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Editorial and Graphic Composition
Walprint Gráfica e Editora Ltd.

The paper on which the ***International Braz J Urol*** is printed meets the requirements of ANSI/NISO Z39, 48-1992 (Permanence of Paper). Printed on acid-free paper.

The ***International Braz J Urol*** is partially supported by the Ministry of Science and Technology. National Council for Scientifc and Technological Development.

The International Braz J Urol, ISSN: 1677-5538 (printed version) and ISSN:1677-6119 (electronic version) is the Offcial Journal of the Brazilian Society of Urology – SBU, has a circulation of 6,000 copies per issue and is published 6 times a year (bimonthly, starting in January - February).
The issue date is up to 2 weeks after the month of issue for the hard copy and up to 1 week after the month of issue for the electronic version. Copyright by Brazilian Society of Urology.

The *International Braz J Urol* is indexed by: EMBASE/Excerpta Medica; SciELO, Lilacs/Latin America Index; Free Medical Journals; MD-Linx; Catálogo Latindex; SCImago, Index Medicus - NLM, PubMed/MEDLINE, ISI - Current Contents / Clinical Medicine and Science Citation Index Expanded.

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International Braz J Urol

Volume 37, number 3 May - June, 2011

CONTENTS

300 Editor's comment
M. Dambros

REVIEW ARTICLE

302 The role of the cell adhesion molecules (integrins / cadherins) in prostate cancer
A. Drivalos, A. G. Papatsoris, M. Chrisofos, E. Efstathiou, M. A. Dimopoulos

CLINICAL UROLOGY

307 Sclerotherapy of hydroceles and spermatoceles with alcohol: results and effects on the semen analysis
Chen Jen Shan, Antonio Marmo Lucon, Rodrigo Pagani, Miguel Srougi (Editorial Comment by A. Saber)

314 Topical betamethasone and hyaluronidase in the treatment of phimosis in boys: a double-blind, randomized, placebo controlled trial
F. J. Nascimento, R. F. Pereira, J. L. Silva II, A. Tavares, A. C. L. Pompeo

320 Oncological and functional outcomes following open radical prostatectomy: how patients may achieve the "trifecta"?
E. Antebi, A. Eldefrawy, D. Katkoori, C. T. Soloway, M. Manoharan, M. S. Soloway (Editorial Comment by A. Tsivian and M. Tsivian)

328 Biochemical recurrence after radical prostatectomy: ıs the dısease or the surgeon to blame?
A. Sımsır, C. Cal, R. Mammadov, I. Cureklıbatır, B. Semercı, G. Gunaydın (Editorial Comment by K. R. M. Leite)

336 Tadalafil rehabilitation therapy preserves penile size after bilateral nerve sparing radical retropubic prostatectomy
Ozgu Aydogdu, Mehmet Ilker Gokce, Berk Burgu, Sumer Baltacı, Onder Yaman (Editorial Comment by O. El-Sibai, A. A. Shafik and F. Iacono, A. Ruffo)

347 Clamp ablation of the testes compar ed to bilateral orchiectomy as androgen deprivation therapy for advanced prostate cancer
AD Zarrabi, CF Heyns (Editorial Comment by A. A. Peclat de Paula)

CONTENTS - *continued from previous page*

CLINICAL UROLOGY - *continued*

328 Biochemical recurrence after radical prostatectomy: ıs the dısease or the surgeon to blame?
A. Sımsır, C. Cal, R. Mammadov, I. Cureklıbatır, B. Semercı, G. Gunaydın (Editorial Comment by K. R. M. Leite)

336 Tadalafil rehabilitation therapy preserves penile size after bilateral nerve sparing radical retropubic prostatectomy
Ozgu Aydogdu, Mehmet Ilker Gokce, Berk Burgu, Sumer Baltacı, Onder Yaman (Editorial Comment by O. El-Sibai, A. A. Shafik and F. Iacono, A. Ruffo)

355 The Lithotripsy Table Height: A Novel Predictor Of Outcome in Shockwave Lithotripsy
E. Ossandon, P. Recabal, C. Acevedo, J. M. Flores, F. Marchant (Editorial Comment by V. A. Mezentsev)

362 Comprehensive Analysis of Etiology on the Prognosis of Urethral Strictures
R. Mathur, G. Aggarwal, B. Satsangi, F. Khan, S. Odiya (Editorial Comment by C. Schwentner)

371 Patient Positioning During Digital Rectal Examination of the Prostate: Preferences, Tolerability, and Results
F. R. Romero, A. W. Romero, R. Tambara Filho, T. B. Filho, F. C.Oliveira Jr. (Editorial Comment by J. Philip, A. Shtricker and O. Kaygisiz)

NEUROUROLOGY

380 Urinary Incontinence Following Surgery for bph: the Role of Aging on the Incidence of Bladder Dysfunction
H. Bruschini, R. Simonetti, A. A. Antunes, M. Srougi (Editorial Comment by P. Grise)

BASIC AND TRANSLATIONAL UROLOGIY

388 New Ex-vivo Organ Model for Percutaneous Renal Surgery
F. Imkamp, C. von Klot, U. Nagele, T. R.W. Herrmann

RADIOLOGY PAGE

395 The Elusive Renal Cell Carcinoma: Reversal Imaging of Arterial Phase to Improve Acuity
E. K. Lang, K. Zhang, Q. Nguyen, D. Thorner, E. Rudman

UROLOGICAL SURVEY

STONE DISEASE

398 The digital flexible ureteroscope: in vitro assessment of optical characteristics
M. Monga

CONTENTS - *continued from previous page*

STONE DISEASE - *continued*

399 **A comparison of treatment modalities for renal calculi between 100 and 300 mm2: are shockwave lithotripsy, ureteroscopy, and percutaneous nephrolithotomy equivalent?**
M. Monga

ENDOUROLOGY & LAPAROSCOPY

400 **Complications and conversions of upper tract urological laparoendoscopic single-site surgery (less): multicentre experience: results from the NOTES Working Group**
F. J. Kim

401 **Living donor kidney transplantation with multiple renal arteries in the laparoscopic era**
F. J. Kim

IMAGING

402 **Comparison of CT Urography and Excretory Urography in the Detection and Localization of Urothelial Carcinoma of the Upper Urinary Tract**
A. Prando

403 **Areas suspicious for prostate cancer: MR-guided biopsy in patients with at least one transrectal USguided biopsy with a negative finding-multiparametric MR imaging for detection and biopsy planning**
A. Prando

PATHOLOGY

405 **The Contemporary Concept of Significant Versus Insignificant Prostate Cancer**
A. Billis

406 **Treatment decision-making for localized prostate cancer: What younger men choose and why**
A. Billis

RECONSTRUCTIVE UROLOGY

407 **Management of Adult Anterior Urethral Stricture Disease: Nationwide Survey Among Urologists in The Netherlands**
S. P. Elliott

409 **The Cleveland Clinic experience with adult hypospadias patients undergoing repair: their presentation and a new classification system**
S. P. Elliott

410 **Cancer control and functional outcomes after radical prostatectomy as markers of surgical quality: analysis of heterogeneity between surgeons at a single cancer center**
A. Bohle

CONTENTS - *continued from previous page*

411 **Adverse renal outcomes in subjects undergoing nephrectomy for renal tumors: a population-based analysis**
A. Bohle

NEUROLOGY & FEMALE UROLOGY

412 **Tape Fixation: An Important Surgical Step to Improve Success Rate of Anti-Incontinence Surgery**
R. Miyaoka

413 **Bladder augmentation and urinary diversion in patients with neurogenic bladder: Non-surgical considerations**
R. Miyaoka

GERIATRIC UROLOGY

413 **The importance of pelvic lymph node dissection in the elderly population: implications for interpreting the 2010 national comprehensive cancer network practice guidelines for bladder cancer treatment**
L. O. Reis

415 **The illusion of prostate-specific antigen decline in patients with metabolic syndrome and insulin resistance**
L. O. Reis

PEDIATRIC UROLOGY

416 **Instituting a conservative management protocol for pediatric blunt renal trauma: evaluation of a prospectively maintained patient registry**
M. C. Wallis

417 **Tonsillectomy does not improve bedwetting: results of a prospective controlled trial**
M. C. Wallis

VIDEO

419 **Kelly A. Swords, Alejandro R. Rodriguez, Mark A. Rich, Hubert S. Swana**
K. A. Swords, A. R. Rodriguez, M. A. Rich, H. S. Swana (Editorial Comment by W. Kassouf)

International Braz J Urol

EDITOR'S COMMENT

The May – June 2011 issue of the International Braz J Urol presents original contributions. The editor's comment highlights some of those papers.

