min before examination and continued for 2 days	1.4%	
(13)	491	Norfloxacin 400 mg, oral, 12-12 h, for one day, initiation following biopsy	11%	< 0.05
		Norfloxacin 400 mg, oral, 12-12 h, for one week, initiation following biopsy	4.9%	
		Control	26%	
(15)	111	Trimethoprim 160 mg + sulfamethoxazole 800 mg, oral, single dose, 60 min before biopsy	6.6%	< 0.05
		Ofloxacin 400 mg, oral, single dose, 60 min before biopsy	4.7%	
(16)	231	Placebo, twice a day, for 3 days	8%	0.003
		Ciprofloxacin 500 mg + tinidazole 600 mg, oral, single dose	2%	
		Ciprofloxacin 500 mg + tinidazole 600 mg, oral, twice a day, for 3 days	3%	
(17)	29	Lomefloxacin 400 mg, oral, 2 h before biopsy	0%	0.05
		Cefazolin, 1 g, IV, 2 h before biopsy	7.6%	
(18)	20	Lomefloxacin 400 mg, oral, 3 h before biopsy, repeating for 2 days after the procedure	0%	No realized
		Lomefloxacin 400 mg + metronidazole 500 mg, oral, each 8 h, both initiating 3 h before biopsy, until 2 days after the procedure	0%	
(19)	110	Cefuroxime, 1.5 g, IV, 20 min before biopsy	5.3%	0.45
		Piperacilin/tazobactan, 4.5 g, IV, 20 min before biopsy	7.2%	

Ref. = reference, N = number of patients, P = p value

Finally, we found that in our patient population the prophylactic effectiveness of schemes using ciprofloxacin was significantly superior to the other groups of antibiotics under study. Our studied showed as well that the use of ciprofloxacin in a single dose 2 hours before the biopsy was equivalent to using it for 3 days. Norfloxacin is a feasible option with a low morbidity and chloramphenicol, in our opinion, should not be used for this purpose.

CONCLUSION

Based on the results of this study we currently recommend in our service the use of ciprofloxacin, in a single dose, 2 hours before TPB.

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EFFECT OF SILDENAFIL IN CAVERNOUS ARTERIES OF PATIENTS WITH ERECTILE DYSFUNCTION

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ABSTRACT

Introduction: Sildenafil citrate is a type 5 phosphodiesterase inhibitor, which has demonstrated excellent results in the treatment of erectile dysfunction. The effect of sildenafil citrate in the cavernous arteries of patients with erectile dysfunction has not been established yet. The objective of this study was to assess the effect of sildenafil citrate in the cavernous arteries of patients with erectile dysfunction, following an intracavernous injection of alprostadil.

Materials and Methods: 29 male patients, with mean age of 53.8 years (32 to 75 years), were prospectively evaluated. The mean time with complaint of erectile dysfunction was 50.5 months (6 to 168 months). Each patient was his own control. Patients underwent a measurement of peak systolic velocity before and after use of sildenafil citrate associated with 5 micrograms of alprostadil, through ultrasonic velocitometry Knoll/MIDUS® system. In the interval between measurements, approximately 15 days, patients used 3 tablets of sildenafil at home with their partners.

Results: Using only 5 mcg of alprostadil, average peak systolic velocity was 23.9 cm/s, and when associated to 50 mg of sildenafil it was 24.8 cm/s. Despite the increase in the flow rate caused by sildenafil, the difference was not statistically significant, $Z_{calculated} = - 0.695$ NS (Wilcoxon test). Twenty one of the 29 patients (72.4%) showed global improvement in sexual performance with the use of sildenafil citrate at home. There was not a statistically significant correlation between the global response to sildenafil citrate and the increase in the peak systolic velocity.

Conclusion: We concluded that, even though the use of 50 mg of sildenafil citrate associated with 5 mcg of alprostadil provides an increase in the peak systolic velocity of the cavernous arteries, there was no statistic difference in relation to alprostadil alone. There was no correlation between the global response to sildenafil and the increase in the peak systolic velocity.

Key words: penis; arteries; penile erection; corpus cavernosum; phosphodiesterases inhibitors
Int Braz J Urol. 2003; 29: 320-6

INTRODUCTION

Erectile dysfunction is the persistent inability to reach or maintain an erection that is sufficient for a satisfactory sexual intercourse (1,2). In Brazil, some degree of erectile dysfunction was found in 39.8% of the studied population (3).

Until 1996, treatments recommended for erectile dysfunction were the vacuum devices, the therapy with injectable vasoactive drugs and penile prosthesis (4), when the first clinical results with the use of sildenafil citrate were published (5,6). The response according to dosage was 60, 84 and 100%, respectively with doses of 25, 50 and 100 mg of sildenafil, compared with a response of 5% from those who received placebo (7). A significant improvement of erections following the use of sildenafil citrate was demonstrated in several trials, reaching a success rate of 70 to 90% (6-10).

Objectively, the action of sildenafil citrate was confirmed by penile plethysmography, with a mean dura-

tion of rigidity above 60% in relation to placebo (11). The effect of sildenafil citrate in the cavernous arteries' flow was confirmed in men without complaints of erectile dysfunction (12), through an increase in the peak systolic velocity with the use of sildenafil citrate that was similar to that obtained with papaverine (13,14).

The objective of this study was to assess the effect of sildenafil citrate in the cavernous arteries of patients with erectile dysfunction, following an intracavernous injection of alprostadil.

MATERIALS AND METHODS

A prospective, comparative, clinical trial was performed, in which the patient was his own control, in 29 male patients, with ages ranging from 32 to 75 years (mean 53.8 years) and with complaints of erectile dysfunction.

The time since settlement of the erectile dysfunction picture ranged from 6 to 168 months (mean 50.5 month). Laboratory analysis consisted of dosage of serum total testosterone, prolactin and fasting glycemia.

After the patient had fulfilled the inclusion criteria, we started the study. The first visit aimed the baseline assessment of cavernous arteries. The patient was conducted to a special, isolated and comfortable room. After some minutes for adapting to the environment, 5 mcg of alprostadil were applied by intracavernous route with a 30-gauge needle. The patient remained resting in this room and with material containing visual erotic stimulation available. Following a 15-minute period, we started the examination. Patients who did not present a satisfactory erection following the drug application were excluded from the study and referred to other type of treatment.

We used ultrasonic velocitometry by the Knoll/MIDUS system (Urometrics, St Paul, Minnesota) for measurement of the peak systolic velocity. The system is comprised by 2 ultrasonic fixed angle transducers (60°). The frequency of each transducer is 8 MHz and it has a measurement capability of blood flow in amplitude from 1 to 200 cm/s. The transducer has a focal distance of 1.2 cm (15).

Measurements were obtained in a standardized way in all patients. With the patient in supine position, the transducers were positioned in the base of the penis and moved laterally until a consistent signal was captured by the earphone and viewed in the computer screen. Data from left and right cavernous arteries were obtained separately. Signals were recorded in high-speed charts in function of time.

Upon completion of the examination, the patient received a box containing 4 tablets of sildenafil citrate 50 mg. The patient was instructed to use 3 tablets at home, with his partner in a period of 15 days, always one hour before the sexual intercourse. The fourth tablet should be taken one hour before the next visit, when a new assessment would be done. The use of sildenafil at home aimed to assess each patient's response to the medication and to compare it with the results obtained in the second assessment.

Before the patient was released, he was instructed about the possibility of priapism, and to come back to the hospital if the erection lasted for 4 hours or more. In the second assessment, in average 15 days after the first one, patients initially answered to the following question: the use of the medication improved your sexual performance in this period? Yes or no? Regardless the answer, a new assessment was performed. Approximately 1 hour after administrating 50 mg of sildenafil citrate, the patient received 5 mcg of alprostadil by intracavernous route in the private room and once more used visual erotic stimulation for 15 minutes, and then was submitted to the measurement of peak systolic velocity, following the same steps of the initial assessment.

All data were classified in tables and submitted to statistical analysis.

In order to study potential differences between the peak systolic velocity of right and left cavernous arteries, both for periods pre- and post-administration of sildenafil citrate, as well as the average for the pre-period in relation to the average for the post-period, we used Wilcoxon non-parametric test for 2 non-independent samples. In order to study potential associations between the peak systolic velocity and the patient's global response to sildenafil citrate, we used the qui-square test (χ^2) for association tables following the Cochran's restrictions and when

present, we used Fisher's exact test. In all cases, the rejection level for the null hypothesis was always fixed in a value below or equal to 0.05 (5%). When the calculated statistic presented significance, we used an asterisk (*) to characterize it, otherwise, we used non-significant (NS).

RESULTS

The tests were performed with total cooperation by the patients, who followed the instructions made. All patients used visual erotic stimulation for performing the examinations. No patient was excluded due to side effects or interruption in the follow-up. Patients returned within the established period of 15 days, with few exceptions, which did not compromise the study's final result.

The measurement of peak systolic velocity was performed separately for right and left cavernous arteries. We used the simple mean between them for comparative analysis, after we had compared the 2 sides that were statistically similar (Figure-1).

Mean values increased from 23.9 cm/s to 24.8 cm/s following the use of sildenafil citrate, however it was not statistically significant in our sampling. The statistical analysis of data obtained is expressed in Table-1.

The response to use of sildenafil citrate at home with the partner was positive in 72.4% of patients. When the groups are divided by age range, the response is enhanced for the group < 50 years, presenting 86.67% of yes answers (p = 0.086), Figure-2.

Comparative analyses between the several variables are presented in Tables-2 and 3.

Adverse events reported by patients were mild headache in 4 patients (13.8%), gastrointestinal upset in 2 (6.9%) and facial rush in 6 (20.7%). One patient (3.4%) presented priapism lasting for 6 hours after the second assessment, when alprostadil was used in combination with sildenafil citrate. The outcome was favorable, requiring only puncture and irrigation of the corpora cavernosa with saline solution, with complete detumescence (Figure-3).

DISCUSSION

The introduction of sildenafil citrate as an option for treating the erectile dysfunction changed urologists' daily practice. The diagnostic arsenal used for investigating the patient was gradually replaced, and many times on request of the patient himself, by a simple test of drug use at home with his partner.

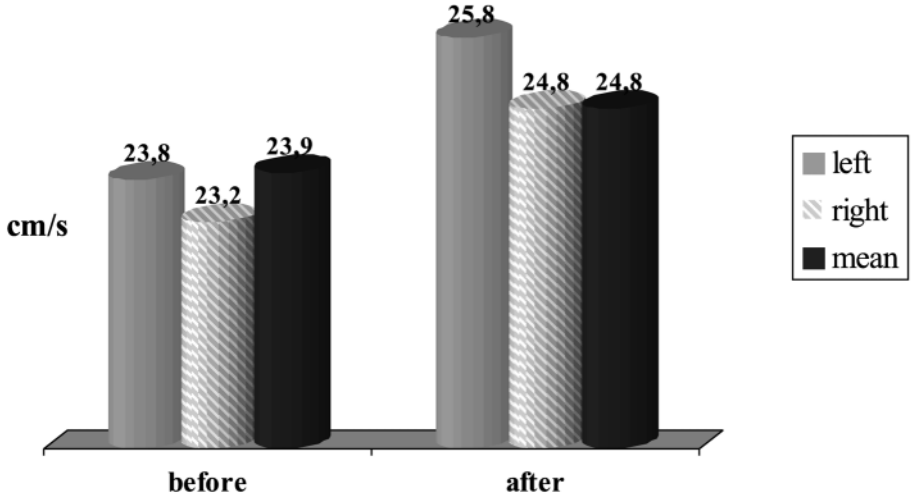

Figure 1 – *Mean values of peak systolic velocity of the cavernous arteries before and after administration of sildenafil citrate.*

Table 1 – *Statistical analysis of differences between the mean peak systolic velocity of cavernous arteries before and after use of sildenafil citrate.*

	N	Mean cm/s	Minimal Value	MaximalValue	Wilcoxon Test
Before	29	23.9	13	39	
After	29	24.8	12	46.5	Z= -0.695 NS

NS – non significant

The mechanism of action of sildenafil citrate was already well established at a cellular level, but there is little information about the effect of the drug on the cavernous arteries' flow during the erection (12-14).

Our sample intended to maximally represent the outpatient profile for erectile dysfunction. Patients' mean age was 53.9 years with a mean time with complaint of 4.2 years. The methodology for obtaining the erection used the routine diagnostic methods for patients with erectile dysfunction. The drug-induced erection test was the choice method for baseline assessment of the cavernous arteries' flow, and at the same time, it selected the patients who could continue in the study.

During the interval period between assessments, patients used sildenafil citrate at home for evaluating their global response to the drug. In this way, we tried to eliminate the stress of an examination room inside a hospital, and also to allow the patient to use the drug in the natural environment where we intended that the medication would act. The assessment of results of the study's domiciliary phase was done with a simple question about improvement and global satisfaction of sexual performance, which in our opinion is the patient's goal. Seventy-two percent of patients reported improvement of erections and stated that they were satisfied with the use of the drug at home. On the second assessment of the cavernous arteries velocitometry, now using sildenafil citrate, we performed once more the drug-induced erection test with 5 mg of alprostadil so that the potential advantage obtained with the sildenafil citrate could be assessed in a reliable way. The use of visual erotic stimulation was warranted by the very mechanism of action of the drug in question. Visual erotic stimulation can reduce the stress factors inherent to the examination and thus to improve the erectile response (16).

Our data were initially analyzed by comparing the peak systolic velocity of the left and right cav-

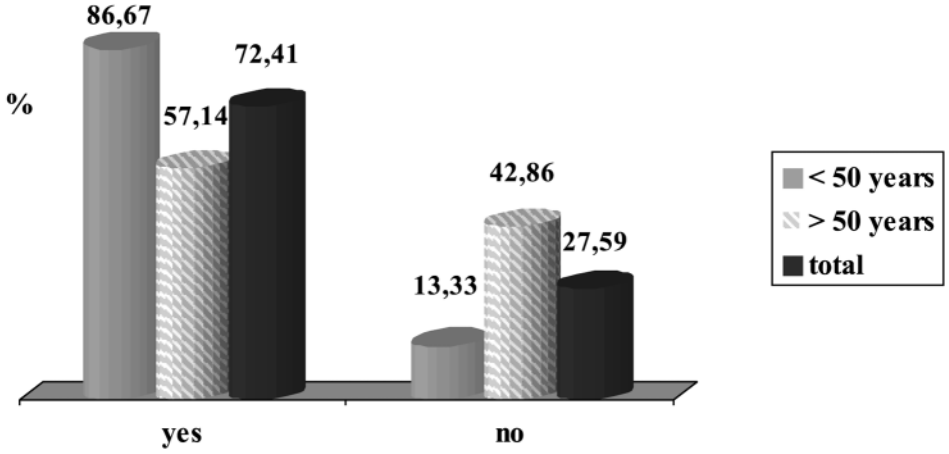

Figure 2 – *Global response to sildenafil citrate according to age.*

Table 2 – *Individuals with peak systolic velocity values = 23 cm/s, according to age and global response.*

Global Response	< 50 Years	> 50 Years	Total
No	0	6	6
Yes	4	7	11
Total	4	13	17

Fisher's exact test, p = 0.1387 or 13.87%, non-significant.

Table 3 – *Individuals with peak systolic velocity values > 23 cm/s, according to age and global response, with statistical results.*

Global Response	< 50 Years	> 50 Years	Total
No	1	1	2
Yes	5	5	10
Total	6	6	12

Fisher's exact test, p = 0.7727 or 77.27%, non-significant.

ernous arteries on the baseline assessment and on the assessment following the use of sildenafil citrate. On the baseline assessment, the mean peak systolic velocity was 23.8 cm/s and 23.2 cm/s for the left and right sides respectively, $Z_{calculated}$ = - 0.313 NS (Wilcoxon test) and on the period following the use of sildenafil citrate, the mean peak systolic velocity was 25.8 cm/s and 24.8 cm/s for the left and right sides respectively, $Z_{calculated}$ = - 0.397 NS (Wilcoxon test).

Since there was no statistically significant difference between right and left sides, we used the average between both sides for assessment of changes obtained with the use of sildenafil citrate. The mean peak systolic velocity on the baseline assessment was 23.9 cm/s and 24.8 cm/s following the use of sildenafil citrate. Despite the increase observed, the difference was not statistically significant, $Z_{calculated}$ = - 0.695 NS (Wilcoxon test), probably due to the small number of patients studied in this sample.

Of the 21 patients who showed improvement of sexual performance, 11 (52.4%) presented a mean peak systolic velocity lower or equal to the median (23 cm/s) and 10 (47.6%) higher than 23 cm/s (p = 0.25 NS, Fisher's exact test), demonstrating that there was no relation between the patient's clinical improvement and the peak systolic velocity.

We analyzed separately those patients with a mean peak systolic velocity following sildenafil citrate above the median (23 cm/s) as for age and global response. The result between the groups was identical. Ten patients responded to sildenafil citrate and 2 did not. Among those who responded, 5 (50%) were from the group of patients with age under 50 years and 5 (50%) above or equal to 50 years, and one from

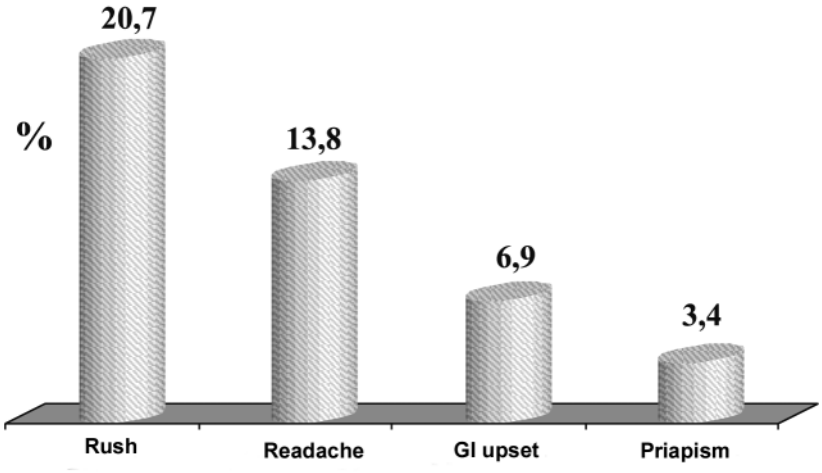

Figure 3 – *Adverse events.*

each group did not respond. There was no difference between age ranges.

In the groups of individuals aged under 50 years, 9 patients responded to sildenafil citrate, with 4 and 5 patients presenting respectively a peak systolic velocity lower or equal and higher than 23 cm/s ($p = 0.6$ NS, Fisher's exact test).

This study analyzed the change in the cavernous arteries flow with the use of sildenafil citrate and its correlation with the patient's clinical response to the medication. We did not try to present an objective confirmation of the drug's pharmacodynamic efficacy, also because the characteristics of the study and the size of the sample did not allow that.

A recent study has assessed the efficacy of sildenafil citrate in 433 men with the diagnosis of erectile dysfunction. Among the several parameters that were studied, the better response to sildenafil citrate in patients with a diagnosis of veno-occlusive dysfunction in relation to the intracavernous injection (17) attracts our attention. The performance of a cavernosometry could give us some additional data in order to fundament the role of the sildenafil citrate in the cavernous veno-occlusive mechanism, and should be used in future studies.

CONCLUSION

The use of 50 mg of sildenafil citrate does not provide an additional increase in relation to that obtained with the use of 5 mcg of alprostadil, of the peak systolic velocity of the cavernous arteries in patients with erectile dysfunction, as measured by ultrasonic velocitometry. There is no correlation between the patient's clinical response to 50 mg of sildenafil citrate and the changes in the peak systolic velocity of the cavernous arteries in patients with erectile dysfunction.

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CHRONIC PENILE STRANGULATION

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ABSTRACT

Chronic penile strangulation is exceedingly rare with only 5 cases previously reported. We report an additional case of progressive penile lymphedema due to chronic intermittent strangulation caused by a rubber band applied to the penile base for 6 years.

A 49-year-old man presented incapacity to exteriorize the glans penis. For erotic purposes, he had been using a rubber-enlarging band placed in the penile base for 6 years. With chronic use, he noticed that his penis swelled. Physical examination revealed lymphedema of the penis, phimosis and a stricture in the penile base. The patient was submitted to circumcision and the lymphedema remained stable 10 months postoperatively.

Chronic penile incarceration usually causes penile lymphedema and urinary disturbance. Treatment consists of removal of foreign devices and surgical treatment of lymphedema.

Key words: penis; lymphedema; compression; device
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INTRODUCTION

While penile incarceration with foreign bodies is generally acute and common enough to be seen by most urologists throughout their careers, chronic penile strangulation by the same mechanism is exceedingly rare and to our knowledge only 5 cases have been reported in the literature (1-3). We report a case of progressive penile lymphedema due to chronic intermittent strangulation caused by a rubber band.