Doctor Romero and colleagues, from Hospital de Clínicas da Universidade do Paraná, Curitiba, Brazil, presented a study to evaluate the preferred position used by Brazilian Urologists to perform digital rectal examination. Two hundred patients answered a questionnaire while undergoing prostate cancer screening. The preferred position was modified lithotomy position reported by 63.4% of Urologists, and left lateral position reported by 42.7% of the patients. Total DRE time was lower in the standing-up position. Pain and urinary urgency scores were similar regardless of the position used, and bowel urgency score was higher in patients positioned kneeling while resting on the table with the hands. Patients were similar in terms of age and PSA level, but there was a significant difference between the standard deviations of estimated prostate weight in left lateral position. There was no difference in prostate asymmetry rate, positive DRE rate or incomplete palpation of the prostate rate among the different positions.

Dr. Joe Philip, Dr.Avraham Shtricker and Dr. Onur Kaygisiz provided editorials on this paper.

Doctor Bruschini and colleagues, from Federal University of Sao Paulo, Brazil, described the causes of incontinence in a group of men following surgery of BPH and analyzed the influence of age on the prevalence of bladder dysfunction. A total of 125 patients with urinary incontinence following surgical treatment for BPH were evaluated. A third group of 21 patients with incontinence following radical prostatectomy was used for comparison. Sphincter insufficiency was the most common etiology of urinary incontinence in the three groups of patients. However, bladder dysfunction was observed in 59.3%, 56.8% and 57.1% of patients who underwent transurethral resection, open prostatectomy and radical prostatectomy, respectively. A logistic regression model for the presence of bladder dysfunction showed that age was a statistically significant predictor. The chances of presenting bladder dysfunction rises 5.3% for each year added to patient age and patients older than 70 years have twice the chance of presenting it.

Dr. Philippe Grise, from Rouen University Hospital-Charles Nicolle, provided an editorial on this paper.

Doctor Nascimento and colleagues, from ABC Medical School, Santo Andre, SP, Brazil, compared the efficacy of three different formulations containing betamethasone valerate versus placebo in the topical treatment of phimosis. Two hundred and twenty boys aged three to ten with clinical diagnosis of phimosis were enrolled. Parents were instructed to apply the formula twice a day for 60 days and follow-up evaluations were scheduled for 30, 60 and 240 days after the first consultation. The results showed that the Betamethasone valerate 0.1%, 0.2% and 0.2% associated with hyaluronidase had equally higher results than placebo in the treatment of phimosis in boys from three to ten years-old. Patients initially with partial or no response can reach complete response after 60 days of treatment.

Doctor Drivalos and colleagues, from University of Athens, Greece, provided an interesting review on the role of integrins and cadherins in prostate carcinogenesis and evaluated the therapeutic potential of their manipulation.

Doctor Ossandon and colleagues, from Hospital Clínico Universidad de Chile, Chile, analyzed the predictive value of the Lithotripsy Table Height (LTH) in SWL outcome. Patient weight, height and age; stone location and size; number of shock waves delivered and LTH used were recorded. LTH was the only independent predictor of outcome. High success rates can be expected if LTH > 218. Patients with lower LTH presented a less effective shockwave conduction, therefore worse stone fragmentation and clearance. These findings may help improve patient selection for SWL therapy.

Dr. Mezentsev, from United Kingdom, provided an editorial on this paper.

Dra. Miriam Dambros
Editor in Chief

Review Article
International Braz J Urol
Vol 37 (3): 302-306, May - June, 2011

The Role of the Cell Adhesion Molecules (integrins / cadherins) in Prostate Cancer

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ABSTRACT

During prostate carcinogenesis the cellular adhesion molecules, i.e.; integrins and cadherins mediate aberrant interactions between glandular epithelial cells and the extracellular matrix. Several integrin α subunits are down-regulated, while β subunits are up-regulated. The expression of several cadherins and catenins has specific prognostic value. There is an association between the expression of the E-cadherin/catenin complex and high grade prostate cancer. Clinical trials evaluating the efficacy of integrin antagonists are ongoing with promising results. In this article we update the role of integrins and cadherins in prostate carcinogenesis and evaluate the therapeutic potential of their manipulation.

Key words: *cadherins; integrins; prostate cancer; review*
Int Braz J Urol. 2011; 37: 302-306

INTRODUCTION

During prostate cancer (PCa) progression, precursor lesions will eventually progress to incurable androgen-independent metastatic disease (1). Among the alterations described in prostate carcinogenesis are aberrant interactions between glandular epithelial cells and the extracellular matrix (ECM), mediated by cell adhesion molecules (CAMs). CAMs are divided into four major categories: cadherins, integrins, selectins and members of the immunoglobulin superfamily. The majority of studies focus on the abnormal expression of cadherins and integrins. In this article, we update current knowledge and their role in prostate carcinogenesis and evaluate the therapeutic potential of manipulating these molecules.

ROLE OF INTEGRINS AND CADHERINS

Integrins

Integrins are transmembrane glycoprotein receptors for ECM proteins. They are composed of two subunits α and β, the combination of which gives them a different specificity and function. Currently, 26 members of the family of integrins have been described (18 α and 8 β subunits) (2). The extracellular domain of integrins has binding sites and upon interaction with the ECM, they form links between cells and ECM components.

Cadherins

Cadherins are transmembrane glycoproteins that mediate intercellular adhesion in the

presence of extracellular calcium (3). Cell-cell adhesion in cadherins is mainly mediated by homotypic interactions. There are about 20 different cadherin molecules currently classified and the most extensively studied are: E- (epithelial), N- (neural) and P- (placental) cadherins. The cadherin complex is composed of the following components: cadherin, intracellular components associated with cadherin (i.e. catenins), and the cytoskeleton (i.e. actin). Catenins (main types are: α-, β- and γ-) are cytoplasmic proteins that interact with the intracellular domain of cadherins, providing anchorage to the microfilament cytoskeleton.

EXPRESSION OF INTEGRINS IN PCA

α subunit

High Gleason score has been correlated with low and/or negative expression of integrin subunit α_3 (4). The expression of α6 subunit diminishes with increasing histologic grade, especially at sites of contact with the basement membrane (5). PCa demonstrates decreased positive staining for subunit α_7, with a further decrease in metastatic disease (6). Other α subunits that have been found down-regulated include α_2, α_4, α_5, and αv (2). Interestingly, $\alpha_{II\beta}$ subunit is expressed only in PCa and not in normal tissue (7).

β subunit

Five β_1 variant subunits have been described and two of them (β_{1C} and β_{1A}) are expressed in normal prostatic epithelium. Decreased β_{1C} steady-state mRNA levels were detected in 94% of PCa specimens compared with normal samples (8). Subunit β_{1A} has been found to be up-regulated in human PCa, as well as, in TRAMP (transgenic adenocarcinoma of mouse prostate) models (9). The expression of β1A promotes cell proliferation and survival by increasing the expression of insulin-like growth factor receptor type 1 (IGFR-1) (9).