CASE REPORT

A 49-year-old single white man was admitted to the hospital because of his incapacity to exteriorize the glans penis. Approximately 6 years prior to admission, he began to use a rubber-enlarging band, acquired in a sex shop, in order to enhance sexual experience and to prolong erection. The rubber-band with 2-cm in diameter was placed in the penile root for approximately 3 hours, 3 to 4 times a week, during the night. With chronic use, he noticed that his penis swelled and that he was unable to ejaculate, but he could maintain prolonged erections, usually over 4 hours without any episode of priapism. He was extremely satisfied with his sexual performance and genital appearance. Two years after the beginning of the rubber band usage, he observed progressive penile swelling and an incapability of exteriorizing his glans penis one year later. However, he only decided to seek medical assistance after 3 years. He denied previous episodes of urinary infection and voiding dysfunction.

Physical examination revealed lymphedema of the penis without scrotal involvement (Figure-1). The penis was covered with dark brown hypertrophic skin and it had a 6.7 cm in diameter. A stricture could be observed in the penile base corresponding to the place on which the band was applied. Phimosis was

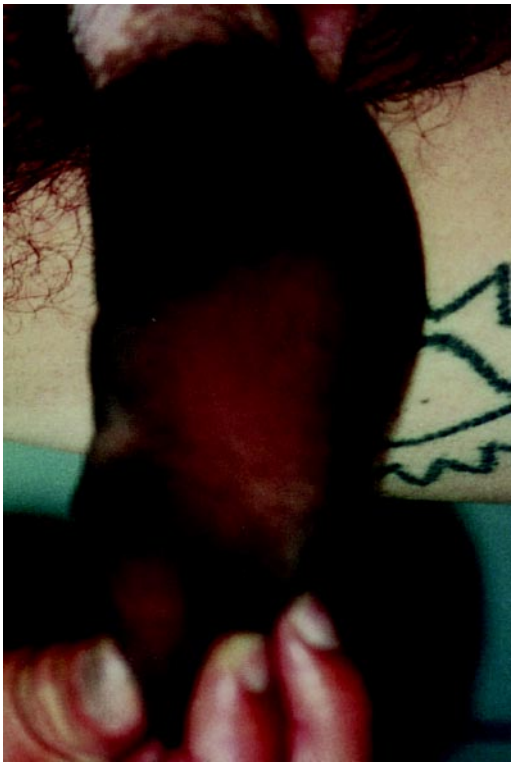

Figure 1 *- Penile lymphedema caused by chronic strangulation.*

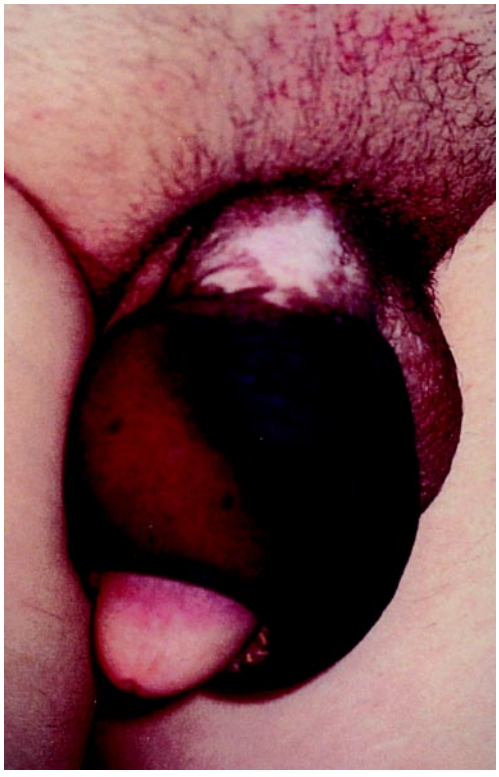

Figure 2 *- Cosmetic result after circumcision.*

present. No skin ulceration, urethral injury, loss of sensation or other alterations were noticed. Urinalysis and urine culture were not suggestive of urinary tract infection.

The patient was advised to stop immediately the rubber-band usage and a month later, we performed a circumcision. Cosmetic result was acceptable (Figure-2) and the patient stated he was well satisfied with function and appearance. Lymphedema remained stable 10 months postoperatively.

COMMENT

Chronic penile strangulation by foreign bodies may be the result of the impossibility to remove the object applied to the penis (1,2) or caused by inappropriate usage of devices developed for autoerotic purposes and to prolong erection (3) that may be regularly acquired at specialized shops.

Chronic penile incarceration usually led to penile lymphedema and may also cause voiding dysfunction (1), urinary infections (1,2), skin ulcerations (1), necrosis (1), urethral cutaneous fistula (2) and colonization of hypertrophic skin (3). Treatment consists of removal of foreign devices and/or medical orientations on the correct usage of erection devices. Surgical treatment of lymphedema may involve lymphangiectomy with covering of denuded areas with skin flaps or full and split skin grafts (3), and in some cases, penectomy and circumcision may be indicated (1,2).

In the present case, we did not indicate removal of all lymphedematous tissue because the patient was satisfied with his penile appearance and sexual performance since the onset of penile lymphedema.

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Case Report
International Braz J Urol Vol. 29 (4): 330-331, July - August, 2003
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BILATERAL AND SYNCHRONIC SEMINOMATOUS TESTICULAR NEOPLASIA

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ABSTRACT

Testicular neoplasia is rare, especially when it is bilateral, and even more when it is synchronic, with its incidence being only 0.17% of germinative tumors of testicles.

We present here the case of a male, 32-year old patient, without children. Patient underwent a bilateral radical orchiectomy, following previous sperm harvest, in a sperm bank. Surgery was performed in 2 stages, with a 12-day interval, with implantation of a silicone testicular prosthesis. The result of anatomicopathological examination revealed bilateral classical seminoma, pT2 on the right side andT1 on the left. He was submitted to bilateral complementary radiotherapy, with 2,500 cGy on each side.

Patient had a good outcome from a medical and oncologic perspective, but a follow-up with psychotherapy was needed.

Key words: testis; testicular neoplasms; seminoma; synchronous neoplasms
Int Braz J Urol. 2003; 29: 330-1

INTRODUCTION

The incidence of germinative testicular tumors in the general population is 0.005%, and accounts for 1% of all tumors that affect men. The risk of a patient having a successive (metachronic) bilateral tumor ranges between 1 and 5% (1). As for synchronic tumors, they are even more rare. Recently a report was described on 2,431 germinative testicular tumors diagnosed and treated from 1978 to 1999, and only 24 of these cases were bilateral, and among them 20 were metachronic, that is, 1% of all tumors. Synchronic tumors were described in only 4 cases (0.17%) (2). The histological type is usually the same in both testicles, however in metachronic ones, histological types can be different.

Synchronous testicular tumors require a bilateral surgical therapy, leading to the patient's sterility.

CASE REPORT

Male, 32-year old patient, married with no children. He had 5-month history of bilateral, hardened, slightly painful, testicular mass, involving practically the entire glands. Ultra-sonography revealed a right testicle measuring 7.8 x 8.4 x 4.2 cm and left testicle measuring 5.4 x 4.0 x 2.7 cm. The main hypothesis was bilateral neoplasia, without excluding a granulomatous process. Tumoral markers were normal. Thorax radiography and abdominal computerized tomography did not reveal metastases. The magnetic resonance imaging of scrotum suggested bilateral testicular neoplasia.

Surgery was indicated following adequate sperm harvests, in sperm banks, for subsequent use. Surgery was scheduled in 2 stages, for reasons of patient safety. The right radical orchiectomy, with previous approach of the spermatic cord, was followed by a silicone testicular implant. The anatomicopathological result was classical seminoma (Boden I-B stage or pT2N0M0), with focal invasion of the tunica albuginea, transposing it and the "rete testis" (Figure-1). The same procedure was performed on the left side, 12 days later, already with a definitive diagnosis. There was only a lymph node measuring 0.5 cm in the spermatic

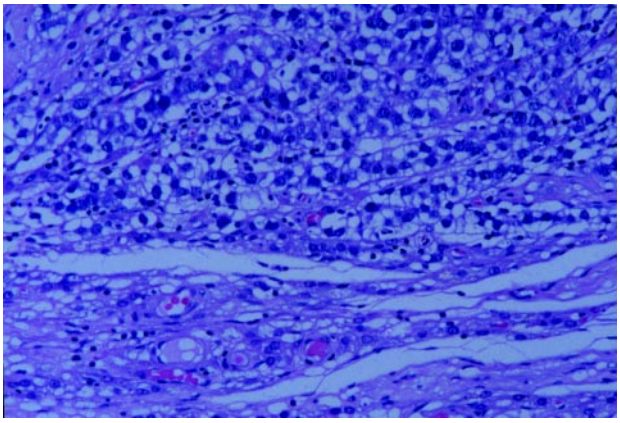

Figure 1 – *Photomicrography of right testicle tumor, showing classical seminoma with invasion of the "rete testis" (HE, X200).*

cord (Figure-2). The anatomicopathological diagnosis was seminoma as well (I-A stage or pT1N0M0), with focal invasion of the tunica albuginea, without transposing the capsule. The lymph node was negative for neoplasia.

As a complementary treatment, the patient was submitted to a conformational radiotherapy, with 2.500 cGy at each side (bilateral iliac and para-aortic chains), 60 days after surgery. He presented a good outcome, and is receiving hormone replacement.

DISCUSSION

Bilateral germinative testicular tumors are rare and, when diagnosed synchronically, they are even rarer. Seminoma is the most common histological type. Current indication for treating such tumors begins with the clinical staging, with orchiectomy being the first step (3). It is hard to evaluate whether a conservative surgery, in bilateral cases, followed by chemotherapy and/or radiotherapy, could provide good results without bilateral testicular ablation, due mainly to the reduced number of cases of studied synchronic tumors. In this particular case, such procedure could not have been possible, since both testicles were involved by the neoplasia, in more than 90% of the normal tissue, with only a small band of tubules with normal aspect (Figure-2). In this case there was a great resistance from patient and his wife, in accepting the bilateral surgical treatment, with a freeze biopsy only, choosing thus to perform a surgery in 2 times, even though we had the clinical diagnosis of neoplasia pre-operatively. Complementary treatment was radiotherapy, due to staging and bilaterality.

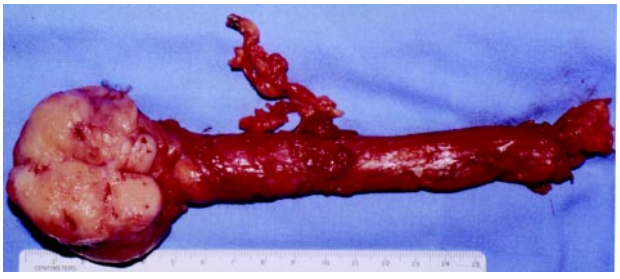

Figure 2 – *Surgical specimen of left side. Note the minimal thickness of normal tissue in the testicle periphery.*

Figure-1 was supplied by Drs. Maria CN Zerbini and Claudia RGCM Oliveira, from Fleury Laboatory, SP

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Surgical Technique

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SLIGHTLY MODIFIED TECHNIQUE OF THE ORIGINAL ESSED PLICATION PROCEDURE FOR CONGENITAL PENILE DEVIATION

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ABSTRACT

Purpose: The Schroeder-Essed plication procedure is a standard technique for the correction of penile curvature. In a retrospective analysis we compared functional results and quality of life (LQ) of the original technique with inverted sutures as described by Schroeder-Essed and our slight modification consisting of horizontal incisions into the tunica albuginea.

Materials and Methods: Twenty-six patients with congenital penis deviation were treated for penile deviation by the original Schroeder-Essed plication with inverted sutures (11 patients) and by the described modification (15 patients). In case of modified technique, horizontal and parallel incisions 4 mm to 6 mm apart and about 8 mm – 10 mm long were made through the tunica albuginea. The outer edges of the incisions were then approximated with permanent inverted sutures (Gore-Tex® 3-0). Mean age was 21.6 years in the first group and 23.2 years in the second group. Average follow-up was 28 months and 13 months, respectively. The preoperative penile deviation angle was > 25° in all patients without difference between the 2 groups.

Results: All patients in both groups reported an improvement in their quality of life and full ability to engage in sexual intercourse. Nine patients (88%) in the first group and 14 patients (93%) in the second group were satisfied with the cosmetic result. In contrast, 10 patients (91%) of the first and 13 patients (87%) of the second group complained of penile shorting. Recurrence of deviation was only noticed in 2 males in the first group (18%).

Conclusions: Our results indicate that this simple modification of the Schroeder-Essed plication offers good functional and cosmetic results. Most patients were satisfied with the penile angle correction results.

Key words: penis; congenital defect; curvature; tunica; reconstructive surgical procedures
Int Braz J Urol. 2003; 29: 332-5

INTRODUCTION

Independent of its etiology, penile deviation may disturb sexual intercourse by difficult vaginal intromission. A simple standard method of congenital curvature repair is the Schroeder-Essed plication procedure (1). We describe and examine a slight modification of this technique consisting of horizontal incisions into the tunica albuginea avoiding cavernous tissue damage and improving adhesion of plicated tunical layers as similar performed by Baskin & Duckett (2). The 2 techniques were analyzed retrospectively by comparing the functional results and life quality (LQ) using standardized questionnaires on their quality of life.

MATERIALS AND METHODS

Between June 1996 and July 2000, 26 patients with congenital penile deviation underwent the origi-

nal Schroeder-Essed plication with inverted sutures (11 patients) and the described modification (15 patients). Mean age was 21.6 yrs in the first group and 23.2 yrs in the second group. Average follow-up was 28 months and 13 months, respectively. The preoperative penile deviation angle was > 25° in all patients without differentiation between the 2 groups, documented by means of auto-photography. Detailed information about possible post-operative discomforts or pain from suture knots, initial irregularities of the penile shaft and shortening of the penis was given to the patients preoperatively. A standardized questionnaire was sent to all patients. Retrospectively we examined quality of life, sexual intercourse, penile deviation, penile shortening, penile sensation, quality of erection, cosmetic result and recurrence.

SURGICAL TECHNIQUE

Surgery was performed under general anesthesia. A tourniquet was set at the base of the penis. An artificial erection was induced by injection of sterile saline solution into the corpora cavernosa through a 19G butterfly needle to determine the degree of deviation. The outer preputial layer is circumferentially incised at the level of the coronal sulcus to facilitate the drop back of the penile shaft skin. The plain of dissection is kept just outside of Buck's fascia in order to preserve the vascular pedicle to the dorsal hooded foreskin. Buck's fascia is elevated on the convex side by avoiding the neurovascular bundle of damage. To straighten the penis, the effect of the tunical plication was simulated by using Allis clamps under careful protection of the dorsal neurovascular bundle and its branches. In case of the original Schroeder-Essed technique plication is made by inverted sutures (1) (Gore-Tex® 3-0). In case of modified technique, 2 parallel horizontal incisions 4 – 6 mm apart and about 8 - 10 mm long are made through the tunica albuginea. The outer edges of the incisions are approximated with permanent inverted sutures (Gore-Tex® 3-0) (Figure-1). A straight penis is confirmed by repeated intra-operative artificial erection. The overlying penile fascia was closed in layers, and a circular dressing with light pressure was applied for a maximum of 2 days.

RESULTS

All patients in both groups undergoing plication for congenital deviation of the penis reported an improvement in their quality of life and full ability to engage in sexual intercourse. The penile deviation was abolished completely in all patients (< 15°). Nine patients (88%) in the first group and 14 patients (93%) of the second group were satisfied with the cosmetic result. No patients reported any changes in penile sensation or in the quality of erections. In contrast, 10 patients (91%) of the first and 13 patients (87%) of the second group complained of penile shorting. Recurrence of deviation was only observed in 2 males in the first group (18%) (Table-1).

Table 1 - *Comparison of Schroeder-Essed procedure and the modified technique.*

Original	CPD		Modification	CPD
100%	11	Improvement of LQ	100%	15
88%	9	Cosmetic result	93%	14
100%	11	Possible cohabitation	100%	15
91%	10	Penile shorting	87%	13
18%	2	Deviation recurrences	0%	0

CPD = congenital penile deviation; LQ = quality of life.

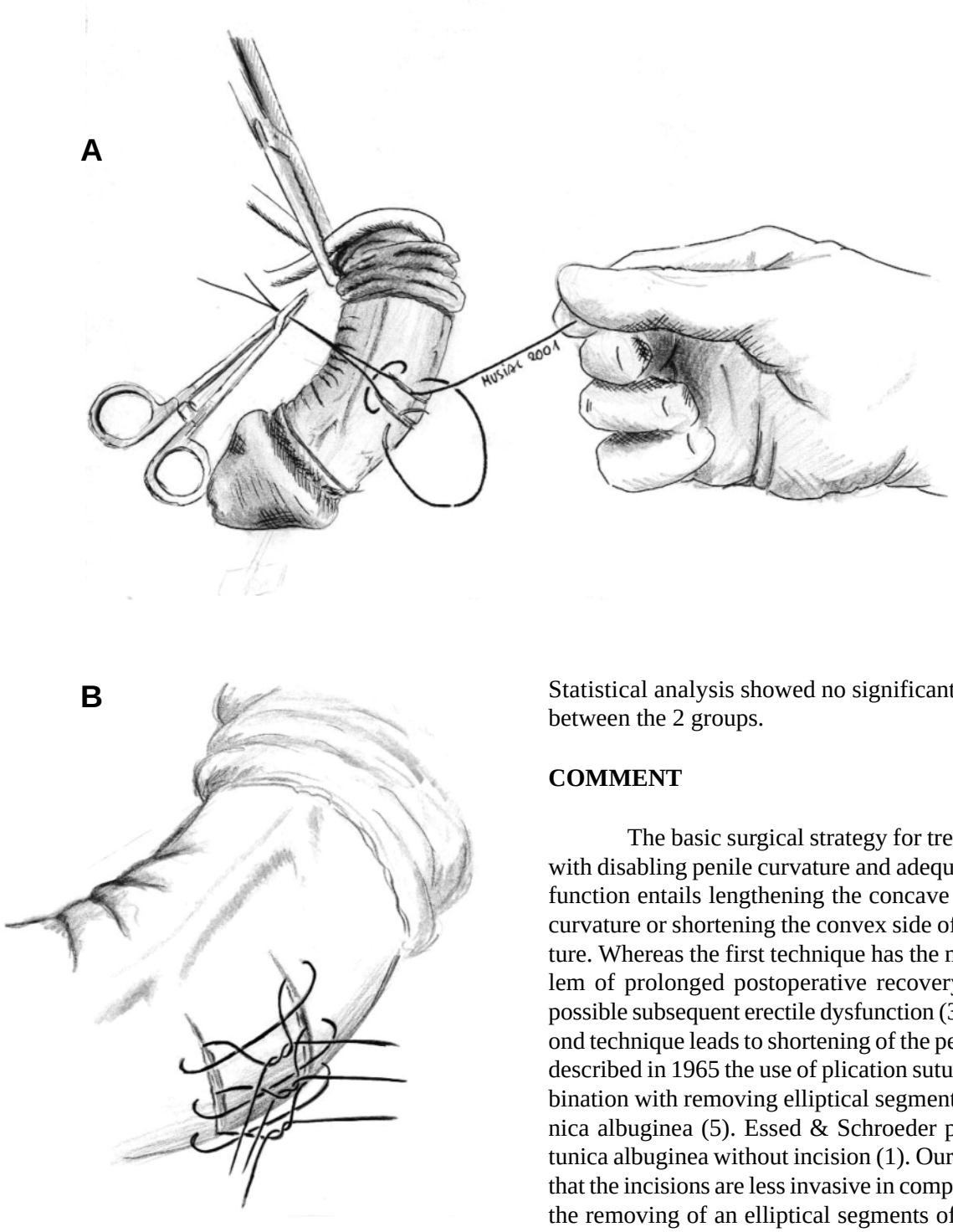

***Figure - 1**, A and B - Slightly modified technique of the original Essed plication procedure with 2 parallel horizontal incisions into the tunica albuginea.*

Statistical analysis showed no significant difference between the 2 groups.

COMMENT

The basic surgical strategy for treating mean with disabling penile curvature and adequate erectile function entails lengthening the concave side of the curvature or shortening the convex side of the curvature. Whereas the first technique has the major problem of prolonged postoperative recovery time and possible subsequent erectile dysfunction (3,4) the second technique leads to shortening of the penis. Nesbit described in 1965 the use of plication sutures in combination with removing elliptical segments of the tunica albuginea (5). Essed & Schroeder plicated the tunica albuginea without incision (1). Our data show, that the incisions are less invasive in comparison with the removing of an elliptical segments of the tunica albuginea but may strengthen the plication by proper healing. We did not see any deviation recurrence or any changing in penile sensation.

CONCLUSIONS

Our results indicate that this simple modification of the Schroeder-Essed plication can provide good functional and cosmetic results for patients with congenital penile deviation. The technique is simple, bloodless, safe and reliable. Most patients were satisfied with the penile angle correction results.

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EDITORIAL COMMENT

This retrospective study compares 2 cohorts of men with congenital penile deviation (chordee without hypospadias). The first group (n = 11) had the original Schroeder-Essed plication using a technique described by Duckett for hypospadia repair. Average follow-up was 28 months for group 1 and 13 months for group 2.