Upregulation of β_3 and β_6 integrin subunits has been described in PCa. Studies have demonstrated expression of the heterodimeric complexes $\alpha v\beta_3$ and $\alpha v\beta_6$, in PCa specimens in contrast with normal controls (10). Integrin $\alpha_v\beta_3$ has been demonstrated to increase cdc2 kinase activity and cdc2 levels in PCA (11). Higher cdc2 levels result in increased cell migration mediated by interaction of cdc2 with cyclin B2 and phosphorylation of caldesmon. It is known that cdc2 and caldesmon are localized in the membrane ruffles of motile cells.

EXPRESSION OF CADHERINS IN PCA

Cadherins

It has been demonstrated that tumor tissues exhibit decreased levels of E-cadherin (12). The expression of this cadherin was significantly correlated with histological differentiation and bones metastasis, but not with lymphatic or vascular invasion (13). Several studies have demonstrated an association between the expression of the E-cadherin/catenin complex and high grade PCa (14). Richmond et al. (15) demonstrated that abnormal expression of the E-cadherin/α-catenin complex was significantly correlated with Gleason score and with a lower survival outcome. In a recent study it has been demonstrated that there is a significant decrease of membrane expression of E-cadherin/β-catenin complex and an increase of cytoplasmatic and nuclear location of the same complex, in high Gleason score prostate cancer (16). A low E-cadherin to high N-cadherin expression switch has been correlated with progression of PCa and high mortality. N-cadherin is not expressed in normal prostate tissue; however, in PCa it has been detected especially in poorly differentiated areas (17). Also, in a number of metastatic lesions, N-cadherin has been found to be homogeneously expressed.

Prostatic tumor tissues were demonstrated to exhibit decreased levels of P-cadherin (12) even when compared with the reduced expression in benign prostatic hyperplasia (BPH). Furthermore, Cadherin-11 is expressed in the stroma of all PCa specimens. A recent study has show the absence of cadherin-10 in irregular cancer profiles in contrast with normal glandular profiles (18).

Catenins

Aberrant expression of all main three catenin types (α, β- and γ-catenin) has been associated with

extra prostatic extension (14). The expression of α-catenin seems to have prognostic value in both local and locally advanced PCa (14,15). The abnormality in α-catenin expression has been found to be associated with high Gleason score, perineural invasion and poor survival. Furthermore, the expression of α-catenin in PCa is up-regulated not only in comparison with normal tissue, but also when compared with the elevated expression in BPH. Hyperplastic prostates differ from normal prostates in the weaker immunoreactions of the two catenins β- and γ- , as well as, in the intracellular distribution of them (19). A recent study has demonstrated that the membranous overexpression of β-catenin is significantly associated with the metastatic prostate cancer cells in the bone and that the high frequency of expression suggests its involvement in the intercellular adhesion of the metastatic cells in the bone. Furthermore, studies have demonstrated that δ-catenin is overexpressed in PCa and is correlated positively with increasing Gleason scores (14).

CLINICAL IMPLICATIONS

Clinical trials that evaluate the efficacy of integrin antagonists as PCa therapeutics are ongoing. Cilengitide, a cyclic Arg-Gly-Asp peptide that inhibits $\alpha v\beta_3$ and $\alpha v\beta_5$, is a promising antagonist of αv integrins. A recent randomized phase II trial assessed the efficacy of different doses of Cilengitide in metastatic hormone refractory PCa patients (20). Forty-four patients were randomized to Cilengitide 500 mg or 2,000 mg IV twice weekly. Median number of cycles was three in both arms and at 6 months two patients on the 500 mg arm and five on the 2,000 mg arm had not progressed, while there was no grade 4 toxicity.

Monoclonal antibodies that inhibit αv integrins have also been studied, usually in conjunction with standard chemotherapy. CNTO 95, an αv integrin monoclonal antibody, was administered (10 mg/kg, once weekly) in combination with docetaxel and prednisone and appeared to be well tolerated (21). MEDI-522 is an antibody against the $\alpha_v\beta_3$ integrin that is being studied in a randomized phase II in combination with docetaxel, prednisone and zoledronic acid [unpublished data].

It is questionable if E-cadherin, β-catenin or α-catenin, can be used individually as prognostic markers. However, a combination of these proteins may be of clinical use as in other tumors (i.e. liver, colorectal). Apigenin is a plant flavone that blocks β-catenin signaling and has been found to suppress prostate carcinogenesis in TRAMP mice (22). Another study (23) has suggested that therapeutic strategies blocking cadherin-11 expression or function, such as anti-cadherin-11 antibodies, may be considered when applying androgen-ablation therapy, because androgen deprivation up-regulates cadherin-11 expression in PCa, and this may contribute to the metastasis of PCa. Finally, a study (24) examined the potential of an N-cadherin inhibitor: ADH1, in reducing tumor angiogenesis ex vivo and delaying tumor progression in vivo. Relevant results have demonstrated that ADH1, does not display antiangiogenic activity in a rat aortic ring assay or antitumor potential in a PC3 subcutaneous xenograft tumor model. Cytotoxic activity was detected in human umbilical vein endothelial cells, PC3, and Tsu-Pr1 cells.

CONCLUSIONS

The molecular pathways by which integrins and cadherins contribute to PCa progression need to be further elucidated. The expression of several cadherins and catenins has specific prognostic value that could be standardized. Finally, designing novel therapeutic approaches based on inhibiting integrin expression and/or downstream signaling is likely to be a promising strategy.

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
February 04, 2011

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Clinical Urology
International Braz J Urol
Vol 37 (3): 307-313, May - June, 2011

Sclerotherapy of Hydroceles and Spermatoceles with Alcohol: Results and Effects on the Semen Analysis

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ABSTRACT

Purpose: To evaluate the success rates of sclerotherapy of the tunica vaginalis with alcohol for the treatment of hydroceles and/or spermatoceles, as well as, evaluation of pain, formation of hematomas, infection and its effects in spermatogenesis .
Materials and Methods: A total of 69 patients, with offsprings and diagnosis of hydrocele and/or spermatocele, were treated during the period from April 2003 to June 2007. Semen analysis was obtained from patients who were able to provide us with samples. The sclerotherapy with alcohol at 99.5% was undertaken as outpatient procedure.
Results: The average volume drained pre-sclerotherapy was 279.82 mL (27 to 1145). The median follow-up was 43 months (9 to 80). A total of 114 procedures were performed on 84 units, with an average of 1.35 procedures / unit and an overall success rate of 97.62%. Of the 69 patients, 7 (10.14%) reported minor pain immediately after the procedure, 3 (4.35%) moderate pain and 2 (2.89%) intense pain. Post-Sclerotherapy spermograms revealed reduction of the parameters regarding: concentration, motility and morphology up to 6 months post procedure , with return to normal parameters 12th months after procedure.
Conclusions: Sclerotherapy of hydroceles and spermatoceles with 99.5% alcohol is an efficient procedure that can be perormed without difficulties, cost-effectiveness, with few side effects and which may be performed in patients who wish fertility.

Key words: *Testis; hydrocele; spermatocele; sclerotherapy; alcohol; spermatogenesis*
Int Braz J Urol. 2011; 37: 307-313

INTRODUCTION

Sclerotherapy has been gaining wider acceptance for the treatment of hydroceles, because of less invasive nature, low morbidity, with faster recovery time. Many different substances have been used as sclerosing agents in the treatment of hydroceles, with variable success rates and side effects (1-4).

Alcohol is easily acquired agent and it has been used as sclerosing agent for renal cysts, liver and thyroid for over two decades, achieving cure rates over 95%, with few side effects and no systemic toxicity. (5-7). Juliano et al. (8) reported use of alcohol as sclerosing agent in hydroceles with a 100% success rate and complain of pain in 26.6% of cases even with testicular cord block with local anesthesia. However, effects if abnormalities in spermatogenesis has not been studied.