The original Schroeder-Essed plication places non-absorbable sutures into the tunica albuginea in such a manner as to shorten the long axis of the penis when these sutures are tied. The problem with this type of plication is that there is no permanent remodeling of the tunica albuginea, and the curvature will recur if and when these sutures ever break. The modification involves making incisions in the tunica albuginea and securing then with sutures. Once healing takes place, even if the sutures break or are absorbed, the curvatures should not recur. The authors found no outcome differences in outcome between the 2 groups. The problem is that follow-up in each of the 2 groups is too short for the presumed benefit of the modification become evident.

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Surgical Technique

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RADICAL CYSTECTOMY WITH PRESERVATION OF SEXUAL FUNCTION AND URINARY CONTINENCE: DESCRIPTION OF A NEW TECHNIQUE

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ABSTRACT

Objective: To describe the original cystoprostatectomy technique which allows the preservation of sexual and urinary function in the majority of treated patients.

Surgical Technique: The described technique presents some details that distinguish it from classic cystectomy: 1) a more efficient control of prostate venous and arterial tributaries; 2) preservation of prostatic capsule and enucleation of prostatic parenchyma, which is removed in block together with the bladder, without violating the vesical neck; 3) no manipulation of the distal urethral sphincteric complex; 4) preservation of seminal vesicles and maintenance of cavernous neurovascular bundles; 5) wide anastomosis between the ileal neobladder and the prostatic capsule.

Comments: The proposed maneuvers allow the performance of radical cystectomy with integral preservation of distal urethral sphincter and of cavernous neurovascular bundles, without jeopardizing the oncological principles.

Key words: bladder; bladder neoplasms; cystectomy; urinary diversion; urinary reservoirs, continence

Int Braz J Urol. 2003; 29: 336-44

INTRODUCTION

Patients who have an invasive bladder cancer, stages T_2-T_4, are currently treated with radical surgery, radiotherapy, chemotherapy or with a combination of these approaches (1). According to available data, radical cystectomy with urinary reconstruction represents the most effective way for treating such cases, accompanied by cure rates that oscillate between 53% to 80%, when there is no regional or systemic extension of the disease (1).

Despite its therapeutic advantages, radical cystectomy represents a major intervention, accompanied by morbidity rates that should not be disregarded. In addition to the inherent post-operative complications, radical cystectomy presented, in the past, 2 serious drawbacks. Until the final 80s, most of these patients underwent an incontinent cutaneous urinary diversion, which constrained them to bear urine-collecting bags, with all the resultant psychological and social drawbacks. Furthermore, almost all male patients developed erectile dysfunction, which compromised their quality of life.

Upon the introduction of orthotopic intestinal neobladders in the urologic practice (2) and the description of the technique that allowed the preservation of cavernous neurovascular bundles (3), the drawbacks of cutaneous ostomies and sexual dysfunction were both mitigated, but they could not be totally avoided. About 10% of patients treated in this way maintain severe diurnal incontinence and almost half of cases remain with nocturnal enuresis for ex-

tended periods (4). On the other hand, even when employing the technique for preserving the cavernous bundles, only 50% of the treated patients evidence penile erections post-operatively (5).

With the purpose of solving these problems, Spitz et al. described in 1999 an alternative technique of radical cystectomy that preserved sexual, ejaculatory, and urinary functions in treated patients (6). Other studies were subsequently published with the same scope (7,8,9) and all of them contemplated, in a common way, maneuvers intended to maintain the integrity of the distal urethral sphincteric complex, responsible for urinary continence, and the cavernous neurovascular bundles, implied in the sexual function. Despite the significant reduction in risks of urinary incontinence and erectile dysfunction, these techniques presented 2 shortcomings witnessed by us in a small number of treated cases. The block transection of the prostate gland along with the vesical neck is accompanied by a more marked bleeding that the one observed when employing classical techniques of radical cystectomy. For the same reason, preservation of the prostatic parenchyma, common to all such new proposed techniques creates the risk of incomplete removal of vesical neoplasia, when it infiltrates and outgrows the vesical neck. For these reasons, we proposed a new technique of radical cystectomy that aims to preserve the integrity of sexual and urinary functions and that allows a greater control of intraoperative bleeding and a more effective resection of tumors located close to the vesical neck.

SURGICAL TECHNIQUE

With the patient under general anesthesia, through a wide median abdominal incision, the bladder is separated from the abdomen anterior wall, maintaining, together with the organ, the parietal peritoneum that covers it superiorly. A bilateral pelvic lymphadenectomy is performed, removing the lymph nodes located around the common, external and internal iliac vessels, and close to the obturator vessels. Distal ureters in both sides are dissected and sectioned close to the bladder.

Subsequently, the bladder is laterally released from the pelvic wall and the vesicoprostatic segment is anteriorly dissected up to the prostatic apex. The preprostatic fat is removed, carefully controlling the superficial branch of the deep dorsal vein of penis at the level of the prostatic apex. The intervention proceeds with transection of lateral peritoneal wings, which fix the vesical dome to the pelvic wall. Inside these sheets, we found the vas deferens, and in a more posterior location, the superior vesical arteries, all of which are sectioned and ligated.

Upon releasing the bladder from the structures that involve it anteriorly, superiorly and laterally, the hemostatic control of arterial and venous vessels that involve the prostate begins. Prostatic arteries, located in the vesico-prostatic sulcus on each side, are ligated with 2 large and deep “figure-of-8” stitches, with vicryl zero, applied next to the origin of such vessels in the inferior vesical arteries (Figure-1). Next, the 3 venous trunks, one medial and two lateral, which run over the anterior prostate surface, from the deep dorsal vein of penis, are controlled. To accomplish this, 2 parallel and transversal rows of 3 zero vicryl stitches are applied; with the first row located more distally, at about 1.5 cm from the vesical neck, and other row more proximally, at 0.5 cm from the neck (Figure-2). These stitches penetrate deeply the prostate capsule and, once they are tied, they control the prostate ascending venous tributaries and the bladder descending branches. They also enable the control of arterial vessels that run in the prostatic capsule. Before incising the prostatic capsule, a third row of 3 zero vicryl stitches is done distally to the previous rows, and are not tied (Figure-2). The anterior portion of the prostatic capsule is incised transversally with an electrocautery, between the first 2 rows of stitches previously tied, until the prostatic parenchyma is reached. Through digital and scissors-aided dissection, the parenchyma is separated from the prostatic capsule, in a maneuver similar to the one performed when an adenoma is enucleated. The urethra is sectioned distally, but the base of the prostate is kept adhered to the vesical neck, forming a single block with the bladder, whose lumen is not violated (Figure-3). Upon the completion of the distal enucleation of the prostate, the more distal capsular stitches are tied and kept repaired. This maneuver allows the definitive control of tributaries of the deep dorsal vein

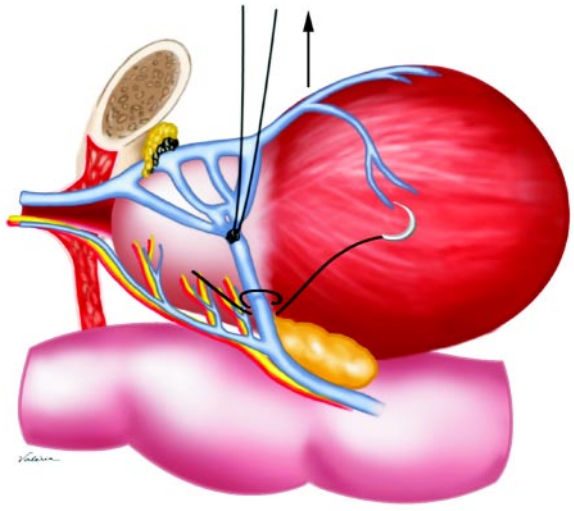

Figure 1 *- Double ligation of prostatic artery.*

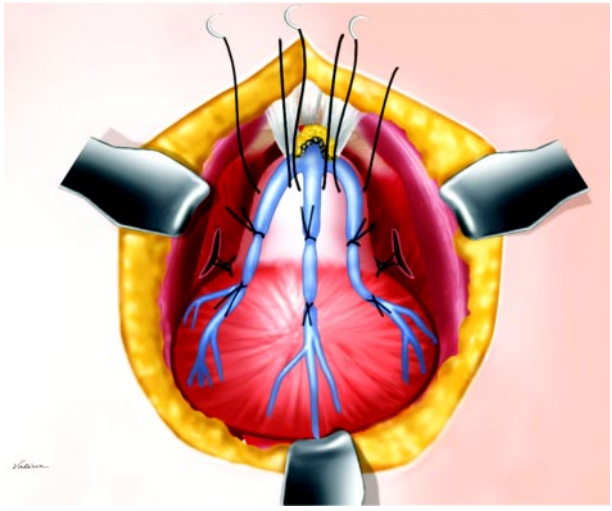

Figure 2 *- Control of ascending and descending venous tributaries.*

of the penis, which often start to bleed in the capsulotomy's distal margin following the prostatic enucleation. Such intercurrence results from the loosening of the previously tied capsular stitches, due to the enucleation of the adenoma.

At this moment, the anterior manipulation of prostate and bladder is interrupted and the posterior dissection of the block is proceeded. In order to create a correct plane between the bladder and the seminal vesicles, which will be preserved, we repaired the vas deferens in both sides at the posterosuperior surface of the bladder. Through digital and scissors-aided dissection, the surgeon advances in caudal direction between the bladder and the vas deferens, and then anteriorly to the seminal vesicles, until the prostatic base is reached (Figure-4). Resuming the anterior dissection of the specimen and maintaining a small sponge between the bladder and the seminal vesicles, the capsulotomy is completed in its posterior half, with a special precaution to avoid damage to the cav-

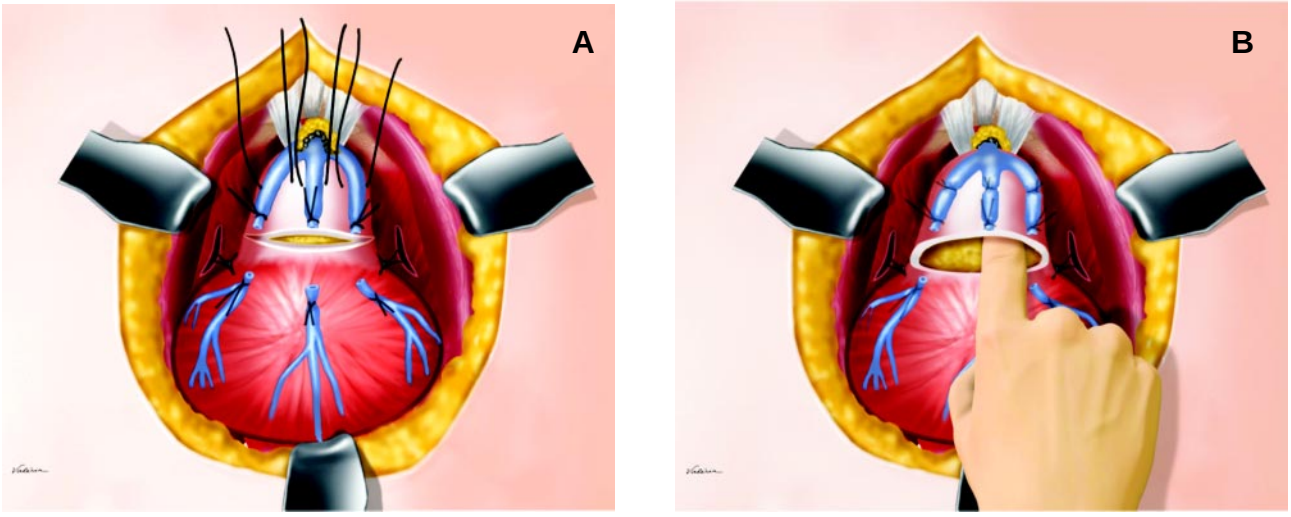

Figure 3 *- A) Anterior capsulotomy. B) Enucleation of the adenoma.*

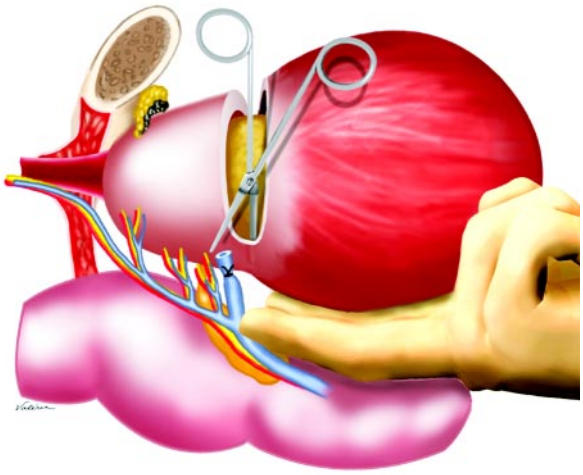

***Figure 4** - Detachment of posterior surface of the prostate.*

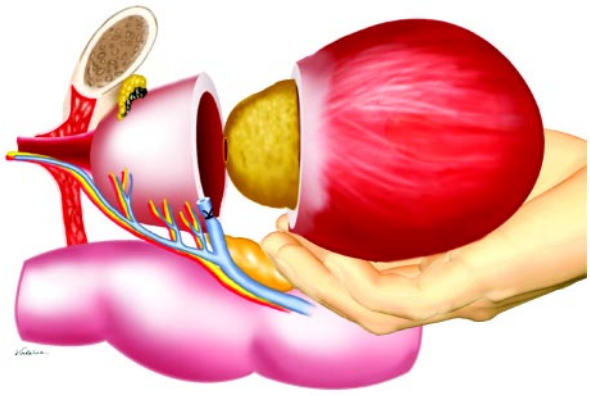

***Figure 5** - Release of bladder-adenoma block, following posterior capsulotomy.*

ernous neurovascular bundles (Figure-5). These maneuvers culminate with the complete release of the bladder-prostatic adenoma block, which will be removed, and the distal prostatic capsule, preserved. Samples of tissue from the distal margin of the capsule are removed and submitted to freezing pathologic study in order to confirm the absence of residual neoplasia.

Cystectomy is completed sectioning the 2 lateral vesical pedicles, performed with the aid of Mixter forceps or hemoclamps applied in craniocaudal direction. The specimen formed by the bladder connected to prostatic adenoma is removed, the prostatic cavity and the capsular margins are revised and small bleeding vessels are controlled with electrocautery or with "figure-of-8" 3-zero vicryl stitches.

The intervention proceeds with the construction of an orthotopic ileal neobladder, for which we use Camey II or Studer techniques (2,10). Once the neobladder is done and double-J catheters are inserted in both ureters, the anastomosis between the neobladder and the remaining distal prostatic capsule is performed (Figure-6). This anastomosis is made with a continuous 2-zero vicryl suture, and before its completion a 20F Foley urethral catheter is placed in the neobladder, and the distal ends of both double-J catheters are tied to it.

Surgery is finished with the installation of continuous suction drains at the level of the anastomosis between the neobladder and the prostate and near the sites of ureteral implantation. These drains are maintained until the 7th post-operative day and the Foley catheter, tied to the double-J catheters, are removed on the 20th day after the intervention.

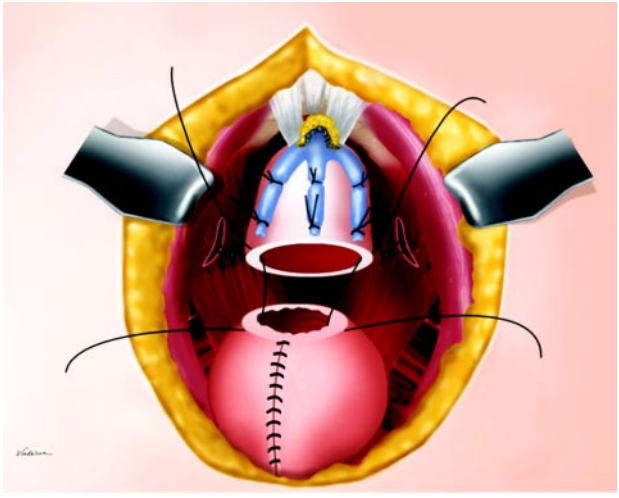

***Figure 6** - Anastomosis between the neobladder and the prostatic capsule.*

COMMENTS

In this work we present an original alternative technique for radical cystectomy, which allows integral preservation of urinary continence and reduces substantially the risks of sexual impotence. In an initial group of 6 treated patients, 5 presented complete diurnal and nocturnal continence immediately after removing the urethral catheter, 3 referred penile erections on the first month and none evidenced positive surgical margins at the level of vesical neck or prostatic parenchyma.

In contrast to the classical radical cystoprostatectomy technique, this method preserves the prostatic capsule, the cavernous neurovascular bundles and is not accompanied by manipulation of the distal urethral sphincteric complex. For such reasons, this technique, which could be referred to as cysto-adenomectomy, has a highly favorable impact over the maintenance of urinary and sexual functions post-operatively. Another advantage of this technique is the fact that it is accompanied by a block removal of bladder and prostatic parenchyma, reducing the risks of incomplete removal of the vesical neoplasia, when it invades the vesical neck and the prostate by intraluminal direct extension.

Under a surgical perspective, this method incorporates maneuvers that allow a quite efficient control of the anterior periprostatic venous trunks and the lateral prostatic arteries (11), significantly reducing intra-operative bleeding. As a matter of fact, none of the 6 patients treated up to now, required blood transfusions during or after surgery.

The only drawback of the cysto-adenomectomy technique, compared with the classic radical cystectomy, is that it does not remove a prostate cancer when this tumor is coincidentally present in addition to the vesical neoplasia (12). To minimize this problem, the cysto-adenomectomy technique must be indicated when the existence of a prostate cancer is highly unlikely, that is, in patients with medical examination and normal serum levels of prostatic specific antigen or, in case of doubt, with negative pre-operative prostatic biopsy.

The first proposal about preservation of sexual and ejaculatory function in radical cystectomy was made in 1999 (6). These authors described a technique that removed the anterior half of the prostate and preserved its posterior portion. After that, 3 more studies were published with the same objective, all of them proposing the preservation of the prostate and bladder resection with distal transection of the specimen at the level of the vesical neck (7,8,9). Despite highly elevated rates of maintenance of sexual and urinary function observed with these techniques, they presented, as a common feature, the risk of violating the bladder tumor and producing positive distal margins, when the neoplasia reaches the vesical neck. This risk was reduced by Colombo et al. (9) and by Vallancien et al. (8) who performed the endoscopic resection of the vesical neck and the prostate previously, but even then, the potential risk of violating the neoplasia persists when the vesical neck is sectioned transversely. In our technique, this possibility is minimized due to the block removal of prostatic parenchyma, vesical neck and bladder.

Another advantage of this cysto-adenomectomy technique in relation to other published approaches is that it implies in removing the specimen in one stage. Both previous endoscopic resection (9) and that performed at the moment of cystectomy (8) increase the length and morbidity of the intervention.

If the ongoing study by our group confirms better preservation of urinary continence and a lower incidence of post-operative sexual dysfunction, this technique may become a preferential method for performing radical cystectomy in men with invasive bladder cancer. In such cases, the method could be employed every time that the presence of a primary prostate cancer is previously ruled out, and when there is no extensive secondary involvement of the prostate gland from the vesical neoplasia.

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EDITORIAL COMMENT

Srougi et al. adapted a few technical maneuvers acquired from years of performing radical and simple prostatectomies and applied them to a cystoprostatectomy with orthotopic neobladder. The objective is to preserve sexual function and improve urinary continence. In my experience patients have excellent daytime continence (< 5% wear pads) although 15% empty by intermittent catheterization. Nighttime incontinence is infrequent since most of my patients wake up at least once per night. I have elected to taper the ileum at the site of the urethral anastomosis which may add to the functional urethral length. I am not certain how important this is.

The issue of preserving erectile function is an important one for a relatively small subset of men who have a cystoprostatectomy and neobladder. The percentage of men who are candidates for this prostate capsule sparing is relatively low among all of the men I evaluate for surgery. The majority of men is older or has advanced local disease and thus they are impotent or the extent of disease makes invasion of the prostate a concern. I believe the patient must be

one who understands the need for subsequent careful monitoring - not only for urothelial cancer but for adenocarcinoma of the prostate.

The men who are most likely to benefit from these modifications of the standard cystoprostatectomy are younger men who have recurrent or persistent high grade Ta, CIS, or T1 bladder cancer and have failed intravesical therapy. Once tumor at the bladder neck (?) and prostatic urethra is excluded they might be reasonable candidates for this approach.

There are some trade-offs when comparing the standard procedure in which the entire prostate and seminal vesicles are removed with Srougi's modification which leaves the prostate capsule and seminal vesicles. This is not much different however, from leaving the neurovascular bundles, bladder neck, and the distal seminal vesicles during a radical prostatectomy with the desire to improve the chance of retaining normal pre-op erectile function. Each case must be carefully judged based on pre and intraoperative findings as well as a variety of patient issues such as age and erectile function before surgery.

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EDITORIAL COMMENT

En bloc removal of the bladder, prostate, ampullae of the vasa deferentia and seminal vesicles is now the paradigm treatment for muscle invasive and recurrent high grade urothelial carcinomas. However, largely due to significant associated morbidities and only modest cure rates when applied as a monotherapy, initial acceptance of this procedure was not broad. Over the past 30-years both medical and urologic oncologists have made dramatic strides to improve the adverse consequences of effectively treating urothelial cancer. Medical oncologists have graduated patients from non-effective, single-agent chemotherapy to the latest less-toxic but efficacious combination of paclitaxel, carboplatin and gemcitabine. With improved survival, urologic oncologists have modified their surgical execution to reduce morbidity and improve the social, sexual and psychological implications of radical cystectomy. Lower urinary tract reconstruction has evolved from simple cutaneous ureterostomies and ileal conduits to continent cutaneous urinary reservoirs, and most recently the continent orthotopic neobladders. Today men and women can safely undergo orthotopic lower urinary tract reconstruction to the intact native urethra while preserving the erectile nerve bundles and importantly, the pelvic plexus supplying these nerve bundles. This has given witness to a dramatic improvements in both the longevity and quality of our patients' lives.

For continuing these forward strides in surgical techniques with their described method, a modification of that previously described by the USC group (authors' reference 6), the authors are to be commended. And we are sure that many innovative surgeons will continue to refine this technique to provide even better outcomes for the patient of tomorrow.

But in this search for minimal morbidity, let's not forget in whom and for what reason the vast majority of radical cystectomies are performed. Today the average male patient requiring cystectomy for bladder cancer is in his sixth decade of life when the reproductive necessity of preserving ejaculatory function has generally long since past. In the end, this

is the one morbidity of standard nerve sparing radical cystoprostatectomy that we see as preserved through this technique, and this is accomplished with a questionable overall improvement in life's quality for the vast majority of men with urothelial carcinoma. We are further puzzled as to the mechanism of antegrade ejaculation following the removal of a functional bladder neck and the necessity for its coordinated closure to provide antegrade emission of deposited seminal fluids.

With a very conscious recognition of the anatomic location of the pelvic plexus lateral to the seminal vesicles and its nervous supply to the erectile nerve bundle as depicted in authors' Figure-1, maintaining the erectile nerve bundles should be no more difficult during radical cystoprostatectomy than radical prostatectomy. We commonly perform retrograde release of the nerve bundles from apex to base during radical cystoprostatectomy as we perform it during radical prostatectomy. Similar to the reports of others, this approach has allowed us to preserve erectile function at rates similar to that seen following isolated radical prostatectomy (1). While this approach obviates ejaculatory function, is this truly an issue for the majority of patients undergoing radical cystoprostatectomy?

We then re-focus on the patients in whom the majority of these surgeries are performed; sixty-year-old men, who also have the highest incidence of prostate cancer (2). Furthermore, we now recognize that a significant number of prostate cancers exist in men with serum PSA below 3ng/ml, the majority of which are clinically significant (3,4). The benefits of a radical cystectomy which preserves the posterior lateral zones of the prostate might quickly fade for the patient and physician alike when the serum PSA starts rising and there is limited hope of performing completion prostatectomy and reconstruction of the orthotopic neobladder.

The authors' approach is certainly appealing when ejaculatory preservation is a quality of life issue. We however caution that this select patient is few and far between. For the young (20 to 30 year-old) male with benign bladder disease necessitating cystectomy (refractory cystitis glandularis) or non-urothelial carcinoma away from the bladder neck in whom fertility is an issue, this technique, offering ejaculatory preservation, even if ejaculation is retrograde into the neobladder where it can be harvested, is alluring. For all others we feel there is little benefit to be gained by this technique over a properly performed nerve sparing cystoprostatectomy

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EDITORIAL COMMENT

The concept of preservation of the prostate at the time of cystectomy for bladder cancer is not new and has been applied sporadically since early in the twentieth century. I first preserved the prostate capsule in 1985 using a technique somewhat similar to Srougi and subsequently in several carefully selected patients. I have been reluctant to publish these cases due to the uncertainty as to whether this technique will be viable in the long term. Clearly, interest in this technique has escalated with this recent report and the larger series of Vallancien et al. from France (1).

While there are some early signs that this technique may be beneficial for some patients, the benefits versus the risks of the technique must be addressed before its widespread use. The benefits include probable decrease in blood loss, probable improved continence, and probable improved erectile function recovery. I emphasize the "probable" aspect because the degree of improvement is certainly unquantified, despite the initial observations of Srougi and my experience as well. A validated Quality of Life instrument suitable to quantify erectile function and incontinence after a cystectomy and neobladder surgery is not currently available; thus the magnitude of improvement from this technique will be debatable until studied in an appropriate fashion.

The risks are also unquantified. Using whole-mount step-sectioning of the prostate, it has been determined that approximately 40% of bladder cancer cystectomy patients may harbor unsuspected urothelial carcinoma in situ in the prostatic urethra or prostatic ducts (2,3). Similarly, 40% to 50% of patients have unsuspected adenocarcinoma of the prostate (most of which are small and of uncertain clinical significance) (3). Since the patient populations with urothelial and adenocarcinomas do not necessarily overlap, 40% to 80% of patients might have a neoplasm in the prostate which may make it unwise to leave the prostate capsule behind. Much of this risk may be obviated by careful patient selection and presurgical screening for prostate cancers as suggested by Srougi, and a frozen section of the adenomatous tissue removed from the prostate. If the frozen section reveals either urothelial or adenocarcinoma at the time of surgery, the prostate capsule and seminal vesicle could be removed. If the frozen section is benign, the neobladder could be sewn to the prostate capsule as described in Srougi's report.

As with many procedures in oncology, the evolution is towards smaller, less extensive operations that still reliably eliminate the cancer but preserve better function (e.g., lumpectomy and radiation for breast cancer or nerve-sparing radical prostatectomy). Maybe it is time for a more critical study of a tailored radical cystectomy for urothelial cancer. Careful patient selection will unquestionably be the most important aspect.

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THE ROLE OF VIDEOLAPAROSCOPY IN THE DIAGNOSTIC AND THERAPEUTIC APPROACH OF NONPALPABLE TESTIS

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ABSTRACT

Objective: Evaluate the results from the first 5 years of experience with laparoscopy for diagnosis and treatment of nonpalpable testes.

Materials and Methods: Medical records of 51 patients submitted to laparoscopic testicular exploration, during a 5-year period, were retrospectively analyzed. Patients' mean age was 65.7 months (median = 48) on the first procedure. The youngest patient was 10 months and the oldest was 14 years old on the first surgery. Twenty-four (47%) patients presented nonpalpable testes bilaterally, 7 (14%) only at the right side and 20 (39%) at the left, totaling 75 testicular units assessed. Patients who had their testes palpated after anesthetic induction were excluded from the study, and in all other cases, surgical management was based on the testicular position and viability. During the post-operative follow-up, surgical success was classified as palpable testis in scrotal sac, with adequate consistency and volume.

Results: Nine (12%) testes were not localized, but their vessels and deferent duct were atrophic. Two (3%) testes were intra-abdominal and atrophic, and 2 (3%) gonads, in the same patient, had a dysmorphic aspect. Nineteen (25%) testicular units were located close to the internal inguinal ring (peeping testes) and, in 22 (29%) units, the spermatic vessels and deferent duct penetrated the internal inguinal ring. Eight (10%) testes were located at a distance of less than 2 cm from the internal inguinal ring and 13 (17%) at a distance greater than 2 cm. The 2 intra-abdominal atrophic testes were removed. Inguinotomy was performed in a total of 41 (54%) cases, reaching a surgical success of 89%. Laparoscopic orchiopexy in one stage, without vascular ligation, was performed in 9 (12%) testes, which presented a distance of less than 2 cm from the internal inguinal ring, also with a surgical success index of 89%. Orchiopexy in 2 stages, with ligation of the spermatic vessels, was performed in 13 (17%) testicular units located at a distance greater than 2 cm from the internal inguinal ring, reaching 77% of good results.

Conclusion: Videolaparoscopy is a safe and effective method for diagnosis and treatment of nonpalpable testis.

Key words: testis; cryporchidism; diagnosis; therapeutics; laparoscopy
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INTRODUCTION

Cryptorchidism occurs in 0.8 to 1.2% of boys at 1 year old (1,2), and in 20% of them, the testis is nonpalpable (3), and it can be absent, intra-canalicular, or intra-abdominal.

The diagnosis and treatment of nonpalpable testes have been controversial, however, in the last 20 years, since the introduction of laparoscopy, they have undergone major changes. First, it became one of the choices diagnostic methods, since imaging scans such as ultrasonography, computerized tomog-

raphy, scintigraphy and magnetic resonance, do not offer a similar accuracy (4-7). In 1992, Jordan et al. (8) introduced the therapeutic application of laparoscopy in patients with nonpalpable testes and, since then, in addition to being a diagnostic method, it has been an option for treating this condition.

This work's objectives were: 1) To analyze the experience of the first 5 years following the introduction of videosurgery for diagnosis and treatment of nonpalpable testes in our service; 2) To access the surgical success of different orchiopexy techniques; 3) To assess the need of exploring the inguinal canal in cases where laparoscopy identifies spermatic vessels and deferent duct penetrating the internal inguinal ring.

MATERIALS AND METHODS

In the period from March 1996 to April 2001, 51 patients underwent diagnostic and therapeutic laparoscopy in our service. Patients' mean age was 65.7 months (median = 48) on the first procedure and 64.58 months (median = 50) on the second surgery. The youngest patient was 10 months and the oldest was 14 years old on the first surgery.

Twenty-four (47%) patients presented nonpalpable testes bilaterally, 7 (14%) only at the right side and 20 (39%) at left, totaling 75 testicular units assessed (Table-1).

Twenty-two (43%) patients presented comorbidities (Table-1). Thirty-nine (76%) patients were White and the others were Mulatto or Black, and there was none patient of Asian origin. Twenty-five (48%) patients underwent pelvic and inguinal ultrasonography, and in only 10 (40%) the result coincided with the surgical finding. Stimulation with β-HCG was performed in 5 (9,6%) patients with bilateral nonpalpable testes, without change of testicular position at the post-treatment assessment.

All patients were submitted to inhalatory and intravenous general anesthesia, followed by testicular palpation. Those patients who had their testes palpated at this moment were excluded from the study and were submitted to inguinotomy. The surgical technique that was employed included gastric stenting, vesical drainage and Trendelenburg's position; infraumbilical incision and the confection of a pneumoperitoneum with Veress needle, insufflating carbon dioxide at pressures of 8 to 10 mmHg. Then a 10 mm trocar was introduced through the incision, enabling the investigation of the peritoneal cavity with an optic (30°) of 10 mm. First, potential injuries to hollow viscera and other organs were assessed; next, the following was evaluated: region of internal inguinal ring, spermatic vessels and deferent duct, testicular size and position, in addition to comparison with the contralateral unit.

In cases of absent testicular structure, with spermatic vessels and deferent in blind sac, the laparoscopic procedure was terminated. When the testis was next to the internal inguinal ring (peeping testes), the inguinotomy was preferred, because, in our experience, such testicular position allows for the classic orchiopexy with good results. If elements of the spermatic cord penetrating the internal inguinal ring were identified, the exploration was proceeded by inguinal route and, when a viable testis was identified, orchiopexy was performed.

Table 1 – *Laterality and associated pathologies.*

Nonpalpable Testis	Frequency	Associated Pathologies
Bilateral	24 (47%)	18 (75%) : 6 DR; 5 MPH; 4 PB; 2 MGD; 1 HP
Right	7 (14%)	2 (29%) : 1 DR; 1 HP
Left	20 (39%)	2 (10%) : 1 DS; 1 KT
Total	51 (100%)	22 (43%)

DR = neuro-psychomotor development retardation; MPH = male pseudo-hermaphroditism; PB = prune-belly syndrome; MGD = mixed gonadal dysgenesis; HP = hypospadias; DS = Down's syndrome; KT = Klippel-Trenounay syndrome.

In all other situations, 2 auxiliary trocars, one of 10 mm and other of 5 mm, were located in both hemiclavicular lines at the level of the umbilicus scar, under direct visualization. Patients with bilateral cryptorchidism were treated in a single time.

When the testis was located at less than 2 centimeters from the internal inguinal ring, the laparoscopic orchiopexy in one stage was performed, which consisted in the distal section of the gubernaculum, if present; dissection of the peritoneum laterally to the spermatic vessels, mobilizing the vessels and the deferent for an extension of 8 to 10 cm of their retroperitoneal position. The vessels were preserved by blunt dissection, avoiding electrocoagulation. Upon completing the dissection, the testis was free of adhesions to the posterior abdominal wall, with the spermatic vessels and the deferent duct. At this moment, a laparoscopic clamp (Grasping or Maryland) was introduced, from a new internal inguinal ring created medially to the obliterated ipsilateral umbilical artery, up to the scrotal sac. A small incision and a sub-dartos pouch were created in the scrotum, through which a 5 mm trocar, followed by a Grasping clamp, were introduced into the peritoneal cavity. The testis was then driven to his position within the sub-dartos pouch in the scrotum, pulled by the gubernaculum, aiming not to injury its vascular supply. The desufflation of the pneumoperitoneum provided an additional extension to the testicular position.

In cases of testes that were more than 2 centimeters away from the internal inguinal ring, the laparoscopic orchiopexy in 2 times was performed, which consisted initially in ligation of the spermatic vessels with metallic clips and their section. The laparoscopic orchiopexy was performed in a second time, usually with a 6-month interval from the first surgery. Closure of the internal inguinal ring was not performed in any case of laparoscopic orchiopexy.

RESULTS

Laparoscopic Findings

Videolaparoscopy defined the intraabdominal anatomy in all cases. Nine (12%) testes were not localized, however their vessels and vas deferens were atrophic. Two (3%) testes were intraabdominal and atrophic and 2 (3%) gonads, in the same patient, had a dysmorphic aspect. Nineteen (25%) testicular units were located next to the internal inguinal ring (peeping testes) and, in 22 (29%) cases, the spermatic vessels and the deferent duct penetrated the internal inguinal ring. Eight (10%) testes were located at a distance of less than 2 cm from the internal inguinal ring, and 13 (17%) at a distance greater than 2 cm.

Surgical Management

The 2 intraabdominal atrophic testes were removed, by laparoscopic approach in one case, and by inguinal approach on the second one.

The 2 gonads with dysmorphic aspect were biopsied by laparoscopy. The histological analysis showed viable testicular tissue in one of them, with laparoscopic orchiopexy without vascular ligation being performed.

Inguinotomy was performed in a total of 41 (54%) cases: in 19 testicular units located next to the internal inguinal ring and in those 22 where the spermatic vessels and the vas deferens penetrated the internal inguinal ring. Among those, 13 units presented anorchia or testicular atrophy on inguinotomy, with the excision of testicular remnants being performed. In the remainder 28 units, open orchiopexy was completed.

Laparoscopic orchiopexy without vascular ligation, in one stage, was performed in 9 (12%) testes: 8 that presented a distance of less than 2 cm from the internal inguinal ring, in addition to the unit with dysmorphic aspect that had been submitted to biopsy.

Orchiopexy with ligation of spermatic vessels in 2 stages was performed in 13 (17%) testicular units located at a distance superior to 2 cm from the internal inguinal ring. The interval between the first and the second procedure was 6 months.

Surgical Result

After a mean follow-up of 11.2 months, the findings of physical examination of the 50 testicular units driven to the scrotum were analyzed in order to evaluate the surgical success, that is, topical testes in the scrotum, with adequate volume and consistency (Table-2).

Of the 28 testicular units that were driven to the scrotum by open orchiopexy, 25 (89%) were palpable in the scrotum with adequate consistency and volume; one (4%) in low inguinal canal and 2 (7%) evolved with atrophy.

Of the 22 testes driven to the scrotum by videolaparoscopy, 9 were driven to the scrotum without vascular ligation, in one stage, with 89% of success and only one (11%) testicular atrophy. 13 were operated by Fowler-Stephens technique with ligation of vessels, in 2 stages, reaching 77% of good results, with 3 (23%) palpable testes in the inguinal canal. Relative to the non-closing of the internal inguinal ring in cases of laparoscopic orchiopexy, no inguinal herniation was identified in the follow-up.

Pathological Study

It was performed in 17 testes: in the 2 intra-abdominal atrophic testes, it revealed cells in the prepubertal developmental stage; in the 2 dysmorphic gonads that were submitted to biopsy, it demonstrated a dysgenic gonad and a rudimentary testis. However, in the 13 units where the spermatic vessels and the vas deferens penetrated the internal inguinal ring, during the inguinal exploration, testicular atrophy or anorchia were identified, demonstrating lack of testicular tissue in 11 cases, scaring tissue in 1 and cells in the prepubertal developmental stage in another.

Second Surgery

Inguinotomy and orchiopexy were performed due to testicular atrophy, detected in the post-operative follow-up, in 3 units: 2 of them were initially located in the internal inguinal ring, and had undergone orchiopexy by inguinal approach on the first surgery, whereas the third unit had been driven to the scrotum by laparoscopy in one step.

DISCUSSION

The main reasons for investigating nonpalpable testes and their position in the scrotum when present, are to preserve fertility, to make the testicular examination easier anticipating the diagnosis of an eventual malignant transformation, in addition to esthetic and psychological factors.

The traditional method for investigating a nonpalpable testis consists in an exploration by inguinotomy, or by lower abdominal approach. Videosurgery was used for this purpose, for the first time, in 1976, by Cortesi et al. (9) and, since then, it has been improved and used, as well, for therapeutic purposes.

Considering the occasional difficulties for driving an abdominal testis to the scrotum, several techniques were described. Orchiopexy by inguinal approach is feasible in cases of testes next to the internal inguinal ring. The procedure by inguinal approach in 2 stages, not used in this series, has the disadvantage of technical difficulty in the second stage, which can lead to testicular injury, or damage of the spermatic cord (10). Autotransplantation, that is not performed in our service as well, requires microvascular surgery techniques and a prolonged hospitalization time (11,12). The ligation of spermatic vessels, as postulated by Fowler & Stephens, has a testicular atrophy index around 30% (13,14); that can be lowered to about 10%, when the procedure is per-

Table 2 – *Surgical result according to the technique employed, excluding testes initially atrophic or absent.*

Technique	Atrophic Testis	Palpable in Inguinal Canal	Palpable in Scrotum	Total
Orchiopexy by inguinal approach	2 (7%)	1 (4%)	25 (89%)	28 (56%)
Orchiopexy by laparoscopic approach (one stage)	1 (11%)	0	8 (89%)	9 (18%)
Orchiopexy by laparoscopic approach (Fowler-Stephens - 2 stages)	0	3 (23%)	10 (77%)	13 (26%)
Total	3 (6%)	4 (8%)	43 (86%)	50 (100%)

formed in 2 stages, allowing the development of collateral circulation (15).

The mean age of patients in our sample was high (mean = 65.7 and median = 48 months), reflecting a probable delay in the diagnosis or in the referral of boys with nonpalpable testes to the tertiary care service. Once the follow-up in our service was initiated, there was no investment in imaging studies or hormone therapy, due to their limited results according to the literature. In this series, 48% of patients underwent ultrasonographic investigation, mostly before referral, and in only 40% of the cases, the findings coincided with the surgical anatomy.

Analyzing the results on a laterality basis, we observed that among the 24 patients (48 testicular units) who presented nonpalpable testes bilaterally, 18 (75%) presented associated pathologies, 10 (21%) absent or atrophic testicular units and 13 (27%) units in "high" position (> 2 cm from the internal inguinal ring). Among the 7 patients who presented nonpalpable testes only at the right side, 2 (28%) presented associated pathologies, only 1 (14%) missing unit and none unit in high position. We observed 20 nonpalpable units only at the left side, with 2 (10%) presenting associated pathologies, 14 (70%) absence or atrophy and none high unit. The highest incidence of associated pathologies in patients with nonpalpable testes bilaterally is probably because patients bearing neuropathies, male pseudo-hermaphroditism, prune-belly syndrome and mixed gonadal dysgenesis, often evolve with cryptorchidism. The analysis based on laterality also suggests that the "high" position of intra-abdominal testes is more frequent in bilateral defects and that anorchia or testicular atrophy are more commonly observed in cases where the defect occurs only at the left side.

One of the purposes of this study was to assess the surgical result of the 3 different techniques that are used in our service. Orchiopexy by inguinal approach and laparoscopic orchiopexy without ligation of vessels presented a surgical success (adequate testicular volume and position) of 89%, whereas laparoscopic orchiopexy in 2 stages (Fowler-Stephens), obtained 77% of good results; values that are consonant to the literature (13-16).

Inguinal exploration, in cases where laparoscopy had identified spermatic vessels and deferent duct penetrating the internal inguinal ring, proved to be necessary, because in 9 cases (41%) viable testes were found and driven successfully to the scrotum. In this sample, such exploration was performed by inguinal approach in all cases, due to the team's larger experience with this approach. However, by retrospectively assessing and based on data from the literature (17-19), we do not see a reason why such exploration is not made by laparoscopic approach, since it has showed to be safe and effective. Such management could avoid the use of 2 approaches (laparoscopy and inguinotomy) for obtaining the same objective.

Schleef et al. (19) suggest the inguinal laparoscopic exploration in cases where one can observe hypoplastic elements of the spermatic cord penetrating the internal inguinal ring. Such study, based also in findings from other works (20-22), suggests the hypothesis that in cases where hypoplastic elements of the spermatic cord penetrate a closed internal inguinal ring, there is never a normal testis in the inguinal canal. In our sample, it was possible to identify 2 cases on the definition above, and in none of them a viable testis was found in the inguinal canal. Our sample of inguinal laparoscopic exploration is still small, with a larger number of studies being required to confirm such hypothesis.