In this current study, we report the success rate of sclerotherapy of the tunica vaginalis with alcohol for the treatment of hydroceles and spermatoceles, as well as, evaluation of pain, formation of hematomas, infection and its effects in spermatogenesis .

MATERIALS AND METHODS

A total of 75 patients, with children, with diagnosis of hydrocele or spermatocele, were

evaluated during April 2003 to June of 2007. The diagnosis was done by clinical examination and confirmed by scrotal ultrasonography. Of the 75 patients, 6 were excluded from the study, 5 for lack of follow-up and one death from procedure non-related cause.

The study included 69 pacients. The mean age was 61 y.o. (28-86 y.o.) . Eleven pacients had bilateral hydroceles, three had hydrocele and spermatocele on the same side and one patient had 2 hydroceles on the same side, totaling 84 units, 49 on the right and 35 on the left.

Of the 84 units treated, one patient had prior varicocelectomy, two had prior ipsilateral inguinal hernia repair, six had history of scrotal injury and 4 underwent open hydrocelectomy.. Semen analysis was analized from patients who were able to provide them before treatment.

Sclerotherapy was performed on an outpatient basis with the patient in normal clothing and without shaving. The patients were placed supine. The puncture area was identified by transillumination of the scrotum avoiding blood vessels. Patients was prepped with polyvinylpyrrolidone iodine and local anesthesia performed with 2% lidocaine hydrochloride without epinephrine. Hydroceles and spermatoceles were drained with a 16 gauge angiocatheter, connected to sterile intravenous tubing per gravity. Gentle manipulation of the scrotum resulted in the total emptying of the hydrocele. In cases when the color of the drainage was not tipical yellow/straw, samples of the fluid were sent for cytologyl to rule out malignancy. Immediatly after drainage, chloridrate of lidocaine at 2% was injected into the cavity between the vaginal tunics, in the proportion of 1% of the volume drained, up to a maximum of 10 mL to prevent pain due to the sclerotherapy,.

The sclerosing agent used was 99.5% alcohol. The volume injected was calculated to be 10% of the volume drained from the hydrocele. The maximum volume injected was of 50 mL of alcohol.

After the withdrawal of the angiocatheter, the site of the puncture was compressed for 5 minutes and the patient was discharged with a scrotal support. No analgesics or antibiotics were used.

The patients were clinically evaluated and semen analizis was collected from patients who were able to ejaculate at 1, 3, 6 and 12 months and annually after the sclerotherapy procedure. The cases of acute total relapse within 1 month post-ptocedure underwent a repeat sclerotherapy. The cases of partial relapse were managed conservatively ascertaining reduction of overallvolume. The cases of late relapse (after 1 month of the procedure) underwent a repeat sclerotherapyat the end of the third month post recurrence.

The following were studied:

- The percentage relapse of the hydrocele after one or more sclerotherapy;
- changes in the spermogram;
- evaluation of post-procedure complications, including, pain, incidence of hematomas, local infection and faster recovery.

Analysis of the Data

A variance analysis for repetitive measures (ANOVA) was used to analyse the sperm concentration (mL), motility, and the average Kruger´s index before and after treatment at 1,3,6 and 12 months by means of Bonferroni´s multiple comparisons (9).

$P < 0.05$ was considered significant.

RESULTS

The average volume drained at the first sclerotherapy was of 279.82 mL (27 to 1145). Of these, 67 samples had a yellow color, corresponding to hydrocele fluid (average volume of 277.3 mL, varying from 27 to 1069 mL; 7 units with a volume greater than 500 mL and two units with a volume greater than 1000 mL), 14 units of white color, corresponding to spermatoceles (average volume of 277.71 mL, varying from 35 to 793 mL; 3 units being greater than 500 mL) and 3 units of blood-colored liquid (average volume of 448 mL, varying from 56 to 1145 mL).

The median follow-up was of 43 months (9 to 80).

Of the 67 units yellowish color fluid, 51 units (76.12%) did not recur after the first application, 14 units (20.9%) after the second, and one unit (1.49%) after the third application. One unit was not cured even after the sixth application. Of note, ten of the 15 units that had a second application had red tinged-colored fluid on the occasion of the second puncture.

Of the 14 clear fluid units, 10 (71.43%) were cured at the first application, 2 (14.29%) were cured at the second and two (14.29%) were cured at the third application. Of the four units which required a second procedure, the two which presented white fluid were cured by the second application, and the two had yellow fluid which stopped after the third procedure.

Of the three units which presented red tinged bloody fluid, two (66%) were cured by the first application, and one required four applications.

A total of 114 procedures were undertaken on the 84 units, with an average of 1.35 procedures on each unit and an overall cure rate of 97.62%.

Of the 69 patients, 7 (10.14%) reported low intensity pain immediately after the procedure, 3 (4.35%) reported moderate intensity and 2 (2.89%) of high intensity pain. Analgesic (Butylescopolamine with oral Dipirone) was given to patients. Only 2 patients with moderate pain and one who had intense pain used the medication. All patients had pain relief 20 to 30 minutes after analgesic use.

None of the cases required chord block. Eight patients (11.59%) had low intensity pain and 1 moderate pain for a period of from 1 to 3 days. Of these, one patient took analgesic once and the other for 2 days. All patients reassumed normal activities after the procedures.

The sperm analysis before the treatment and one, three, six and twelve months after the sclerotherapy of 22 patients, are given in the Figures 1-3 and the Table-1 which follow.

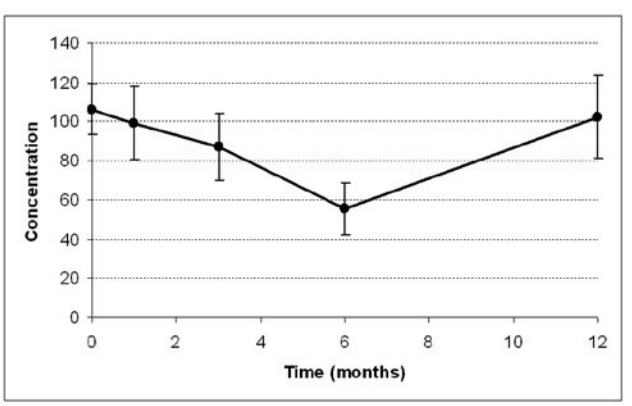
We compared sperm analysis before treatment, and 1, 3, 6 and 12 months after sclerotherapy.

The sperm analysis revealed decreased parameter values for concentration, motility and strict morphology (Kruger´s Index) up to the 6th months after the procedure, with no statistical significance. However, there was a return to the baseline sperm analysis parameters prior to the procedure after 12th months from the procedure.

DISCUSSION

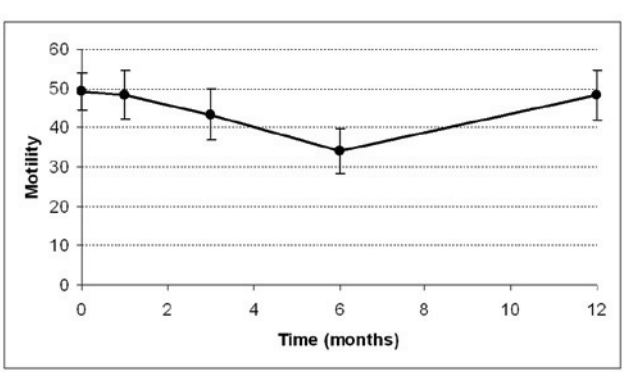
Hydrocelectomy is considered the gold standard for the treatment of hydroceles and remains to be the most efficient treatment modality (10), it is, however, a procedure which needs to be carried out in the operating room, often with spinal or general anesthesia, increasing the cost of care compared to sclerotherapy. Also social and medical recovery is approxinately 15 days post-

Figure 1 *- Variation of sperm Concentration per mL over time.*



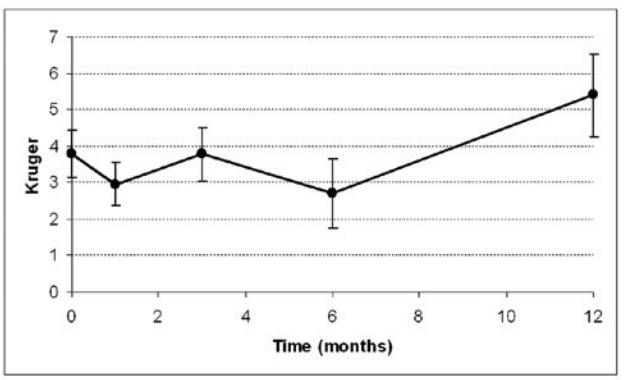
There was no statistically significance on the variation of the sperm concentration over time (p = 0.245).

Figure 2 *- Variation of sperm Motility over time.*



There was no statistically significance on the variation of the motility over time (p = 0.434).

Figure 3 *- Variation of Sperm Morphology (Kruger) over time.*



There was no statistically significance on the variation of morphology over time (p = 0.069).

hydrocelectomy (1). After sclerotherapy the return to normal activities is immediate (11).

The success rate after sclerotherapy varies from 20% (12) to 100% (2,3,8) depending on the sclerosing agent used. In this present study, the overall result of 98%, with an average of 1.3 applications, is highly satisfactory to the patient. In a previous study using 2.5% phenol, this rate was only achieved with 1.9 applications (11).

Pain occurs in almost all cases of hydrocelectomy and may last up to a month, while with sclerotherapy it is much less frequent and depends on the agent and the method of application. Agents such as Tetracycline causes most pain, requiring hospitalization for pain management (13,14). According to Juliano et al.(8), the use of alcohol resulted in slight pain in 26.6%, of patients who underwent sclerotherapy and testicular cord block with 2% xylocaine,. Twelve patients (17.39%) had pain during the procedure, 7 (10.14%) defined as mild pain, 3 (5.35%) moderate pain and 2 (2.89%) intense pain. Of these only 3 patients (2 had moderate pain and 1 intense pain) took medication with Butylescopolamine with oral Dipirone. All 3 patients had relief from their pain within 20 to 30 minutes. The best effective regional anesthesia is the intra vaginal testicular block since we inhibit the sensory pain receptors in the tunica vaginalis. (15). Eight patients(11%) had pain during the first few days after the procedure, seven had mild pain and one moderate pain for 1 to 3 days. No patients had to interrupt their daily normal activities.

Hematoma after classic hydrocelectomy was reported in up to 40% of patients in Moloney`s comparative study (1), but in modified hydrocelectomy this complication has been reduced (16,17). In sclerotherapy this complication rate is much lower, varying between 0 and 5% (18). In this present study there was no single case of hematoma. Small puncture guided by transillumination and local pressure after the procedure probably decrease the rate of this complication.

Fever reported by Yamamoto et al (3) associated with the use of OK-432 in 75% of the cases, was not seen in our patients. This side effect depends on the type of sclerosing agent used, and occurs also with the use of Etanolamine in 15% of patients (19), with sodium Tetradecyl Sulfate in up to 9% (20) and with Tetracycline in up to 7.5% (21).

Table 1 *- Concentration of spermatozoids per ml, motility and Kruger´s índex before treatment and one, three, six and twelve months after the treatment with sclerotherapy in 22 patients. Average value and p value on each occasion in comparison with those prior to treatment.*

	Before treatment	1 month	3 months	6 months	12 months
Concentration	106.22	99.10 (0.206)	87.20 (0.20)	55.33 (0.071)	102.33 (0.985)
Motility	49.37	48.44 (0.695)	43.39 (0.283)	34.15 (0.138)	48.33 0.856)
Kruger´s Index	3.79	2.94 (0.176)	3.78 (0.454)	2.69 (0.694)	5.40 (0.093)

Local infection after schlerotherapy was reported by Musa18 in 12% of his cases, but no similarly high rate has been confirmed by other authors. In this present study we had no single case of infection.

The assessment of sclerosing agents on spermatogenesis is important. Studies should include patients who have offsprings. Osegbe (22) reported a reduction of 78% in the concentration of the sperm analysis 6 months after sclerotherapy of hydrocele with tetracycline. In our earlier research, in a study which compared hydrocelectomy with sclerotherapy we found a slight reduction in the concentration of sperm per milliliter at 6th and 12th months, with no statistical significance. The reduction occurred on both groups that underwent sclerotherapy or hydrocelectomy (11). In this present study we found a reduction in the parameters up to 6t months, with no statistical significance, but at the 12th month these abormalities returned to baseline parameters.

CONCLUSIONS

We conclude that sclerotherapy of hydroceles and spermatoceles with 99.5% alcohol is a procedure of great efficiency, easy application, is cost-effective, with few side effects , and it may be applied to patients that desire fertitlity in the future.

ABBREVIATIONS

ML - Milliliter; % - percent

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
November 16, 2010

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EDITORIAL COMMENT

In this article, Chen JS et al. tried to study the efficacy of sclerosis of the tunica vaginalis with 99.5% alcohol regarding the cure rate of hydroceles and spermatoceles, post- procedural pain, hematoma, infection and effect on spermatogenesis. They found that this procedure is of great efficiency, easy application, economic, with few collateral effects and which may be applied to persons who have not yet constituted their families.

Aspiration of the hydrocele fluid and sclerotherapy may be simple, safe and inexpensive, but less effective than hydrocelectomy regarding patient satisfaction and the overall success rate (1). Many sclerosing agents have been used, such as Tetradecyl sodium sulfate, Tetracycline, adhesive fibrin, Quinacrine, Polidocanol, absolute alcohol and talc powder. However, the results have been inconsistent (2).

Standard hydrocelectomy may cause postoperative discomfort, temporary limitation of normal activities and complications, such as hematoma, infection, persistent swelling, chronic pain and decreased fertility (3).To avoid these postoperative discomfort, the pull-through technique advocated by Onol et al., enables the surgeon to remove large hydrocele sacs through a small incision and with minimal dissection under direct vision of the testicular structures (3). A new minimally access hydrocelectomy through 2 cm scrotal skin incision and excision only of disc of the parietal tunica vaginalis about double of the skin incision dimension was recently published with encouraging outcome (4).

Finally, Hydrocelectomy is practiced as the gold standard technique for the treatment of hydrocele worldwide. Aspiration and sclerotherapy is cheap, less invasive and safe compared to hydrocelectomy. However, the outcomes are inconsistent because of lack of uniformity in methods and sclerosing agents used (5). So, Aspiration and sclerotherapy is a viable first-line therapeutic option in the management of hydroceles (1).

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Clinical Urology
International Braz J Urol
Vol 37 (3): 314-319, May - June, 2011

Topical Betamethasone and Hyaluronidase in the Treatment of Phimosis in Boys: a Double-Blind, Randomized, Placebo-controlled Trial

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ABSTRACT

Purpose: To compare the efficacy of three different formulations containing Betamethasone Valerate versus placebo in the topical treatment of phimosis. As a secondary goal, we compared the outcomes after 30 and 60 days of treatment.
Materials and methods: Two hundred twenty boys aged 3 to 10 years old with clinical diagnosis of phimosis were enrolled. Patients were randomized to one of the following groups: Group 1: Betamethasone Valerate 0.2% plus Hyaluronidase; Group 2: Betamethasone Valerate 0.2%; Group 3: Betamethasone Valerate 0.1% or Group 4: placebo. Parents were instructed to apply the formula twice a day for 60 days and follow-up evaluations were scheduled at 30, 60 and 240 days after the first consultation. Success was defined as complete and easy foreskin retraction.
Results: One hundred ninety-five patients were included at our final analysis. Group 1 (N = 54), 2 (N = 51) and 3 (N = 52) had similar success and improvement rates, all treatment groups had higher success rates than placebo(N = 38). After 60 days of treatment, total and partial response rates for Groups 1, 2 and 3 were 54.8% and 40.1%, respectively, while placebo had a success rate of 29%. Success and improvement rates were significantly better in 60 days when compared to 30 days.
Conclusions: Betamethasone Valerate 0.1%, 0.2% and 0.2% in combination with Hyaluronidase had equally higher results than placebo in the treatment of phimosis in boys from three to ten years-old. Patients initially with partial or no response can reach complete response after 60 days of treatment.