Those who oppose to laparoscopy for diagnosis and treatment of nonpalpable testes claim that the procedure is longer, brings a risk of long-term adhesions, in addition to subjecting the patients with testis, or testicular remnants, in inguinal canal, to a needless procedure in 48 to 64% of cases (23-25). In 54% of the children in this sample, the exploration of the inguinal pathway was performed by inguinotomy after the laparoscopic identification of spermatic vessels penetrating the internal inguinal ring. Nevertheless, data from the literature (19-22) show that even in these cases it is possible to perform orchiopexy by laparoscopic exploration of the inguinal pathway. This approach would have the advantage of avoiding the performance of an inguinotomy in patients whose procedure had already been initiated by laparoscopic route.

Evaluating the literature data about false-negative inguinal explorations (26), in addition to the risk of in-situ carcinoma in cryptorchid testes (27-28), we should engage in the definitive laparoscopic diagnosis. It is worth to remember that some laparoscopic procedures were canceled, with an inguinotomy performed, due to palpation of the testis after anesthetic induction. This results from the fact that the muscle relaxation and the immobilization of the child contribute to testicular palpation. Despite of this, in 9 cases, testes located in the inguinal canal were not palpated. Laparoscopy allowed their correct localization and their treatment by inguinal approach.

CONCLUSION

Laparoscopy showed to be a safe and effective method for assessment and treatment of nonpalpable testes. It enabled that intraabdominal anatomy was accurately defined in all cases, providing higher safety in dissection of delicate structures, under direct visualization. If also offered a fast recovery to the patient, with excellent esthetic results. Non-closure of the internal inguinal ring did not result in inguinal hernia.

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EDITORIAL COMMENT

Laparoscopy is already a recognized method for assessment and treatment of nonpalpable testes, and the experience presented by the authors confirms such data.

The therapeutic sequence for the several laparoscopic findings is well defined in this work, giving importance to the reference of distance from the testis to the internal inguinal ring. Therefore, if the distance is less than 2 cm, the orchiopexy can be performed immediately, since the dissection allows to obtain a sufficient length of the spermatic vessels to comfortably fix the testis to the scrotum (most of the times, that occurs when it can be taken to the internal orifice of the contralateral inguinal canal). On the other hand, when the initial distance is greater than 2 cm, probably a sufficient length will not be obtained, even with exhaustive dissection, thus it is more prudent to make the vascular ligation only, and to perform the orchiopexy in a new procedure after 6 months.

Contrarily to the authors, I consider that the identification of the testis next to the internal inguinal ring is a formal indication for laparoscopic orchiopexy, inclusively when it is located within the hernial sac ("peeping testis"). However, it is fundamental that the deferent, which can insinuate further beyond the testis, through the internal orifice of the inguinal canal, forming a loop in the hernial sac wall, is carefully dissected, avoiding its injury. For that, it is necessary to pull the hernial sac into the abdominal cavity, in order to make its visualization easier. Due to the low testicular position, the length of spermatic vessels and deferent rarely constitutes a limiting factor to the success of primary laparoscopic orchiopexy.

In the discussion, the authors suggest the possibility of laparoscopic dissection of the inguinal canal to treat canalicular testes, when vessels and deferent are identified penetrating the obliterated internal inguinal orifice. In my opinion, this is a haz-

ardous proposal, since in some cases the testis is viable, but is located below the external orifice of the inguinal canal, that is, in the inguinal subcutaneous tissue, consequently in a site of difficult access by laparoscopic approach. Moreover, there is a significant risk of trauma to the testis, deferent and spermatic vessels with this laborious dissection, making the orchiopexy unfeasible. Such strategy would be warranted only if all canalicular testes should be removed, due to being atrophic, what is not confirmed by the authors' own sample. Additionally, in case of atrophic or vestigial canalicular testes, the inguinotomy allows that, following the orchiectomy, testicular prostheses are inserted at the same time.

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SAFYRE™: A READJUSTABLE MINIMALLY INVASIVE SLING FOR FEMALE URINARY STRESS INCONTINENCE

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ABSTRACT

Introduction: SAFYRE™ is a readjustable and minimally invasive sling for the treatment of stress urinary incontinence (SUI). It is as a pubovaginal sling placed in the medial third of the urethra. The initial experience is described.

Materials and Methods: Forty-five patients (mean age = 59 years) underwent a SAFYRE™ implant to treat SUI. Physical examination and urodynamic study were performed before surgery. All patients presented symptoms of SUI and 20% also reported mild urgency. Approximately 60% of this group had a previously failed anti-incontinence procedure. Urethral hypermobility was diagnosed in 40% of the patients and intrinsic sphincter deficiency (ISD) in 60% of the cases.

Results: The average follow up period was 10 months. The mean operative time was 20 minutes. Dystopia repair was performed whenever necessary, during the same procedure. The average hospital stay was 24 hours. In 11% of the implants, bladder perforation occurred. During the postoperative period, 9 patients (20%) developed transient urgency symptoms. During the initial follow up period, 90% were found to be continent, 3% reported an improvement and 7% were unchanged.

Conclusion: SAFYRE™ is a safe and quick procedure that allows postoperative readjustment. This technique may be an attractive alternative in the management of SUI, should the good result obtained so far prove to be long lasting.

Key words: urinary incontinence, stress; prostheses and implants; reconstructive surgical procedures
Int Braz J Urol. 2003; 29: 353-9

INTRODUCTION

Autologous pubovaginal sling is the choosen treatment for complex cases of stress urinary incontinence (SUI) (1). Preference for autologous material was largely due to 2 basic concerns: implant infection and urethral erosion (2).

On the other hand, the use of synthetic slings transforms major surgeries into minimally invasive procedures and also reduces operative time and hospital stay as well as postoperative discomfort and the recovery period (1).

The readjustable and self-anchoring SAFYRE™ sling has recently been added to the existing therapeutic arsenal. It is a tension-free, synthetic sling, placed at the mid urethra that makes urethral erosion unlikely.

According to the integral continence theory (3), the medial and distal third regions of the urethra are the most important regions in urinary continence because of the insertion of the pubourethral ligament and the pelvic muscle floor (4). Should postoperative urinary leakage or retention occurs, this innovative device allows for tension readjustment (3).

Slings are now being used more often and the SAFYRE™ system, which has imbibed these new concepts, is an attractive alternative for the surgical treatment of SUI. The authors present their first experience with this readjustable sling.

MATERIALS AND METHODS

Patients

An open prospective non-randomized clinical study involving SUI patients was conducted after receiving the approval of the Hospital Ethics Committee.

From February 2001 to July 2002, 45 patients with SUI diagnosis underwent the SAFYRE™ implant. The patient's ages ranged from 42 to 72 years (mean age 59 years). The work-up for incontinence included clinical examination and urodynamic study.

After the surgery, the recall was monthly for clinical assessments. At these monthly recalls, the patients were questioned about presence of spontaneous micturition, involuntary urinary leakage, bladder irritative symptoms, vaginal or suprapubic pain and questions related to the degree of satisfaction with the procedure.

Besides history, a physical examination was performed during follow-up to access continence and to verify signs of infection or erosion of the vaginal wall.

The surgical results were classified according to Blaivas & Jacobs (5) into 3 categories: a) cured - absence of incontinence; b) improved - frequency of incontinence episodes less than once every 2 weeks; c) failure - frequency of incontinence episodes more than once a week.

During preoperative evaluation, all patients showed urinary leakage during repeated Valsalva maneuvers. None of them presented significant degree of atrophic vaginitis, even among post-menopausal patients. The gynecological examination revealed the presence of mild cystocele in 13 patients (30%), 90% of the cases was grade I and the rest grade II. Rectocele was diagnosed in 4 patients (9%) and only cases of grade II cystocele were repaired. The dystopias were corrected during the SAFYRE™ implant surgery.

Urodynamic evaluation disclosed urethral hypermobility in patients with Valsalva leak point pressure (VLPP) above 90 cm H_2O and intrinsic sphincter deficiency when VLPP was less than 60 cm H_2O. Intermediate VLPP values were analyzed along with clinical information to establish the diagnosis (6,7). Using these criteria, 18 patients (40%) were diagnosed as intrinsic sphincteric deficiency and in 27 patients (60%) urethral hpermobility. Patients who presented involuntary detrusor contractions during bladder filling or infravesical obstruction were excluded from the study but those with irritative symptoms without urodynamically proven involuntary contractions were included. Although urodynamically proven detrusor instability does not have a significant effect on surgical outcome, this decision was based on the concept regarding the postoperative improvement of sensory urgency, as described previously (8). Patients with involuntary detrusor contractions were excluded from this initial study due to the less favorable prognosis regarding post-operative irritative symptoms (9).

Urgency in association with urinary leakage symptoms was reported by 20% of the patients while 60% of the patients reported a history of previous surgical treatment for incontinence; the one most commonly performed was the anterior vaginal repair (Table-1).

Material

SAFYRE™ consists of a polypropylene mesh that acts as a urethral support, held between 2 self-anchoring tails made of polydimethylsiloxane polymer. These tails are the basis of the readjust able self-anchoring system. In order to minimize the surgical damage to pelvic floor natural support structures, a special 3.5 mm in diameter needle, allows for both suprapubic and transvaginal approaches, according to the surgeon best skills. The versatile needle is assembled for trans-

Table 1 – *Previous surgical procedures for stress urinary incontinence.*

Technique	N	(%)
None	18	40.0
Anterior repair (Kelly plication)	13	28.9
Retropubic colpossuspension	5	11.1
Pubovaginal sling	5	11.1
Periurethral injection	3	6.7
Needle suspension	1	2.2
Total	45	100.0

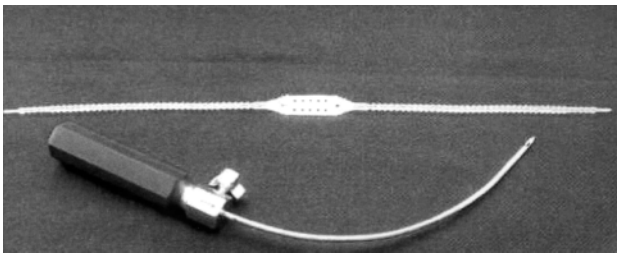

Figure 1 - *SAFYRE™* sling set.

vaginal approach when the hooked extremity is introduced inside the needle holder, and for supra pubic approach when assembled the other way (Figure-1).

Surgical Technique

Two 0.5 cm transverse incisions are made close to the superior aspect of the pubic bone 5 cm apart. A longitudinal vaginal incision, 1.5 cm in length is made, starting 1 cm from the urethral meatus. Notice that this incision is not allowed encroaching on the bladder neck. Dissection is done to create a 1 cm tunnel lateral to the urethra for the introduction of the needle. First, the needle is advanced through the vaginal tunnel until the perforation of pelvic floor at the level of the mid-urethra. Then, it is redirected against the back of pubic bone and advanced continuously to the previously made landmarks in the suprapubic area (Figure-2). Cystoscopy is performed to rule out bladder perforation. After the removal of the holder, SAFYRE™ is attached to the needle and pulled out to the suprapubic area (Figure-3). The same maneuvers are repeated on the other side. The proper tension of the sling is adjusted maintaining a Metzenbaum scissors between the urethra and the sling, to prevent undue tension (Figure-4). The extremities of the sling are cut and the Metzenbaum scissors removed (Figure-5). No further fixation is needed and the incisions are closed in the usual manner. An indwelling catheter is left in place overnight.

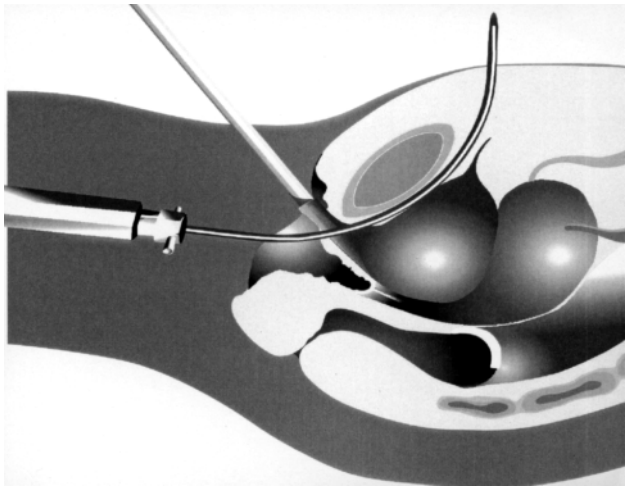

Figure 2 - *After perforation of the endopelvic fascia, the needle is directed through the retropubic space close to the pubic bone.*

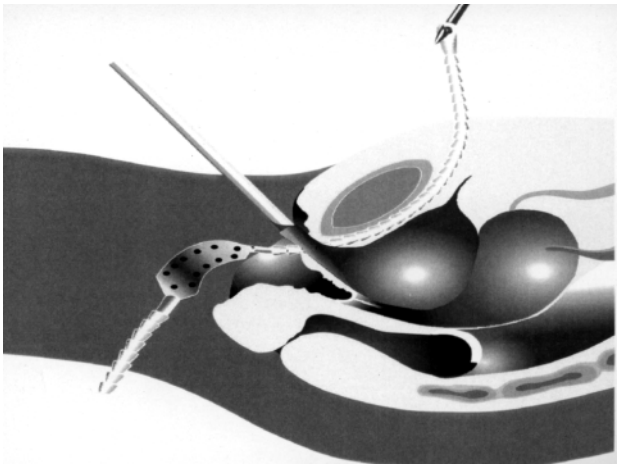

Figure 3 - *SAFYRE™ is attached to the needle and pulled out to the suprapubic area.*

Readjustment Technique

The procedure to tight the SAFYRE™ can be performed under local or spinal anesthesia. As the extremities of the polydimethylsiloxane tails can be easily palpable in the subcutaneous tissue, local anesthesia with lidocaine 1% solution seems to be the method of choice. Usually, the readjustment of only one tail is enough, without risk of significant deviation of the urethral axis. A small incision is made over the palpable tail extremity (close to the superior aspect of the pubic bone) and it is gentle dissected and grasped using a haemostatic clamp. Then, it is pulled carefully, until the proper tension is achieved. During this maneuver, a cystoscope sheath should be maintained inside the urethra, to prevent over correction. The bladder is filled with saline solution before the procedure, so the patient can be asked to cough

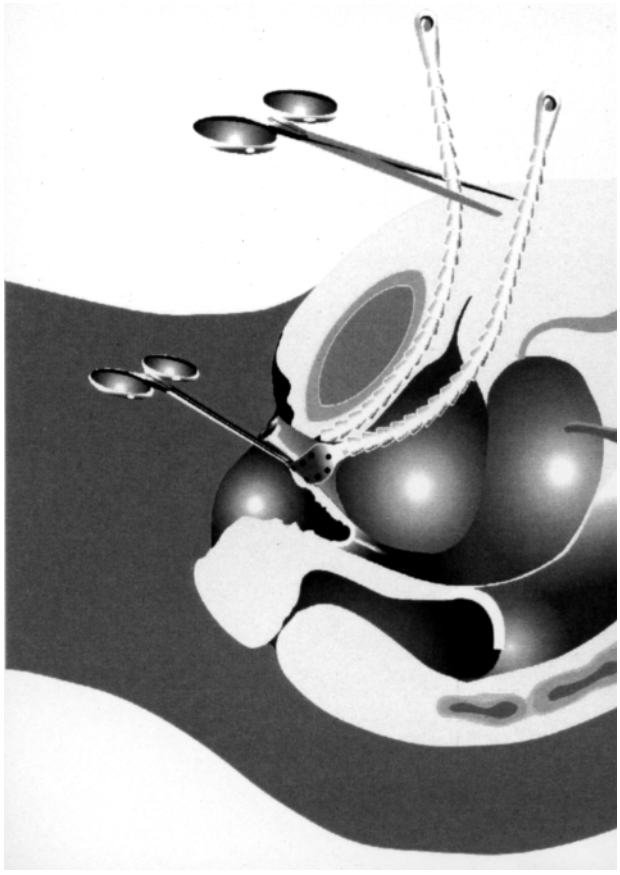

Figure 4 *- A Metzenbaum scissors is placed between the tape and the urethra for proper tension adjustment.*

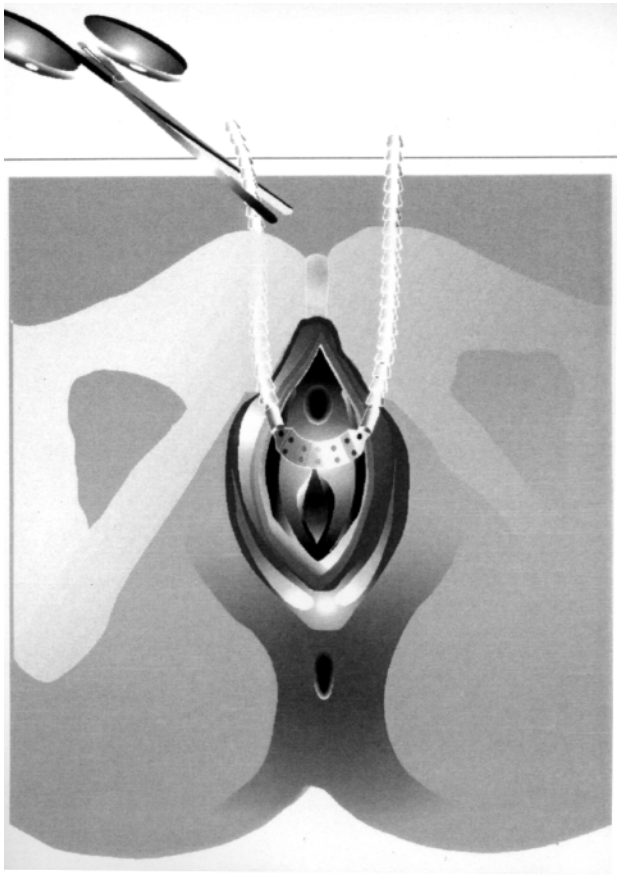

Figure 5 *- The final aspect of the sling in place.*

and to do repeated Valsalva maneuvers to check if leakage occurs. Prophylactics antibiotics are used for 3 days. Generally, the readjustment is proposed before 30 days postoperative, but theoretically it can be done at any time after the procedure, because of the formation of a fibroblastic pseudocapsule surrounding the polydimethylsiloxane tails of SAFYRE™, that permits easy dissection and mobilization of the tails inside this pseudocapsule, whenever it became necessary.

The procedure to loosen the SAFYRE™ can be performed under spinal, intravenous or local anesthesia. When local anesthesia is used, both suprapubic area (including rectus muscle and fascia) and anterior vaginal wall (including urethropelvic fascia) have to be anesthetized with lydocaine 1% solution. A longitudinal vaginal incision, 1.5 cm in length is made, starting 1 cm from the urethral meatus, and the polypropylene mesh is dissected from the urethropelvic fascia. The tails are dissected bilaterally, grasped with haemostatic clamps and pulled back, until a Metzenbaum scissors or a right-angle clamp can be interposed between the mesh and the urethra. A Foley catheter is left in place overnight and prophylactics antibiotics are used for 3 days.

RESULTS

The follow up period ranged from 2 to 17 months, the mean follow up period was 10 months. The mean duration of the procedure was 20 minutes (15 to 35 minutes) and the mean hospital stay was 24 hours (from 12 to 36 hours). All procedures were performed under spinal anesthesia. Perforation of the upper lateral wall of the bladder occurred in 5 patients

(11%), including, 2 patients that have been previously submitted to a retropubic colpossuspension and to an anterior repair as well. A Foley catheter was left in place for 48 hours and the patients presented no complications.

The diagnosis of urinary retention was done when the residual volume, obtained by post micturition urethral catheterization, was higher than 100 ml. Patients which could not present spontaneous micturition in the immediate post-operative period were maintained in a clear intermittent catheterization program until 4 weeks post-operatively when a loosening procedure was performed if retention had persisted. All of the patients that presented spontaneous micturition in early post-operative period showed post-void residual less than 100 ml and were considered without retention. Following the above criteria, postoperative urinary retention occurred in 3 patients (6.7%) that had not presented spontaneous micturition after 4 weeks post-operatively. All underwent sling tension loosening under local anesthesia and voided spontaneously, with completed relief of irritative symptoms and with a mean post void residual volume of 60 ml after the procedure.

There were 4 cases (9%) of vaginal wall infection but no vaginal or urethral wall erosion. Transient irritative voiding symptoms were reported by 9 patients (20%) during the immediate postoperative period (up to 4 postoperative weeks). None of the patients presented pelvic floor defects that required surgical correction during the follow-up.

According to Blaivas & Jacobs criteria (5) after 10 months mean follow up, 40 patients (90%) were considered cured, 2 (3%) reported significant improvement and 3 patients (7%) were dissatisfied with the procedure and were considered as failures.

DISCUSSION

Pubovaginal slings and the retropubic urethrocystopexies are the procedures that can lead to the best continence results in long-term follow up (1). Autologous pubovaginal slings, however, imply in a considerable period of surgical training and the inconvenient need for a donor site to obtain the fascia to be used in the surgery as well as the risks of infra-vesical obstruction and voiding dysfunction (3). Retropubic urethrocystopexies, on the other hand, imply an abdominal incision with increased morbidity and hospital stay, high costs when performed using a laparoscopic access and a time consuming learning curve (4). Therefore all efforts towards the development of minimally invasive techniques are justifiable.

From a conceptual standpoint, the SAFYRE™ corresponds to a sling. So, the creation of a suburethral support zone increases urethral resistance and diminishes the rotational as well as the descending movement of the urethra when abdominal pressure increases. Additionally, it improves the coaptation of the urethral lumen at rest and under stress. However, contrary to the classical pubovaginal slings, the SAFYRE™ is applied in the middle third of the urethra, where the pubourethral ligaments responsible for natural stability of the urethra are inserted (10). The SAFYRE™ self-anchoring system is created by a sequence of 4 mm cones, creating a hook-like effect on the pelvic fascias and the abdominal rectus muscle as well (11,12).

Although most patients had previously undergone an anti-incontinence procedure, no complications or technical operative difficulties were noticed. Contrary to previous reports, rejection of implanted material was not observed with this synthetic sling (2).

SAFYRE™ insertion is tension-free and is not restricted by the size of the bladder neck as in conventional slings (12,13). Urinary retention occurred in 6.7% of the patients according to the criteria adopted. The diagnosis of post-operative obstruction following anti-incontinence surgeries is a matter of concern. Besides the different urodynamic criteria proposed, the diagnosis is underestimated and most of patients without complete retention were diagnosed in the late post-operative period, usually after they had presented with urinary tract infection. Besides the possibility of retention relief after 4 weeks post-operatively, we advise the loosening procedure by these period in order to avoid the fibrotic reaction around the sling and to allow for the patients to return to their habitual activities as soon as

possible. The unique feature of SAFYRE™ allows for postoperative tension readjustment without difficulties. These patients underwent sling readjustment under local anesthesia and voided spontaneously, with completed relief of irritative symptoms and with a mean post void residual volume of 60 ml.

Although this study have not compared SAFYRE™ to other minimally invasive techniques, such as Tension-free Vaginal Tape (TVT®) or similar, there are specific and significant differences concerning the biochemical and biomechanical properties of this device. As opposed to TVT® or other polypropylene minimally invasive slings, the smooth surface of SAFYRE™ mesh allows for easy primary adjustment during the implant and even during eventual readjustment, besides keeping its resistance and shape due to its low deformity rate. Moreover, the elasticity of polymetylsyloxane tails can provide fine movements according to the changes of patient's abdominal pressure, acting as a dynamic support. Furthermore SAFYRE™ self-anchoring system is unique as far as postoperative readjustibility is concerned. The procedure is minimally invasive and no large abdominal incision is required for harvesting fascia, neither to fix the sling to the aponeurosis of the abdominal rectus muscle as in classical slings. Its readjustability allows for late adjustments of sling tension in patients presenting persistent incontinence or urinary retention, avoiding major surgeries such as urethrolysis or the need for another sling insertion, reducing costs. The coherence of the physiological principles involved in female urinary incontinence, cure rate over 90% and the uncontestable benefits of postoperative tension readjustments make this procedure a promising step forward in the surgical management of SUI.

CONCLUSION

SAFYRE™ is a safe and quick procedure, easy to perform and to learn, and allows for postoperative readjustment under local anesthesia. This unique and innovative feature is a major advantage for the individual patient and makes SAFYRE™ an attractive alternative in the management of SUI, should the good results prove to be long lasting.

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UROLOGICAL SURVEY

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EDITORIAL COMMITTEE

STONE DISEASE

Computerized tomography guided access for percutaneous nephrostolithotomy

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Purpose: Access for percutaneous nephrostolithotomy (PNL) using conventional fluoroscopic guidance may carry an increased risk of damage to surrounding organs in patients with renal calculi and aberrant anatomy. In these situations cross-sectional anatomical imaging may facilitate safe percutaneous access. We describe our experience with computerized tomography (CT) guided percutaneous access for such patients undergoing PNL.

Materials and Methods: Between June 2000 and December 2001, 154 patients underwent PNL at our institution. Five of these patients (3%) required a total of 6 percutaneous access tracks under CT guidance. All patients in this group had anatomical abnormalities precluding standard access to the collecting system without risk to adjacent organs. These abnormalities included a retrorenal colon in 2 and a severely distorted body habitus due to spinal dysraphism in 3.

Results: Percutaneous access was achieved without complication in all cases. At subsequent PNL 5 of the 6 renal units (83%) were rendered completely stone-free.

Conclusion: CT guided percutaneous access is infrequently required for PNL. However, there is a select group of patients with anatomical anomalies that may predictably require this procedure to facilitate safe and efficacious PNL.

Editorial Comment

Aside from bleeding, the most common cause of morbidity associated with percutaneous nephrostolithotomy (PCNL) is injury to surrounding organs. With widespread use of CT imaging for the diagnosis of renal and ureteral calculi, anatomic features associated with risky percutaneous renal access are often identified. As the same time, patients with stones who are known to be at risk for anatomic anomalies often undergo CT imaging to evaluate the anatomic relations of the kidney to facilitate fluoroscopically-guided percutaneous access. For example, if CT shows that the spleen is located quite posteriorly and underlies the upper pole of the kidney in its lateral aspect, then the percutaneous puncture can be directed more medially under fluoroscopic guidance.

Matagla and colleagues, however, used CT guidance directly to obtain percutaneous renal access in patients at risk of injury with fluoroscopically-guided access. In doing so they reduced the chance of adjacent organ injury and increased the likelihood of satisfactory percutaneous renal access for PCNL. Although the risk of encountering a retrorenal colon, the most common cause (albeit rare) of colonic injury during PCNL, may not be sufficiently high to justify pre-operative CT imaging in all patient candidates for PCNL, those patients with known anatomic anomalies should undergo cross-sectional imaging as part of the routine preoperative planning process. For those few patients in whom percutaneous renal access cannot be safely obtained under fluoroscopic guidance, CT-guided access offers an effective means of achieving safe, optimal renal access.

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Variability of renal stone fragility in shock wave lithotripsy

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Objectives: To measure, in an in vitro study, the number of shock waves to complete comminution for 195 human stones, representing six major stone types. Not all renal calculi are easily broken with shock wave lithotripsy. Different types of stones are thought to have characteristic fragilities, and suggestions have been made in published reports of variation in the fragility within some types of stones, but few quantitative data are available.

Methods: Kidney stones classified by their dominant mineral content were broken in an unmodified Dornier HM3 lithotripter or in a research lithotripter modeled after the HM3, and the number of shock waves was counted for each stone until all fragments passed through a sieve (3-mm-round or 2-mm-square holes).

Results: The mean +/- SD number of shock waves to complete comminution was 400 +/- 333 per gram (n = 39) for uric acid; 965 +/- 900 per gram (n = 75) for calcium oxalate monohydrate; 1134 +/- 770 per gram (n = 21) for hydroxyapatite; 1138 +/- 746 per gram (n = 13) for struvite; 1681 +/- 1363 per gram (n = 23) for brushite; and 5937 +/- 6190 per gram (n = 24) for cystine. The variation for these natural stones (83% +/- 15% coefficient of variation) was greater than that for artificial (eg, gypsum-based) stones (17% +/- 8%).

Conclusions: The variability in stone fragility to shock waves is large, even within groups defined by mineral composition. Thus, knowing the major composition of a stone may not allow adequate prediction of its fragility in lithotripsy treatment. The variation in stone structure could underlie the variation in stone fragility within type, but testing of this hypothesis remains to be done.

Editorial Comment

A number of clinical series have attempted to retrospectively correlate stone composition with success of shock wave lithotripsy (SWL). However, the ability to predict stone composition preoperatively on the basis of density on plain radiographs or attenuation on CT has been disappointing. Likewise, inconsistency in stone fragmentation among stones of similar composition has further limited our ability to predict SWL outcomes.

Williams and associates evaluated a series of human stones of different compositions as well as artificial stones to assess their susceptibility to and variability of fragmentation with SWL in vitro. Although uric acid and hydroxyapatite stones required the least and struvite and cystine stones the most shock waves to comminute, the variability within each group of stones with similar composition was remarkably high, suggesting that secondary factors, such as additional mineral components or variation in internal structure, also contribute to the overall susceptibility of a stone to SWL fragmentation.

This relatively simple but important study suggests that recent attempts to determine stone composition on the basis of radiographic characteristics may provide less predictive information than previously hoped. Although some generalizations may be made about susceptibility of stones of certain compositions to SWL fragmentation, in any individual case the outcome is less certain due to the large variability in response of stones to shock waves. Thus, knowledge of stone composition in and of itself may provide insufficient evidence on which to base patient selection for SWL.

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ENDOUROLOGY & LAPAROSCOPY

Laparoscopic nephrectomy: assessment of morcellation versus intact specimen extraction on postoperative status

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Purpose: We compared pathological evaluation and postoperative recovery in patients undergoing transperitoneal laparoscopic nephrectomy at our institution with morcellated vs intact specimen extraction.

Materials and Methods: A prospective evaluation of 57 consecutive patients undergoing radical and simple transperitoneal laparoscopic nephrectomy was reviewed. One patient was excluded from study due to transitional cell carcinoma, which was detected intraoperatively. The 33 morcellated specimens were extracted at the umbilical port and the 23 intact specimens were extracted through a midline infraumbilical incision. Data were obtained on narcotic requirements, hospital stay, complications, estimated blood loss, mass size based on preoperative imaging, specimen weight and extraction incision length.

Results: Mean incision length in the morcellated and intact specimen removal groups was 1.2 and 7.1 cm, respectively ($p < 0.001$). No significant differences in pain or recovery were noted between the 2 groups. Two cases of microscopic invasion of the perinephric adipose tissue in the intact specimen group were up staged from clinical T1 to pT3a disease. No change in patient treatment was made based on this information.

Conclusions: We did not find a significant difference in surgical time, pain or hospital stay. Only incision length was statistically significant. Postoperative recovery appeared to be similar in these 2 groups. With modern imaging modalities information on pathological stage did not alter patient treatment.

Editorial Comment

Although prospective, this study was non-randomized. The authors report that "the decision to morcellate or perform intact extraction was based solely on patient preference". There were some differences between the groups, including patients that were older (mean age of 54.6 vs. 61.5 years, $p = 0.03$) and larger (BMI of 31.7 vs. 27.9) in the morcellated group. The mean operative time was only 11 minutes longer in the morcellated group. Unfortunately, the authors did not report the operative time for extraction separately. It would have been informative to compare the operative time after complete dissection of the kidney, to determine if the longer extraction time in the morcellated group was outweighed by the longer time to close the incision in the intact extraction group. Entrapping a specimen in the Cook LapSac is a challenging task, which the authors appropriately bemoan in their discussion section, and I would think that in most surgeon's hands it would take longer to entrap and morcellate a specimen than to close the 7.1 cm average incision for intact extraction. That the authors of this study managed to perform morecellation in only 11 minutes longer than they took to perform intact extraction, especially given the greater BMI in the morcellated group, is a testament to their skill. The major finding of this study is the lack of benefit in terms of patient convalescence in the morcellation group, despite the smaller incision. This leaves cosmetics as being the only advantage of morcellation. There are a number of potential advantages to intact extraction. With intact extraction, pathological staging is possible. There is a growing body of evidence, however, that there is little prognostic difference between clinical T1 renal cancers that are confirmed as pT1 and those that are upstaged to pT3a. In addition, there is concern that morcellation might increase the risk of port implantation. Fortunately, there have been only 3 reported cases of port site implantation of renal cell carcinoma, and 2 of them occurred after inappropriate blind morcellation in a plastic bag. My conclusion is that port site implantation is not a significant concern with renal cell carcinoma

and that there is minimal benefit to the pathological staging provided by intact extraction. Given this, and the findings of this study, the only difference between intact extraction and morcellation is improved cosmetics in the last. As such, I prefer morcellation unless the specimen is very large (> 750 grams), in which cases I use hand-assistance (and therefore intact extraction) to simplify dissection and entrapment.

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Prospective randomized comparative study of the effectiveness and safety of electrohydraulic and electromagnetic extracorporeal shock wave lithotriptors

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Purpose: We compared the efficacy of 2 shock wave energy sources, electrohydraulic (Dornier MFL 5000, Dornier MedTech, Wessling, Germany) and electromagnetic (DLS, Dornier Lithotriptor S, Dornier MedTech), for the treatment of urinary calculi.

Materials and Methods: A prospective randomized study of 694 patients with urinary stones was conducted during 12 months to compare the efficacy of the 2 machines. Entrance criteria were radiopaque single or multiple stones at any location within the kidney or the ureter, 25 mm or smaller that had not previously been treated by any means. Patients with congenital anomalies were excluded from this study with all other contraindications for extracorporeal shock wave lithotripsy. Following lithotripsy a plain abdominal film and tomograms were done 1 week after each session to determine if there were residual stones and assess the need for re-treatment. Patients were evaluated 4 weeks after lithotripsy by plane abdominal x-ray and spiral computerized tomography. Success was defined as no residual stones. Univariate and multivariate statistical analyses were performed for different variables that may have an impact on the success rate, including the type of lithotriptor. Comparisons of treatment parameters, complications and success rate for both lithotriptors were done.

Results: Of 9 variables examined with univariate analysis 6 had a significant impact on the success rate. Of these 4 maintained their statistical impact on multivariate analysis. These were side, site of the stones, renal morphology and type of lithotriptor. Treatment time was significantly shortened for DLS (54 ± 32.9 minutes compared to 65.7 ± 44.7 for MFL, $p < 0.001$). The re-treatment rate was lower for DLS at 34% versus 51.6% for the MFL ($p < 0.001$). The overall success rate was 85.4%. It was 88.5% for DLS compared to 82.4% for MFL ($p = 0.03$). No statistically significant difference between the lithotriptors was noted for ureteral calculi ($p > 0.05$). The success rate was higher in the DLS group for renal stones especially lower caliceal and pyelic stones ($p < 0.05$). The success rate was higher in DLS group for stones 10 mm or smaller, 92.8% versus 85.3% for MFL ($p = 0.03$). The success rate was comparable in both groups for stones larger than 10 mm (81.8% for DLS versus 77.9% for MFL, $p > 0.05$). No statistically significant difference was found in the complication rate for the groups. Steinstrasse were noted in 4% of patients treated with MFL and 3% of those treated with DLS. Subcapsular hematomas were noted in 2 patients in each group. No procedures after extracorporeal shock wave lithotripsy were needed in either group.

Conclusions: The electromagnetic lithotriptor (Dornier lithotriptor S) has significant clinical advantages over the electrohydraulic lithotriptor (Dornier MFL 5000) in terms of treatment time, re-treatment rate and success rate, although there is no difference in the complication rate.

Editorial Comment

As nice as it would be to conclude that this study provides definitive evidence with regards to one energy source over another, as the authors would like us to believe as suggested by their stress on the energy source rather than the particular lithotriptor throughout the text, it does not do that. Other differences between the lithotriptors make this conclusion invalid. The focal zone is 224 mm^2 in the MFL and 175 mm^2 in the DLS. The number of shock wave delivered was not provided. One might conclude reasonably, however, that indeed the DLS is a better machine than the MFL – primarily owing to the lower retreatment rate. Since the MFL is no longer in production, this information is not all that useful. One finding in the study that is very useful, however, is the minimal (0.6 %) rate of hematoma formation overall, despite the use of sensitive CT scans for surveillance. Other studies have suggested that hematoma formation might be more frequent with either machine, and given the sensitive radiographic assessment in this study I find this reassuring.

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IMAGING

Multidetector CT angiography for preoperative evaluation of living laparoscopic kidney donors

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Purpose: The purpose of this study was to determine the accuracy of multidetector CT (MDCT) angiography as the primary imaging technique in the evaluation of living kidney donors.

Material and Methods: Seventy-four consecutive living kidney donors (30 men, 44 women; mean age, 41.7 years) who underwent MDCT were evaluated. CT examination was performed with 120 mL of IV contrast material at an injection rate of 3 mL/sec and a pitch of 6. In every case, arterial and venous phase volumetric data sets were acquired at 25 and 55 sec, respectively. Scans were reconstructed at 1-mm intervals for three-dimensional (3D) imaging using a volume-rendering technique. Axial CT images and 3D CT angiography were evaluated prospectively by one reviewer and retrospectively by two reviewers who had no knowledge of surgical results. Surgical correlation for the location of primary and accessory renal arteries, early branching of the renal arteries, and renal vein anomalies was made.

Results: Seventy-two subjects underwent left nephrectomy, and two subjects underwent right nephrectomy because supernumerary left renal arteries were detected on preoperative CT angiography. Eighteen supernumerary renal arteries (two arteries to 16 kidneys and three arteries to one kidney) to 74 kidneys underwent nephrectomy. CT and surgical findings agreed in 93% of subjects (the average of three reviewers; range, 89–97%). Two small accessory renal arteries were missed by all three reviewers. Those arteries were diminutive and were thought to be insignificant by the surgeons. Early branching of the renal arteries was shown in 14 arteries, and CT and surgical findings agreed in 96% (the average of three reviewers; range, 93–97%). Renal vein anomalies were present in eight subjects, and CT and surgical findings agreed in 99% of the cases (range, 96–100%).

Conclusions: MDCT angiography is highly accurate for detecting vascular anomalies and providing anatomic information for laparoscopic living donor nephrectomy.

Editorial Comment

Radiological imaging plays an important role in the evaluation of potential living related kidney donors since anatomical and functional assessment of the donor kidney is mandatory. This is particularly critical when laparoscopic donor nephrectomy is performed. As we know, arterial and venous anomalies are more frequently found in the left kidney. Since this kidney is usually preferred for laparoscopic nephrectomy, the demonstration of arterial or venous anomalies is essential for the success of the surgical procedure. Single-slice helical CT angiography with advanced 3-D techniques provides detailed description of the vascular, parenchymal, and collecting system and is considerately a method with high accuracy for detecting vascular anomalies and provides anatomical information. It may be used as the primary tool for donor evaluation since additional useful information can be obtained: cortical cysts, duplex collecting system, hydronephrosis and renal stone. Recently several reports have shown high accuracy of single-slice CT angiography in demonstrating accessory arteries (78-98%), early arterial branching (89-99%), and renal / perirrenal venous anatomy (90–99%) as pointed out in this manuscript. These rates are not significantly different from those obtained with MDCT, 89–97%, 93–97% and 96–100%, respectively. The use of the recent technology of multi-slice CT known also as multi-detector CT, has several advantages over single-slice technology (better vascular opacification and higher spatial resolution) and few but important drawbacks (higher dose of ionizing radiation and potentially nephrotoxic contrast agents). In order to avoid such problems one might consider using MR angiography, which is also very important method for the preoperative evaluation of living kidney donors. Preoperative CT and MR angiography of the renal arteries in renal donors demonstrate substantial agreement and similar high rates of accuracy. MR angiography has the advantage of avoiding ionizing radiation and potentially nephrotoxic contrast agents.

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Contrast enhances color Doppler endorectal sonography of prostate: efficiency for detecting peripheral zone tumors and role for biopsy procedure

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Purpose: We evaluated the accuracy of contrast enhanced color Doppler endorectal ultrasound to guide biopsy for the detection of prostate cancer.

Materials and Methods: A total of 85 patients were evaluated with gray scale and color Doppler before and during intravenous injection of ultrasound contrast agent made of galactose based air micro bubbles. Our biopsy protocol was performed during contrast injection. An additional 18 directed cores were obtained based on contrast-enhanced imaging. Diagnostic efficiency with and without contrast medium injection for detecting prostate cancer was compared based on biopsy results.

Results: Cancer was identified in a total of 58 biopsy sites in 54 patients. Gray scale imaging revealed 96 abnormal hypoechoic nodules or irregular zones inside the outer gland, of which 48 were malignant on

pathological evaluation. Contrast enhanced color Doppler had higher sensitivity (93%) than unenhanced color Doppler (54%), while specificity increased only 79% to 87% for enhanced imaging. Nine of 10 isoechoic suspicious zones were depicted with enhancement, while unenhanced Doppler detected 7 of them. There was no significant difference between the intensity of enhancement and tumor Gleason scores.

Conclusions: Contrast enhanced color Doppler endorectal sonography increases the detection of prostate cancer. Improvement in sensitivity was high, while the difference in specificity was not as pertinent. It is accurate when using a common and routine application ultrasound unit. This technique is easy to perform and not time-consuming. Obtaining additional biopsy cores of suspicious enhancing foci significantly improves the detection rate of cancer.