Key words: *phimosis; child; therapy; Betamethasone 17-valerate*
Int Braz J Urol. 2011; 37: 314-319

INTRODUCTION

Phimosis is an usual condition in which the foreskin cannot be retracted passed the glans penis (1). At birth, there is usually a physiologic phimosis or inability to retract the foreskin because congenital adhesions exist between the prepuce and the glans. By 3 years of age, 90% of foreskins can be retracted, and less than 1% of males have phimosis by 17 years of age (2).

In the last decades, the first line treatment was circumcision. In the 90's, many authors introduced topical steroids as a nonsurgical alternative in the treatment of phimosis. Potential advantages included less trauma and lower cost (3), avoidance of anesthesic and surgical complications such as hemorrhage, pain, infection, urinary obstruction and esthetic problems (4).

A variable number of topical steroids have been proposed (5). Triancinolone, Hydrocortisone, Betamethasone, Clobetasone and Monometasone, among others, have been used with varied results and different therapeutic schemes. Reported success rates range from 65% to almost 90% (Table-1). However, double-blind, randomized, placebo-controlled trials for the treatment of phimosis are

Table 1 - *Placebo-Controlled, Randomized Trials with topical steroids in the treatment of phimosis*

Author / Year	Steroid	Steroid potency	N	Follow-up (months)	Success Topical Steroid X Placebo	p
Letendre (1) 2009	Triamcinolone 0.1%	High (Level 3)	43	2	76% X 39%	0.0086
Espósito (5) 2008	Mometasone furoate 0.1%	Very High (Level 2)	240	20 (6-30)	65.8% X 16.6%	< 0.0001
Pileggi (4) 2007	Mometasone furoate 0.1%	Very High (Level 2)	110	2	88% X 52%	< 0.05
Lee (12) 2006	Hydrocortisone	Low (Level 7)	78	1	89.7% X 20.5%	< 0.05
Lund (14) 2005	Betamethasone	Very High (Level 2)	137	18	74% X 44%	< 0.05
Yang (10) 2005	Valerate betamethasone 0.06% X Clobetasone butyrate 0.05%	Very High (Level 2)	70	4.3 X 19.1 Weeks	81.3% X 77.4%,	0.63
Yilmaz (11) 2003	Betamethasone 0.05%	Very High (Level 2)	98	2	68% X 37.5%	-
Lindhagen (15) 1996	Propionate clobetasol	Highest (Level 1)	30	2	77% X 50%	-
Zampieri (13) 2005	Betamethasone 0.05%	Very High (Level 2)	247	6	96%	< 0.001
Freitas (6) 2006	Betamethasone 0.2% + Hyaluronidase	Very High (Level 2)	427	9	92.1%	-
Marques (16) 2005	Betamethasone 0.5%	Very High (Level 2)	70	4	94.2%	-

scarce, and very few were found reporting the association between Betamethasone and Hyaluronidase. According to Freitas (6), "Hyaluronidase is an enzyme obtained from bovine testicles that acts on Hyaluronic acid, reducing intercellular viscosity and causing the tissue to become more permeable to the absorption of drugs" (p. 384). Favorito (7) reports that Betamethasone plus Hyaluronidase alters the elastic fibers in the prepuce-glans mucosa, allowing their separation.

Today, reasons for performing circumcision include the recurrent balanoposthitis, pathological phimosis defined as non-retractile, scarred foreskin, persistent physiological phimosis that wasn't resolved by other means after 10 years of age, and Balanitis Xerotica Obliterans (8).

We have designed a double-blind, randomized, placebo-controlled trial evaluating the efficacy of three different formulations containing Betamethasone Valerate and placebo in the topical

treatment of phimosis and evaluated the complete and partial response rates after 30 and 60 days of treatment.

MATERIALS AND METHODS

From August 2006 to November 2007, 220 boys aged three to ten years old referred from primary care facilities to our clinic with clinical diagnosis of phimosis were evaluated to entry at our prospective double-blinded study, which was previously approved by the Ethics Committee of the ABC Medical School. Detailed information about treatment options and an Informed Consent were provided to the parents. Exclusion criteria were a) previous treatment; b) signs of current Balanitis or Balanitis Xerotica Obliterans (foreskin or meatus stenosis, hypocromia, foreskin inflammatory process); c) recurrent UTI (surgery is indicated in these cases); d) non-agreement with any of the Informed Consent terms and e) non compliance to treatment procedures.

Patients were randomized to one of the four groups of intervention according to a computer-generated random choice determined by a research assistant: Group 1 (Betamethasone Valerate 0.2% + Hyaluronidase), Group 2 (Betamethasone Valerate 0.2%), Group 3 (Betamethasone Valerate 0.1%) or Group 4 (cream placebo group). The four groups format would allow the researcher to determine the optimal formulation containing Betamethasone, considering that the formulations used were the ones available in the market.

All patients were evaluated by the same pediatric urologist on all consultations, to avoid biases in outcome interpretation. On the first consultation, boys were evaluated and phimosis type was assessed according to the Kayaba classification (9) as shown in Table-2. Patients with phimosis type 4 were included because even if this is a lesser degree of the disease, however it is an abnormal condition and needs treatment. The assigned ointment was provided by a research assistant and parents were instructed to use a small amount twice a day for 60 days applying subtle traction on the foreskin (retracting maneuvers). The formulations were specifically designed for the study by the same pharmacy. Follow-up consultations were scheduled at 30 and 60 days. Patients whose treatments were successful were also scheduled to a follow-up consultation 180 days after the first consultation. Compliance with the treatment, adverse effects, complications, and type of phimosis were then assessed. Data collection was performed by a third person based on patients' files.

Cure (success) was defined as complete, easy foreskin retraction with total exposure of the glans after 60 days of treatment. In patients who were not cured, or had partial response were defined as improved degree of phimosis to a better level according to Kayaba's classification. Recurrence was defined as presence of phimosis at 240 post-operative days. For the patients that weren't cured, surgical treatment was performed.

Cure, improvement, complication, and drop-out rates were assessed for each treatment group at each consultation. Statistical analysis was performed using the Fisher's Exact and One-Way ANOVA tests and p values ≤ 0.05 were considered for statistical differences.

Table 2 - *Classification of prepuce type showing presence or absence of tight ring (9).*

Type I	No retraction of prepuce at all
Type II	External urethral meatus exposure only
Type III	Glans exposure halfway to sulcus of corona
Type IV	Glans exposure to above corona at site of preputial adhesion
Type V	Easy exposure of whole glans

RESULTS

Two hundred twenty patients were enrolled, of whom 195 were included at our final analysis. Eleven patients (5%) were excluded due to non-compliance with the application of the ointment and 16 patients (7.3%) were lost to the follow-up but were considered in the analysis before they dropped out. Exclusion and drop-out rates were no different among the four groups of treatment ($p = 0.232$ and 0.939, respectively). Eight children dropped out of treatment before the 30 days consultation, 6 children dropped out between the 30 days and 60 days consultation. Two children who were cured at 60 days did not attend to the follow up consultation, at 180 days.