Editorial Comment

Color Doppler ultrasound (CDUS) has already been proved to be of a great value as a complementary method for the detection of prostate cancer during transrectal guided biopsy. Although it has proven utility, unfortunately, this method is not used routinely in many centers. Some of the reasons may be explained by the fact that CDUS of the prostate requires high resolution modern equipments (with power Doppler), dedicated and experienced sonographer and appropriate control settings. The use of energy Doppler (Doppler angiography, power Doppler) is better than velocity Doppler in order to demonstrate subtle area of abnormal flow (areas with increased neovascularity). This occurs because energy Doppler is not dependent of the angle of the ultrasound beam. The use of microbubbles as an echo-contrast improves the ability of CDUS to better demonstrate the neovascularity associated with cancer. We have found that this phenomenon is particularly useful in large prostate gland (> 60 grams), prostate gland with isoechoic peripheral zone and prostate gland showing 2, 3 or more suspicious areas. Obviously 2 or 3 cores of the area with abnormal flow must be taken additionally to the cores obtained by the systematic biopsy. In our department routinely used CDUS without and with echo-contrast demonstrated respectively, 8% and 15% of cancer not seen on gray-scale US examination (isoechoic cancer) (1). The authors present a high sensitivity and specificity of the contrast enhanced CDUS (93 and 87% respectively). Other studies has been shown that Doppler angio-sonography (power Doppler) with eco-contrast increased the detection of prostate cancer from 38 % to 85% with an 80% specificity (2). There is no doubt that power Doppler ultrasound, preferably with eco-contrast should be used routinely during transrectal biopsy of the prostate. This technique is particularly helpful in normal appearance prostate gland (mainly those larger than 60 grams), prostate with more than one suspicious area and in patients with negative biopsies and rising PSA.

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UROGENITAL TRAUMA

Improvement of hemostasis in open and laparoscopically performed partial nephrectomy using a gelatin matrix-thrombin tissue sealant (FloSeal)

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Objectives: Long-term follow-up studies have demonstrated that effective local tumor control and long-term tumor-free progression rates can be achieved by nephron-sparing surgery. However, hemostasis is a major issue, and the lack of effective means of hemostasis has limited the wider use of the laparoscopic approach to nephron-sparing surgery.

Methods: Between January 2001 and April 2002, 25 patients with renal cell carcinoma were treated with partial nephrectomy using a two-component tissue sealant (FloSeal). The median age was 54 years (range 42 to 71). The follow-up time was 1 to 12 months (median 3.5). The tumor diameter ranged from 2 to 5 cm (median 2.8). Fifteen cases were performed by open retroperitoneal surgery, and 10 cases were performed laparoscopically. The two-component tissue sealant (consisting of a gelatin matrix granula component and a thrombin component) was applied after resection of the tumor and before perfusion of the kidney. The following parameters were recorded: time until complete hemostasis was achieved; decrease in postoperative hemoglobin level; postoperative bleeding; and presence or absence of a perirenal hematoma 24 hours and 10 days postoperatively by ultrasonography.

Results: After application of the tissue sealant for 1 to 2 minutes to the moist resection site, hemostasis was immediate in all cases. During the laparoscopically performed partial nephrectomies, a laparoscopic applicator was used to avoid wasting the tissue sealant within the dead space of the instrument. When reperfusion of the kidney was established, hemostasis was maintained. The decrease in postoperative hemoglobin level ranged from 0.3 to 1.2 points (median 0.7). None of the patients required blood transfusions. No postoperative bleeding occurred. The ultrasound examination 24 hours and 10 days postoperatively demonstrated the absence of a significant perirenal hematoma.

Conclusions: The two-component tissue sealant FloSeal provided immediate and durable hemostasis in open and laparoscopically performed partial nephrectomies. The tissue sealant may provide a tool to expand the possibilities of laparoscopic nephron-sparing surgery.

Editorial Comment

Major bleeding is an issue for both renal trauma surgery and partial nephrectomy. In this study, the authors validate the use of a novel thrombin hemostatic agent that works much better than any similar material from the past, for use against bleeding seen in laparoscopic partial nephrectomy. Although not specifically a trauma study, I believe that the hemostasis seen in this study could also be welcome in renal trauma surgery (renorrhaphy). In the past, few hemostatic agents had been truly helpful in stemming hemorrhage from the bleeding kidney, and intraoperative and postoperative blood loss remained a problem. Worse, during some renal trauma surgery, potentially salvageable kidneys were removed iatrogenically because of brisk bleeding. Now, the invention of highly concentrated thrombin in a gelatin matrix (FloSeal; Baxter) allows the stemming of even spurting blood, and forms a clot, which is both strong and lasting. This will surely decrease the nephrectomy rate during attempted renorrhaphy.

Company literature shows Floseal stopping bleeding from experimentally lacerated porcine heart and inferior vena cava. The clot that is formed is not pushed out by the pressure of blood, even in the heart. I have

personally validated these findings in pigs, where FloSeal stopped bleeding from stab wounds to the liver, spleen and kidney almost instantaneously, and stopped bleeding from lacerated IVC after 3 minutes of light pressure with a moist sponge. In humans, I have used FloSeal in open partial nephrectomy with identically excellent results to this paper. No renal vessels needed ligation, and no persistent or late bleeding was seen. A second application of Floseal is sometimes needed if the first application does not stop all the bleeding. Warm ischemia time is decreased to minutes, even in large partial nephrectomy cases.

In this study, Floseal was used in 25 partial nephrectomy patients as the sole means of bleeding control. 15 had open operations and 10 had laparoscopic surgery. Average time to complete hemostasis was less than 2 minutes, and no patients had postoperative bleeding. Finally, it appears that a very effective hemostatic agent is available for our everyday use.

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Effect of an institutional policy of nonoperative treatment of grades I to IV renal injuries

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Purpose: Nonoperative treatment of serious renal injuries has been advocated and yet to our knowledge the optimum level of operative treatment has not been established to date. We report a unique data set, in which patients with severe renal injuries were treated with an ultraconservative nonoperative approach during a period when urological consultation was not available at a major urban trauma center.

Materials and Methods: We retrospectively reviewed the charts of 51 patients identified with renal trauma in the Detroit Receiving Hospital trauma database from 1997 to 2001.

Results: Injuries were grades I to V in 15, 7, 11, 14 and 4 cases, respectively, and had a tendency toward serious injury. Renorrhaphy was never performed. Nephrectomy was done sparingly, only for grade V renal injuries and only in patients who were exsanguinating from the kidney. Two of the 4 patients with grade V injury died of multiple injuries, including massive head injuries. Only 2 of the patients treated nonoperatively (4%) had complications, including fever and hematuria in 1 each.

Conclusions: This data set seems to support an ultraconservative approach of limiting renal surgery to only patients with active exsanguination. The nephrectomy rate for 14 grade IV injuries, including some gunshot wounds to the kidney, was 0%. When comparing this rate with that in the literature, we would expect it to be 1 patient to as high as 10. This approach was safe and resulted in a low complication rate of 4%. Series in which more aggressive therapy for renal injuries is advocated should compare favorably to ultraconservative therapy if aggressive therapy is to continue to be widely advocated.

Editorial Comment

Most renal trauma literature is written by urologists, but at many centers the General Surgery trauma team not the urologist dictates what therapies are provided to injured patients. In some cases the trauma surgeons may elect not to consult the urology service, or they may elect to remove a briskly bleeding kidney even before urology can be notified. At our trauma center, the trauma surgeons, many of them internationally famous

names, correctly (I believe) determined that most severely injured kidneys healed without the need for surgery. Even 6 patients with gunshot wound were given a trial of conservative therapy - all of them successfully. Only those who where actively bleeding to death (in the estimation of the attending general surgeon) had renal surgery, and that was a speedy nephrectomy in all cases. In this way, these surgeons have turned classic urologic trauma teaching on its head, reducing the operative rate over that reported in previous urologic series, and most importantly decreasing the rate of nephrectomy towards 0% for Grade I-IV injuries. This series mirrors the general trend towards conservative therapy in trauma, and reports like it must be closely followed by anyone with an interest in treating renal injury. Less is turning out to be more in the field of renal trauma. While it takes more courage to observe the patient than go to the operating room, it may ultimately turn out to be the best treatment in the majority of patients.

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PATHOLOGY

Multiple measures of carcinoma extent versus perineural invasion in prostate needle biopsy tissue in prediction of pathologic stage in a screening population

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The capacity of perineural invasion by carcinoma in prostate needle biopsy tissue to independently predict pathologic stage in radical prostatectomy tissues remains uncertain. We sought to determine, in a prostate specific antigen-based screening population, the ability of needle biopsy histologic grade, tumor extent, and perineural invasion to independently predict pathologic stage and margin status in the whole prostate gland. Perineural invasion, Gleason grade, percentage Gleason pattern 4/5 carcinoma, and multiple measures of needle biopsy tumor extent, including number of positive cores, percentage of positive cores, total percentage of carcinoma, greatest percentage of carcinoma in a single core, and total carcinoma length in millimeters, were captured for 215 men from a prostate specific antigen-based screening program diagnosed with prostate cancer in a median of six procured needle biopsy cores. Pathologic stage and surgical margin status were evaluated in corresponding completely embedded radical prostatectomy specimens. A logistic regression model was used to relate the endpoints of extraprostatic extension by carcinoma and/or positive margins to needle biopsy tissue findings. In univariate analyses, total percentage of carcinoma ($p = 0.003$), greatest percentage of carcinoma in a single core ($p = 0.004$), total tumor length in millimeters ($p = 0.009$), and fraction of positive cores ($p = 0.02$) were all significantly associated with extraprostatic (pT3) carcinoma, whereas all five measures of carcinoma extent in needle biopsy tissue were related to positive margins. Correlation coefficient determinations showed that all five measures of needle biopsy carcinoma extent were highly interrelated. In multivariate analyses, total percentage of carcinoma was significantly related to pathologic T stage ($p = 0.003$) and positive margins ($p = 0.0002$). In a multivariate model with the radical prostatectomy whole gland endpoint of either pT3 disease or positive margins, fraction of positive cores ($p = 0.00001$) was the only variable with significant predictive value. Perineural invasion by carcinoma in needle biopsy tissue was detected in 11% of cases. Neither presence

nor absence of perineural carcinoma nor number nor percentage of positive nerves related to pathologic stage in univariate or multivariate analyses. Amount of carcinoma in prostate needle biopsy tissue, using multiple measurements but not perineural invasion, is a significant histologic attribute predictive of pathologic stage and margin status for men with prostate specific antigen screening detected prostatic carcinoma. Reporting of several measures of carcinoma extent in needle biopsy tissue is recommended.

Editorial Comment

The significance of perineural invasion in needle biopsies is a controversial issue. Bastacky et al. (Am J Surg Pathol. 1993; 17: 336-41) from Johns Hopkins University found perineural invasion in 20% of needle biopsies with a specificity of 96% to predict extraprostatic extension. According to these authors, measuring perineural invasion on needle biopsy helps to identify extraprostatic extension and may help in planning nerve-sparing radical prostatectomy in the decision of whether to sacrifice part or all of the neurovascular bundle on the side of the biopsy. Based on this study, in 1994, the American College of Pathologists recommended to include this finding in the pathology report.

Egan & Bostwick (Am J Surg Pathol. 1993; 17: 336-41) from Mayo Clinic found perineural invasion in 36% of needle biopsies with a specificity of 70% to predict extraprostatic extension. However, in a multivariate analysis, only pre-operative PSA, extent of tumor in the biopsy and Gleason grading were statistically significant. The authors conclude that the finding of perineural invasion in needle biopsy of prostatic carcinoma has no independent predictive value for the presence of extraprostatic extension. Accordingly, they recommend no longer routinely evaluate this finding in biopsy specimens.

The paper of this editorial comment favors the findings of Egan & Bostwick. However, the controversy is far from being settled. More studies are needed for a clear significance of perineural invasion in needle biopsies.

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Comparisons of outcome and prognostic features among histologic subtypes of renal cell carcinoma

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Our objective was to compare cancer-specific survival and to examine associations with outcome among the histologic subtypes of renal cell carcinoma (RCC). We studied 2385 patients whose first surgery between 1970 and 2000 was a radical nephrectomy for sporadic, unilateral RCC. All RCC tumors were classified following the 1997 Union Internationale Contre le Cancer and American Joint Committee on Cancer guidelines. There were 1985 (83.2%) patients with clear cell, 270 (11.3%) with papillary, 102 (4.3%) with chromophobe, 6 (0.3%) with collecting duct, 5 (0.3%) with purely sarcomatoid RCC and no underlying histologic subtype, and 17 (0.7%) with RCC, not otherwise specified. Cancer-specific survival rates at 5 years for patients with clear cell, papillary, and chromophobe RCC were 68.9%, 87.4%, and 86.7%, respectively. Patients with clear cell RCC had a poorer prognosis compared with patients with papillary and chromophobe RCC ($p < 0.001$). This difference in outcome was observed even after stratifying by 1997 tumor stage and nuclear grade. There was no significant difference in cancer-specific survival between patients with papillary and chromophobe RCC (p =

0.918). The 1997 TNM stage, tumor size, presence of a sarcomatoid component, and nuclear grade were significantly associated with death from clear cell, papillary, and chromophobe RCC. Histologic tumor necrosis was significantly associated with death from clear cell and chromophobe RCC, but not with death from papillary RCC. Our results demonstrate that there are significant differences in outcome and associations with outcome for the different histologic subtypes of RCC, highlighting the need for accurate subtyping.

Editorial Comment

Molecular genetics had an impact on classification of renal cell tumors. The genetic alterations affect the biology of the tumor cells, in respect of proliferation, cell death, differentiation, and cell adhesion; these very properties play a role in determining both the morphology and the behavior of tumors. Most of the pathologists use classifications of renal tumors based on cytomorphologic and genetic characteristics. According to the Heidelberg classification (J Pathol. 1997; 183: 131-3) and the 1997 workshop held in Rochester, Minnesota, USA (Cancer 1997; 80: 987-9) the clasification of renal cell tumors is based on these characteristics. The benign tumors are papillary adenoma (must have < 5mm in greatest diameter), oncocitoma and metanephric adenoma and the malignant tumors are conventional (clear cell) renal carcinoma, papillary renal carcinoma, chromophobe renal carcinoma, collecting duct carcinoma and unclassified cell carcinoma. Sarcomatoid carcinoma is not a particular tumor. Sarcomatoid change has been found to arise in all of the types of carcinoma in this classification, as well as in urothelial carcinoma of the renal pelvic mucosa.

The paper of this editorial comment is a timely study to make valuable this classification for the urologists. The authors studied the prognostic features among the several histologic subtypes of renal cell carcinoma. Patients with clear cell renal cell carcinoma had a poorer prognosis compared with patients with papillary and chromophobe renal cell carcinoma with no significant difference in cancer-specific survival between patients with papillary and chromophobe renal cell carcinoma. The paper also disclosed the need and importance for reporting tumor size, sarcomatoid component, grading and tumor necrosis. Tumor size, presence of a sarcomatoid component, and nuclear grade were significantly asociated with death from clear cell, papillary, and chromophobe renal cell carcinoma. Histologic tumor necrosis was significantly associated with death from clear cell and chromophobe renal cell carcinoma, but not with death from papillary renal cell carcinoma.

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INVESTIGATIVE UROLOGY

Immune mechanisms in bacillus Calmette-Guerin immunotherapy for superficial bladder cancer

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J Urol. 2003; 170: 964-9

Purpose: Of all medical disciplines it is exclusively in urology in which immunotherapy for cancer has an established position today with intravesical bacillus Calmette-Guerin (BCG) against superficial bladder carcinoma recurrences. BCG is regarded as the most successful immunotherapy to date. However, the mode of action has not yet been fully elucidated. We provide a thorough overview of this complex field of research.

Materials and Methods: Rather than simply reporting all experimental data available for better understanding the involved immune mechanisms, we chose to provide comprehensively only information supported by several independent pathways of evidence.

Results: Major findings made during the last few years include systematic analyses of patient material, detailed in vitro studies and investigations in animal models, which have led to a substantially greater understanding of the mechanisms involved.

Conclusions: The efficacy of BCG is based on a complex and long lasting local immune activation. The bladder as a confined compartment, in which high local concentrations of the immunotherapy agent and effective recruitment of immune cells can be achieved, serves as an ideal target organ for this type of immunotherapy approach.

Editorial Comment

Intravesical BCG against superficial bladder carcinoma recurrences is regarded as the most successful immunotherapy to date. However, the mode of action has not been fully elucidated yet. Since the immuno-activating properties of BCG were discovered, investigations have been carried out to ascertain the functional mechanism. All investigations to date have shown that not one single functional mechanism, but a whole series of immunological phenomena are involved.

Doctors Boehle and Brandau, world leading researchers on BCG in superficial bladder carcinoma, present in this article the most recent knowledge on this form of immunotherapy. They describe the major findings made during the last few years when systematic analyses of patient material, detailed in vitro studies and investigations on animal models have led to a substantially greater understanding of the mechanisms involved. This review explains why BCG therapy is currently considered the most successful immunotherapy of solid tumors, and therefore, must be read by every urologist interested in bladder cancer.

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Racial differences in androgen receptor protein expression in men with clinically localized prostate cancer

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J Urol. 2003; 170: 990-3

Purpose: Black American men experience disproportionate mortality from prostate cancer (CaP) compared with white American men. Differences in outcome may stem from differences within the androgen axis. Since serum testosterone levels appear to be similar by race in men with CaP, we measured and compared androgen receptor (AR) protein expression in malignant and benign prostate tissue from black and white men who underwent radical prostatectomy for clinically localized CaP.

Materials and Methods: Archived radical prostatectomy specimens obtained from 25 white and 25 black men had AR protein antigen retrieved and immunostained. AR protein expression from CaP and benign tissue was assessed by 2 methods. Automated digital color video image analysis was used to measure the

percent area immunostained for AR protein and the intensity of expression (mean optical density). Visual scoring was performed to compare results with automated values.

Results: In black compared with white men malignant nuclei were 27% more likely to immunostain for AR ($p = 0.005$) and in immunopositive nuclei AR protein expression was 81% greater ($p = 0.002$). Visual scoring of malignant nuclei revealed that AR immunostaining was significantly increased in black vs white men (171 ± 40 vs 149 ± 37, $p = 0.048$). In immunopositive benign nuclei AR protein expression was 22% greater in black than in white men ($p = 0.027$). Visual scoring of benign nuclei revealed 20% increased immunostaining in black vs white men, although this difference did not attain statistical significance ($p = 0.065$). Racial differences in AR protein expression were not explained by age, pathological grade or stage, although serum prostate specific antigen levels were higher in black men (9.7 ± 7.5 vs 15.5 ± 12.2 ng/ml, $p = 0.049$).

Conclusions: AR protein expression was 22% higher in the benign prostate and 81% higher in the CaP of black African compared with white men. CaP may occur at a younger age and progress more rapidly in black than in white men due to racial differences in androgenic stimulation of the prostate.

Editorial Comment

Although some controversies still exist, data on age adjusted deaths from CaP obtained from the Surveillance, Epidemiology, and End Results database from 1990 to 1998 in the USA revealed that Black American men have 2.3 times greater mortality from CaP than white American men. Previous works demonstrated that Black men are more frequently diagnosed with higher tumor volume, more advanced tumor stage, higher Gleason grade and higher prostate specific antigen (PSA) levels than white men are. The reasons for such findings are still not well understood.

This is the first study measuring and comparing androgen receptor (AR) protein expression in malignant and benign prostate tissue from black and white men who underwent radical prostatectomy for clinically localized CaP. The authors found that AR protein expression was 22% higher in the benign prostate and 81% higher in the CaP of black compared with white American men. Based on these findings, the authors speculated that CaP might occur at a younger age and progress more rapidly in black than in white men due to racial differences in androgenic stimulation of the prostate.

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RECONSTRUCTIVE UROLOGY

Gastrocystoplasty in patients with an areflexic low compliant bladder

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Eur Urol. 2003; 44: 260-5

Aim: This study was performed with the aim of evaluating gastrocystoplasty as a method of management of patients with an areflexic low compliant bladder.

Patients and Methods: We performed gastrocystoplasty in 30 patients (19 males and 11 females) with an areflexic low compliant bladder. The mean age of the patients was 23.4+/-11 years (range 4-32). The etiology

of lower urinary tract dysfunction was myelodysplasia in 26 patients and spinal cord injury in 4. Twenty-three patients had normal renal function and 7 had impaired renal function (creatinine 2.0-5.0mg%). Additionally, 4 patients had an artificial urinary sphincter implanted and seven had an antireflux procedure performed.

Results: Renal function remained stable or improved in 29 patients. Postoperatively, there was a 225% increase from mean preoperative capacity and a 52% decrease from the preoperative end filling pressure. Nineteen patients voided spontaneously and 11 used clean intermittent catheterization to empty the bladder. Twenty-five patients were continent with augmentation alone, four with augmentation and artificial sphincter implantation while one remained incontinent, as sphincter implantation could not be performed due to the young age of the patient. Five patients (17%) had transient hematuria and dysuria after augmentation. There were no mortalities and complications included prolonged urinary leakage in one patient and mild gastric bleeding in another two.

Conclusion: The use of the stomach for augmenting the areflexic low compliant bladder is clearly advantageous over other tissues as it increases bladder capacity and compliance with consequent achievement of continence and preservation of upper tracts. An artificial urinary sphincter can be safely implanted in the same session. Because of its inherent fibromuscular properties, the gastric patch contributes to the force of urination resulting in better bladder emptying. Patients with impaired renal function are protected from hyperchloremic metabolic acidosis.