Pre-treatment analysis of phimosis (9) indicated type I in 128 patients (58.2%), II in 41 patients (18.6%), III in 47 patients (21.4%) and IV in 4 patients (1.8%).

Mean and median age of the patients were 5.1 and 5.0 years old, respectively (SD = 2.02). No difference was observed among the 4 Groups of treatment regarding mean age ($p = 0.088$) or phimosis type ($p = 0.88$).

At 30 and 60 days, groups 1, 2, and 3 had higher cure and improvement rates than group 4 (placebo) ($p < 0.001$) (Table-3). No difference was noticed among groups 1, 2, and 3 related to total and partial response rates after 30 or 60 days ($p = 0.362$ and $p = 0.666$, respectively).

The results for groups 1, 2, and 3 together after 30 days of treatment had a complete response in 31.3% and partial response in 55.8%. After 60 days, these figures had improved to 54.8% and 40.1% respectively ($p < 0.001$).

Complete and partial response rates according to the pre-treatment phimosis types were similar between the groups, as shown in Table-4 ($p = 0.074$).

Minor complications were observed in 3 patients (1.4%): 2 balanoposthitis and 1 paraphimosis, which could be manually reduced. These 3 patients could complete the 60-day course of treatment successfully and were considered in the final analysis. Recurrence was observed in 5 cases (2.4%). Neither complications nor recurrence rates were related to the group of treatment or to the degree of phimosis ($p = 0.134$).

DISCUSSION

In the last decade there has been an increasing interest all over the world to use topical steroid as an alternative to the standard circumcision treatment.

Our data shows that betamethasone is effective in the treatment of phimosis, when compared to placebo, regardless of the pre-treatment type, confirming what was observed by Freitas (6). All three groups were superior to placebo at 30 or 60 days after the treatment was initiated. However, the association of Betamethasone plus Hyaluronidase was not superior to Betamethasone alone in 0.1% or 0.2% concentrations. This finding shows that the addition of Hyaluronidase does not improve patients' responses, probably indicating that the alteration of the elastic fibers that cures phimosis (6) is due to the steroid alone. However, this study's sample may not be powerful enough to detect differences between 0.1% and 0.2% concentrations of Betamethasone.

It is important to point out that the concentration we used was higher than the majority of similar studies. For example, studies by Yang (10) and Yilmaz (11) used Betamethasone at a 0.06% and 0.05%, while in our study the ointment had at least 0.1% concentration. We choose a higher concentration, as Freitas et al. (6) did, justified by the perspective of a more effective treatment with a small rate of side effects, since lower concentrations seem to be less effective. Even then, the cure rates were lower than most of the works presented in Table-1, such as Pilegi's (4) and Lee's (12), that reached a cure rate close to 90% percent. However, in these cases, partial responses (e.g. non complete exposure of the glans or remaining adhesions) were considered success. Therefore, the lower cure rates we achieved was probably due to two aspects: a more strict criteria for cure, that applied only to patients with total exposure of the glans with no reminiscent adherences; and a more strict inclusion criteria, that excluded children younger than three years-old, who present spontaneous resolution of phimosis in 90% of the cases (2).

Table 3 - *Outcome after 60 days according to treatment Groups (number of patients and percentage).*

Outcome at 60 days				
Groups	Cure	Partial **Response**	No Change	n
1	31(57.4%)	19(35.2%)	4(7.4%)	54
2	30(59.0%)	19(37.3%)	2(3.7%)	51
3	25(48%)	25(48%)	2(4%)	52
4	11(29%)	8(21%)	19(50%)	38
Total	**97(49.8%)**	**71(36.4%)**	**27(13.8%)**	**195**

Table 4 - *Outcome according to pre-treatment phimosis type.*

	Outcome after 60 days			
Phimosis Type	**Cure (%)**	**Partial Response (%)**	**No Change (%)**	**n**
I	48 (53%)	41 (46%)	1 (1%)	90
II	15 (54%)	12 (43%)	1 (4%)	28
III	8 (33%)	10 (41%)	6 (25%)	24
IV	3 (100%)	0	0	3

The similar cure and improvement rates in all 4 types of phimosis correspond to the work of Zampieri (13), in which the application of betamethasone along with foreskin stretching had similar results to all types of phimosis. Although phimosis type III seems to have a lower cure rate in absolute numbers, it was not statistically different from the other types of phimosis.

According to our findings, it is recommended to extend the treatment period to 60 days, since the results at this time were significantly better than at 30 days. Lund (14) also used a similar treatment period (4 weeks plus another 4 weeks for nonrespondents), reaching an optimal cure rate after 8 weeks of treatment. The same ideal time span was reported by Freitas (6). According to their results and ours, it seems that 60 days (or 8 weeks) are a secure and effective time for this topical treatment before considering surgical alternatives.

Recurrence rates at 240 days (2.4%) were lower than other studies with similar methods (8). However, the shorter follow-up period is a limitation of this study, since it could be extended to one year to better assess long term treatment failures.

Dropout rates were lower between 30 and 60 days than before 30 days, indicating that the two month period did not affect treatment compliance. Also, there weren't significant complications in the period between the second and third consultations. The abandonment rates were relative low, since we had 7.3% of children leaving treatment, while Lund (14) had 18% of abandonment, although their follow up period was longer. Our data confirms that, since it is a less invasive treatment that has a good rate of cure and improvement, with few complications and good adherence by the family, the topical treatment should be considered as the first therapeutic option.

CONCLUSIONS

Betamethasone Valerate at 0.1%, 0.2% and 0.2% associated with Hyaluronidase had higher cure rates than placebo in the treatment of phimosis in boys aged three to ten years old and is related to a negligible rate of side effects and of recurrence. The association of Betamethasone plus Hyaluronidase had similar results as Betamethasone alone in 0.1% or 0.2% concentrations in this period of treatment. Patients who showed no response or partial response after 30 days can show complete response after 60 days of treatment, without compromising the rate of adherence to treatment.

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
January 04, 2011

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Clinical Urology
International Braz J Urol
Vol 37 (3): 320-327, May - June, 2011

Oncological and Functional Outcomes Following Open Radical Prostatectomy: How Patients May Achieve the "trifecta"?

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ABSTRACT

Purpose: The desirable outcomes after open radical prostatectomy (RP) for localized prostate cancer (PC) are to: a) achieve disease recurrence free, b) urinary continence (UC), and c) maintain sexual potency (SP). These 3 combined desirable outcomes we called it the "Trifecta". Our aim is to assess the likelihood of achieving the Trifecta, and to analyze the influencing the Trifecta .
Materials and Methods: A total of 1738 men with localized PC underwent RP from 1992-2007 by a single surgeon. The exclusion criteria for this analysis were: preoperative hormonal or radiation therapy, preoperative urinary incontinence or erectile dysfunction, follow-up less than 24 months or insufficient data. Post-operative Trifecta factors were analyzed, including biochemical recurrence (BR).. We defined: BR as PSA $\geq$ 0.2 ng/mL, urinary continence as wearing no pads, and sexual potency as having erections sufficient for intercourse with or without a phosphodiesterase-5 inhibitor.
Results: A total of 831 patients met the inclusion criteria. The mean age of the entire cohort was 59 years old. The median follow-up was 52 months (mean 60, range 24-202). The BR, UC and SP rates were 18.7%, 94.5%, and 71% respectively. Trifecta was achieved in 64% at 2 year follow-up, and 61% at 5 year follow-up. Multivariate analysis revealed age at time of surgery, pathologic Gleason score (PGS), pathologic stage, specimen weight, and nerve sparing (NS) were independent factors.
Conclusions: Age at time of surgery, pathologic GS, pathologic stage, specimen weight and NS were independent predictors to achieve the Trifecta following radical prostatectomy. This information may help patients counseling undergoing radical prostatectomy for localized prostate cancer.