Editorial Comment

For a long time the areflexic low compliant urinary bladder with a dysfunctional urinary sphincter due to spinal cord trauma or congenital diseases such as myelodysplasia was treated with supravesical continent or incontinent urinary diversion. The rationale for treating patients with a supravesical diversion was to preserve renal function in the long term as well as to avoid further incontinence and its sequelae.

Ileal and colonic segments are mainly used to augment small capacity bladders with an intact sphincter. However, colo- or ileocystoplasty alone can rarely restore volitional voiding in truly neurogenic lower urinary dysfunction and may be contraindicated in patients with impaired renal function.

The authors of this paper tried to functionally restore the lower urinary tract in 30 young patients with myelodysplasia or spinal cord injury by using a pedicled gastric patch instead of an ileocolonic segment. It is remarkable that postoperatively 19/30 patients could void spontaneously with insignificant residual urine, incontinence was reduced to 1/30 patients with the help of an artificial urinary sphincter and deterioration of renal function occurred only in 1/30 patients.

Whether the good results obtained in this study are due to the better compliance, different innervation and a larger smooth muscle mass of gastric patches compared to lower intestinal segments is difficult to judge from such a small study. But it clearly shows that we successfully can and therefore should make every effort to restore function of the native lower urinary tract instead of simply doing a supravesical urinary diversion in patients with a long life expectancy knowing the long term complications and socioeconomic consequences of a stoma bag in these patients.

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Is there a role for bladder preserving strategies in the treatment of muscle-invasive bladder cancer?

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Eur Urol. 2003; 44: 57-64

Single modality bladder sparing therapy for muscle-invasive bladder cancer, including transurethral resection, systemic chemotherapy or radiotherapy have been demonstrated to result in insufficient local control of the primary tumor as well as decreased long-term survival of the patients when compared to radical cystectomy. Therefore, multimodality treatment protocols that aim at bladder preservation and involve all of the aforementioned approaches have been established. Arguments for combining systemic chemotherapy with radiation are to sensitize tumor tissue to radiotherapy and to eradicate occult metastases that have already developed in as many as 50% of patients at the time of first diagnosis. It has been shown that the clinical outcome observed with this approach approximates that after radical cystectomy. Additionally, a substantial number of patients survive with an intact bladder. However, bladder preserving approaches are costly, and require close co-operation between different clinical specialists as well as very close follow-up. The good long-term results obtained after cystectomy and creation of an orthotopic neobladder make the possible advantage of a bladder preservation strategy questionable in consideration of quality of life issues. Additionally, side effects related to bladder sparing therapy may result in an increased morbidity and mortality in those patients who in fact need to undergo surgery due to recurrent or progressive disease. Multimodality bladder sparing treatment is a therapeutic option that can be offered to the patient at centers that have a dedicated multidisciplinary team at their disposal. However, radical cystectomy remains the standard of care for muscle-invasive bladder tumors.

Editorial Comment

In the majority of cases bladder reconstruction is necessary after radical cystectomy due to bladder neoplasms. Despite the fact that the majority of both male and female patients with bladder cancer are nowadays eligible for an orthotopic bladder substitution the search for bladder preserving strategies thus avoiding any bladder reconstruction continues.

The review by Kuczyk et al. outlines the results of the more recent protocols of multimodality bladder preservation in locally advanced transitional cell cancer of the bladder. All studies lack a control group – cystectomy monotherapy – to which patients were randomly assigned. But in selected patients, 5-year survival rates with an intact bladder between 36 and 41 % was obtained. However, the multimodality strategies to achieve a complete long term response were complex, costly, cumbersome for patients and treating physicians, and required a certain infrastructure available usually only in large centers. Despite all the efforts some patients still required a salvage cystectomy, which tends to be technically more difficult and often does not allow features which might be important for the patients' future quality of life such as nerve preservation for potency, or an orthotopic neobladder with good results regarding continence. Another aspect are recurrent superficial tumors in the initially successfully treated preserved bladders which may be seen even beyond 5 years.

Surprisingly mortality in the multimodality therapy group was higher in some series than in contemporary radical cystectomy studies (up to 4 % due to chemotherapy vs. 1-2% due to perioperative mortality). A quality of life advantage in the bladder preserved patients has not been substantiated to date. In fact it may be difficult to prove in some series were patients suffer from reduced bladder capacity, severe urgency, and repeat surgery due to superficial tumor recurrences in the long term. Therefore one may conclude that cystectomy in combination with a refined technique of bladder reconstruction to date remains the best option to treat locally advanced bladder cancer. We should continue to search for ways to treat these with

bladder preserving strategies, however, only under strict protocols and only in large centers with good interdisciplinary cooperation.

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UROLOGICAL ONCOLOGY

Practical considerations in permanent brachytherapy for localized adenocarcinoma of the prostate

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Urol Clin North Am. 2003; 30: 351-62

Prostate brachytherapy has become an accepted treatment modality for localized prostate cancer. Long-term biochemical and biopsy data confirm the early positive impressions that brachytherapy is as valid a treatment option as radical prostatectomy or EBRT. Quality-of-life data also look promising, but more follow-up data are needed. Is brachytherapy as good as or perhaps better than radical prostatectomy? This question cannot be answered yet. Well-controlled, randomized studies are needed. In the meantime, the clinician will have to rely on the available published data.

Permanent interstitial brachytherapy for the management of carcinoma of the prostate gland

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J Urol. 2003; 169: 1643-1652

Purpose: We summarize the permanent prostate brachytherapy literature, including biochemical outcomes, quality of life parameters and areas of controversy.

Materials and Methods: The permanent prostate brachytherapy literature was reviewed using Medline searches to ensure completeness.

Results: Using various planning and intraoperative techniques the majority of the brachytherapy literature demonstrates durable biochemical outcomes for patients with low, intermediate and high risk features. For low risk patients there is no advantage to combining supplemental external beam radiation therapy with brachytherapy. In addition, supplemental external beam radiation therapy may not improve biochemical outcomes for patients at intermediate and high risk if the target volume consists of the prostate with a generous periprostatic margin. There is no defined role for adjuvant hormonal manipulation. Although a reliable set of pretreatment criteria to predict implant related morbidity is not available, severe urinary and rectal morbidity is rare. The incidence of brachytherapy induced erectile dysfunction is significantly greater than initially reported but the majority of patients respond favorably to sildenafil.

Conclusions: Continued refinements in brachytherapy planning and implementation techniques, postimplantation evaluation and continued elucidation of the etiology of urinary, bowel and sexual dysfunction should result in further improvements in biochemical and quality of life outcomes.

Editorial Comment

These two papers essentially cover all available knowledge on the clinical application on permanent interstitial seed brachytherapy for prostate cancer.

Next to radical prostatectomy, permanent interstitial prostate (low-dose-rate, LDR) brachytherapy has become an accepted modality for treating localized prostate cancer. These papers are very thorough and up-to-date overviews on the history, the technical aspects, the treatment results and side effects of this new therapeutic option. Based on previous ultrasound inventions in Europe, the technique was refined basically in the US and realized on biplanar linear array ultrasound probes. This tool, together with an expert technique, forms the basis of a successful brachytherapy. Furthermore, software advances for the preplanning and the procedure resulted in new programs that now can accurately monitor each seeds position and radiation contribution.

Patient selection is crucial for successful therapy and the ideal candidate has low risk prostate cancer, defined as PSA of 10 or less, Gleason score of 6 or less and clinical stage T2a or less. Patients who present with more advanced features will require additional therapy, which is also addressed in depth in the articles.

The important aspect of doses is also focussed in detail. Generally, a dose of 140 Gy can be considered as threshold, as doses of less than 140 Gy had inferior results. Doses of 140 Gy and higher had outcomes comparable to radical prostatectomies.

The treatment results of studies all over the world are given for low risk patients, and also for patients with high-risk cancer. Low risk patients treated with brachytherapy have treatment results comparable to radical prostatectomy results. High-risk patients if treated in combination with hormones and/or external radiation therapy do fairly well with still room for improvement.

Treatment morbidity and side effects are also given in detail and are clearly inferior to radical prostatectomy results. Urinary retention rates vary between 1.5 to 34%, whereas late urinary complications including stricture, incontinence, and proctitis are very rare, given the right dose and technique.

An important aspect is the results on erectile dysfunction. Here, brachytherapy clearly has an advantage over radical prostatectomy, with potency preservation rates in the seventies to nineties, if brachytherapy is given alone. These data still can be improved by edition of files.

In summary, permanent interstitial prostate cancer brachytherapy has become an accepted treatment modality for localized prostate cancer. Therapeutic validity is high and side effects are very low as compared to other curative alternatives. Therefore this technique will represent a clear option in the armamentarium of the urologic surgeon.

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FEMALE UROLOGY

Effective treatment for mixed urinary incontinence with a pubovaginal sling

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J Urol. 2003; 170 (2 Pt 1): 494-7

Purpose: We assessed the results of autologous fascia pubovaginal sling (PVS) in women with mixed incontinence using a validated outcome score and identified risk factors for failure.

Materials and Methods: A total of 131 women who received a PVS for sphincteric incontinence (SUI) confirmed by history, physical examination and/or videourodynamic study (VUDS) were identified from a database during the accrual dates 1995 to 2001. Patients with a urethral diverticulum, neoplasm or urinary fistula were excluded. Patients with SUI who also complained of urinary urge incontinence (UUI) and/or had detrusor instability that reproduced incontinence symptoms during VUDS were diagnosed with mixed incontinence (MUI). Patients completed a urological questionnaire, 24-hour voiding diary, pad test, VUDS and cystoscopy preoperatively. The diagnosis of SUI and UUI was further confirmed by physician interview. In patients with MUI detrusor overactivity was classified according to urodynamic criteria. At least 1 year postoperatively the validated Urinary Incontinence Outcome Score (UIOS) was calculated from a 24-hour diary, pad test and questionnaire, and outcomes in patients with SUI and those with MUI were compared. The study was powered a priori to detect a 20% difference in outcome score. Cured patients (UIOS 0) were compared with those who were not cured (UIOS 1 or greater) and univariate analysis was applied to identify the correlates of failed PVS.

Results: Of the 131 patients evaluated 33 with a diverticulum or fistula were excluded and 98 underwent PVS. Patient age was 45 to 84 years (median 66). Followup was 1 to 7 years (median 3). A total of 46 patients (48.5%) had simple SUI and 52 (51.5%) had MUI. Two patients were lost to followup (2%) and the procedure was presumed to have failed. There were no differences in age, hormone status, previous surgery or pelvic organ prolapse between patients with SUI and MUI. The cure/improved rate was 97% in 44 SUI cases and 93% in 47 MUI cases, which was a nonsignificant difference ($p = 0.33$). Analysis of the MUI group showed that patients who were cured and not cured had similar age, parity, urethral angle, bladder capacity, leak point pressure and pad tests. Patients with MUI who were cured had a higher number of voids in 24 hours on preoperative voiding diary (12 vs 8, $p = 0.01$), while those who were improved or in whom treatment failed had a greater number of urgency (5.6 vs 4.1, $p < 0.05$) and UUI (5.1 vs 3.0, $p < 0.01$) episodes. Univariate analysis of MUI cases showed that an increasing number of preoperative urgency and urge incontinence episodes correlated directly with PVS failure ($r = 0.33$, $p = 0.038$ and $r = 0.35$, $p = 0.048$, respectively). In contrast, an increasing number of voids correlated with successful PVS ($r = 0.4$, $p = 0.01$).

Conclusions: Women with SUI and concurrent urge incontinence or detrusor instability have a successful PVS outcome at a rate comparable to that in women with simple SUI, in contrast to our previous findings. Increasing episodes of urgency and urge incontinence on the preoperative voiding diary correlated directly with surgical failure, while voiding frequently was associated with cure.

Editorial Comment

The authors review 131 patients who underwent an autologous rectus fascial pubovaginal sling performed by the same surgeon. Pre-operatively, the patients completed a urologic questionnaire, 24 hour voiding diary, pad test, video urodynamics and cystoscopy. One year postoperatively the patients completed a 24 hour voiding diary, pad test, questionnaire and physical examination with a full bladder. In addition, they completed a validated urinary incontinence outcome score (UIOS) (1). The treatment outcome in patients with the preoperative diagnosis of stress urinary incontinence was compared to the outcome in patients with preoperatively diagnosed mixed urinary incontinence.

This is a very elegant and well written paper. It offers multiple points to ponder for those surgeons treating urinary incontinence. The data the paper presents is very fair, unbiased and clear. The use of the Urinary Incontinence Outcome Score draws very firm lines between what is considered a cure, improved, and a failure (1). I use this outcome score as well when analyzing data and urge the reader to consider using it in his practice. One of the true highlights of this paper is in the discussion section, especially reviewing the outcome

data presented and pondering whether a selection bias may have been found in the authors of this paper in view of their impressive previous research into this population group. The caveats they extend to the reader for the use of a pubovaginal sling with mixed urinary incontinence should be strongly reviewed and considered.

Reference

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Preoperative urodynamic evaluation may predict voiding dysfunction in women undergoing pubovaginal sling

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J Urol. 2003; 169: 2234-7

Purpose: We determine which urodynamic parameters can best predict postoperative voiding dysfunction following pubovaginal sling surgery.

Materials and Methods: The records of 98 consecutive women who had undergone pubovaginal sling surgery with allograft fascia lata between July 1998 and July 2000 were reviewed. Urodynamic and follow-up data were sufficient for evaluation for 73 patients. Urodynamic and clinical parameters were correlated with urinary retention, time to return of efficient voiding and development of post-operative urgency symptoms.

Results: Average time to return of efficient voiding was 3.92 days (median 3). Of 21 women who voided without a detrusor contraction, urinary retention developed in 4 (23%) versus 0 of 48 who voided with detrusor contraction ($p = 0.007$). Urinary retention was defined as the need to perform even occasional self-catheterization. All 4 women with urinary retention had a detrusor pressure of greater than 12 cm H_20 (0 in 3, 4 in 1). None of the women with a detrusor pressure of greater than 12 cm H_2O had urinary retention ($p = 0.047$). The presence of Valsalva voiding in women without detrusor contraction did not affect the incidence of urinary retention (11.1%) compared to those who did not demonstrate Valsalva voiding (5.1%) ($p = 0.603$). Peak flow rate, detrusor instability on preoperative urodynamics and post-void residual urine volume were not associated with postoperative urinary retention. Finally, post-void residual urine volume predicted delayed return to normal voiding ($p = 0.001$). There were no other urodynamic parameters that were significantly associated with urinary retention, delayed return to normal voiding or postoperative urgency symptoms including peak flow rate, capacity or compliance.

Conclusions: Women who void without or with a weak detrusor contraction are most likely to have urinary retention postoperatively. Therefore, we conclude that preoperative urodynamic evaluation may be used to counsel women regarding the risk of urinary retention following the pubovaginal sling procedure.

Editorial Comment

The authors review the urodynamic parameters and follow-up data on 73 patients who had undergone pubovaginal sling with allograft fascia lata. They characterized post-operative dysfunctional voiding patterns as urinary retention, delayed return to normal voiding and de novo urgency. The urodynamic patterns analyzed

to define post-operative dysfunctional voiding patterns included detrusor voiding pressure at maximum flow rate, detrusor instability, peak flow rate, post-void residual, cystometric bladder capacity and bladder compliance. Out of the 73 post-operative women reviewed, 4 women were in urinary retention and 9 different women took greater than 7 days to resume their post-operative voiding. The 4 women in urinary retention all voided without a detrusor contraction. One of those women voided with Valsalva maneuvers while the other three in urinary retention voided without a Valsalva maneuver. Of the 7 women who were noted to void by Valsalva maneuver, one had a delayed return to efficient voiding. Three patients developed de novo urgency and one of the three had detrusor instability on pre-operative urodynamics while two did not.

This paper is quite notable with regard to emphasizing the importance of pre-operative urodynamic evaluation prior to an anti-incontinence procedure and to commenting on the post-operative voiding function of Valsalva voiders. Many times with a physical examination and history consistent with stress urinary incontinence, surgeons will question the need to put patients through a urodynamic testing. The value of a urodynamic testing denoted by this article would include characterizing the woman's voiding pattern with regards to the use of a detrusor contraction or not, in addition to documenting detrusor instability. Preparation for potential post-operative difficulties is of immeasurable value in the field of voiding dysfunction. However, as stated by this paper, most women who void without a detrusor contraction will not have urinary retention after an anti-incontinence operation such as a sling. Perhaps these patients do normally void with a detrusor contraction but that the urodynamic study was unable to identify or characterize same thus obscuring the true voiding difficulties of patients who void without a detrusor contraction and who undergo a suburethral sling.

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PEDIATRIC UROLOGY

Antibiotics and surgery for vesicoureteric reflux: a meta-analysis of randomised controlled trials

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Arch Dis Child. 2003; 88: 688-94

Aims: To evaluate the benefits and harms of treatments for vesicoureteric reflux in children.

Methods: Meta-analyses of randomised controlled trials using a random effects model. Main outcome measures were incidence of urinary tract infection (UTI), new or progressive renal damage, renal growth, hypertension, and glomerular filtration rate.

Results: Eight trials involving 859 evaluable children comparing long term antibiotics with surgical correction of reflux (VUR) and antibiotics (seven trials) and antibiotics compared with no treatment (one trial) were identified. Risk of UTI by 1-2 and 5 years was not significantly different between surgical and medical groups (relative risk (RR) by 2 years 1.07; 95% confidence interval (CI) 0.55 to 2.09, RR by 5 years 0.99; 95% CI 0.79 to 1.26). Combined treatment resulted in a 60% reduction in febrile UTI by 5 years (RR 0.43; 95% CI 0.27 to 0.70) but no concomitant significant reduction in risk of new or progressive renal damage at 5 years (RR 1.05; 95% CI 0.85 to 1.29). In one small study no significant differences in risk for UTI or renal damage were found between antibiotic prophylaxis and no treatment.

Conclusion: It is uncertain whether the identification and treatment of children with VUR confers clinically important benefit. The additional benefit of surgery over antibiotics alone is small at best. Assuming a UTI rate of 20% for children with VUR on antibiotics for five years, nine reimplantations would be required to prevent one febrile UTI, with no reduction in the number of children developing any UTI or renal damage.

Editorial Comment

This paper reviews randomized controlled trials of children with vesicoureteral reflux. Only eight trials were felt to be adequate for analysis. Nonetheless, the conclusion that the authors reach is that there are few differences in the results of antibiotic treatment vs. surgical treatment. Indeed, the only difference demonstrated was a 60% reduction is febrile UTI at 5 years. The authors calculate that 9 to 17 children would require antireflux surgery to prevent one UTI during the five-year follow-up. If indeed there is limited benefit, the authors intimate that even voiding cistourethrograms (VCUG) may not be needed. All children could be treated with antibiotics. Furthermore, the only study that reviews the results of no antibiotic treatment for patients with reflux showed no significant differences between groups. If this data holds up, it is conceivable that no VCUG would be needed in these children and no antibiotics would be necessary except for treatment of acute UTI.

On the other hand, the paper also documents the weaknesses in those trials. The studies all have significant problems. Even accounting for the weaknesses of the studies of medical vs. surgical management, it is likely that longer follow-up would show an even larger difference in febrile UTIs. Similarly, longer follow-up might well show benefits of antibiotic use in children with reflux, as the single study reported had only 29 children and 14 months of follow-up. It seems that the main point of this manuscript is that more studies are needed to obtain scientific data that enable optimal decision-making.

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Treatment of vesico-ureteric reflux: a new algorithm based on parental preference

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Objective: To assess parental preference (acknowledged in treatment guidelines as important when choosing therapy) about treatments for vesico-ureteric reflux (VUR, commonly associated with urinary tract infection and which can cause long-term renal damage if left untreated), as at present there is no definitive treatment for VUR of moderate severity (grade III).

Subjects and Methods: The parents of 100 children with grade III reflux (38 boys and 62 girls, mean age 4 years, range 1-15) were provided with detailed information about the three treatment options available for treating VUR (antibiotic prophylaxis, open surgery and endoscopic treatment), including the mode of action, cure rate and possible complications, and the practical advantages and disadvantages. They were then presented with a questionnaire asking them to choose their preferred treatment.

Results: Most parents preferred endoscopic treatment (80%), rather than antibiotic prophylaxis (5%) or open surgery (2%); 13% could not decide among the three options and endoscopic treatment was recommended.

Conclusion: Given the strong preference for endoscopic treatment we propose a new algorithm for treating VUR; endoscopic treatment would be considered as the first option for persistent VUR, except in severe cases where open surgery would still be recommended.

Editorial Comment

The authors examine parental preferences in choices of treatment for vesicoureteral reflux. Using 100 families of children with Grade III/V reflux as a test group, the authors presented information on 3 treatment options (antimicrobial therapy, open surgery and endoscopic injection). 80% chose endoscopic therapy vs. only 2% for open surgery and 5% for antimicrobial therapy!

The parental choices in this case are striking. On the other hand, the choices are based primarily on the counseling. In particular, the account of open surgery described a hospitalization of 7-10 days and a follow-up voiding cistourethrogram (VCUG). In our hospital, the majority of patients go home the next day after antireflux surgery and VCUG are only done if patients have persistent hydronephrosis or UTI. This difference in practice may make an enormous difference in parental choice. Nonetheless, it is important to recognize the emotional appeal of endoscopic therapy.

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