Key words: *Radical Prostatectomy; treatment outcome; prostate cancer; recurrence*
Int Braz J Urol. 2011; 37: 320-327

INTRODUCTION

Open Radical prostatectomy (RP) is an effective treatment for clinically localized prostate cancer. In the era of PSA screening, patients are often diagnosed with low grade, low stage prostate cancer. Consequently, disease free survival (DFS) rates approach 90% at 5 years post TP. (1). Other approaches, like radiation therapy, provide similar DFS. Treatments with comparable DFS rates should be evaluated in terms of quality of life (QoL) including continence and erectile function, as well as cancer control.

Better knowledge of pelvic anatomy, improvements in surgical technique (2), and early detection (PSA), have led to improved oncological results and reduced adverse functional outcomes (3). Full continence, erectile function, and absence of biochemical recurrence (BR) represent the Trifecta, the most desired outcomes following TP (4). BR is assessed with serial serum PSA measurements. However, QoL outcomes being subjective in nature are tabulated as an objective endpoint. Although the methodology of assessing the outcome is critical, there are no universally accepted guidelines for

quantifying and reporting urinary incontinence and erectile dysfunction (ED) after RP.

Several endpoints have been used to evaluate postoperative UC. The rates following RP vary from 70-95% (5-10). Although different definitions have been applied, urinary incontinence is more accurately reported than ED given that it can be quantified and qualified (pads or no pads, leakage or not).

Assessment of erectile function lacks uniformity. Erectile function encompasses different factors: partial recovery, adequate rigidity, ability for intercourse and overall sexual satisfaction. In addition, reported rates need to be correlated with age, preoperative function, oncologic outcomes, surgical technique and use of medication or devices to assist in the treatment of ED.

The aim of our study is to present our Trifecta results and to analyze the factors that may influence these results. The ultimate clinical objective is to better inform patients by assessing each individual's risks and his probability of achieving Trifecta using preoperative and postoperative variables.

MATERIALS AND METHODS

A total of 1738 men with localized PC underwent RP from 1992-2007 by a single surgeon (MSS). RP is performed through a Pfannenstiel incision with bilateral standard pelvic lymphadenectomy and "en-bloc" resection of the prostate. A unilateral or bilateral nerve-sparing approach was performed when feasible (3). The exclusion criteria for this study were: neo-adjuvant hormonal (n = 310) or radiation therapy (n = 24), preoperative urinary incontinence (n = 6) or erectile dysfinction (n = 320), follow-up less than 24 months or incomplete data on UC, SP or BR (n = 247). Our final cohort included 831 patients. The factors affecting UC, SP or BR were analyzed. We defined: a) BR as PSA ≥ 0.2 ng/mL, b) urinary continence as wearing no pads and c) sexual potency as having erections sufficient for intercourse with or without phosphodiesterase-5 inhibitors. The ability to perform a nerve sparing procedure was assessed from the surgeon's operative note defining whether one or both neurovascular bundles were spared. A procedure was recorded as "non-nerve sparing" when there was no intention to spare the neurovascular bundles and when there was uncertainty the nerves were preserved.. Quality of Life (QoL) data was collected during each clinical encounter and subsequent chart review. During the past 2 years, patients completed the sexual health inventory for men (SHIM) (11) and International Consultation on Incontinence Questionnaire (ICIQ), (12) on each postoperative visit and data was collected. Patients were considered potent if their SHIM score was 3-5 on the third question of the questionnaire. Urinary continence was defined as bother score of "0" and/or no pads. A patient was considered to have achieved Trifecta if he had UC, SP and was free of BR.

Risk stratification was performed using the D'Amico criteria (13,14). Low risk included clinical stage T1c or T2a, PSA < 10 ng/mL and biopsy Gleason sum (GS) ≤ 6. Intermediate risk included clinical stage T2b, PSA between 10 and 20 ng/mL or biopsy GS of 7. High risk was defined as clinical stage T2c or more, PSA > 20 ng/mL or biopsy GS ≥ 8.

Statistical analysis was done using the SPSS software version 17. A two-sided p-value of 0.05 or less was considered statistically significant. Data were expressed as numerical values and percentages for categorical variables; and as mean ± SD for continuous variables. For normally distributed data, analysis of variance (ANOVA) was used to analyze overall differences. For data that was not normally distributed, the non-parametric Kruskal-Wallis test was used to analyze overall differences. Chi-square or Fisher's exact test was used to compare the categorical data among the groups. Kaplan-Meier analysis was performed to estimate the long term outcome regarding biochemical recurrence (BR). Univariate and multivariate analyses were performed using logistic regression models with the intent of testing the independent effect of each predictor on the outcomes of interest that represent the Trifecta. Predictors included age at surgery, PSA, clinical stage, biopsy Gleason sum, pathologic Gleason sum and stage, nerve sparing procedure, and specimen weight.

RESULTS

A total of 831 patients were included in this analysis. Clinical and pathologic patient characteristics are shown in Table-1. Mean age was 59 (range 35 to 77) and median preoperative PSA was 5.8 ng/mL. 68% of patients had biopsy Gleason score of 6 or less, and 85% were clinical stage ≤ T2a. Unilateral and bilateral nerve sparing procedures were performed in 17.5% and 63.5% of patients respectively, and 19% of patients were considered to have had a non-nerve sparing procedure. The following rates for pathologic Gleason sums were recorded: 49% for Gleason 6, 42% for

Table 1 - *Preoperative and postoperative patient characteristics (n = 831).*

Age	
Mean (median)	59.5 (60)
Range	35 - 77
< 65 years	652 (8.5%)
> 65 years	179 (21.5%)
Preoperative Biopsy Gleason score	
6 or less	568 (68.5%)
7	212 (25.5%)
8 or more	51 (6%)
Clinical T stage	
T2a or less	706 (85%)
T2b	84 (10%)
T2C or more	41 (5%)
PSA (ng/mL)	
Mean (median)	6.9 (5.7)
0 -4.0 ng/mL	132 (15.9%)
4.1 – 10.0 ng/mL	582 (70.0%)
> 10.0 ng/mL	117 (14.1%)
Nerve sparing	
None	159 (19%)
Unilateral	147 (17.5%)
Bilateral	525 (63.5%)
Risk group stratification	
Low	436 (52%)
Intermediate	288 (35%)
High	107 (13%)
Pathologic stage	
T2	688 (82.8%)
T3a	88 (10.6%)
T3b	55 (6.6%)
Pathologic Gleason	
6 or less	409 (49%)
7	350 (42%)
8 or more	72 (9%)

Gleason 7 and 9% for Gleason 8-10. 83% of the patients were pT2.

After a median follow-up of 52 months (mean 60, range 24-202), the rates of BR was 19%; SPwas 71%; and UC was 94.5%. When stratifying patients according to the preoperative D'Amico classification, BR occurred in 12% of the low risk group, 21% in the intermediate group and 38% in the high risk group ($p < 0.001$). The Kaplan-Meier estimated biochemical recurrence free survival of 92% at 2 years post-op, 84% at 5 years and 66% at 10 years.

The overall UC rate had median follow-up of 54 months and UC rate of 94.5%. The UC rates were not significantly different ($p = 0.90$) in the low (94%), intermediate (94%) and high risk (93%) groups. The overall postoperative SP rate was 71%. The potency rates in the low, intermediate and high risk groups were 74%, 69% and 67% respectively ($p = 0.28$).

Trifecta was achieved in 56% of patients in the entire cohort with a median follow-up of 54 months, in 64% at 2 years (n = 831) and in 61% at 5 years (n = 352). Trifecta rates in the low, intermediate and high risk groups were 62%, 52% and 43% respectively ($p < 0.001$) (Table-2). Patients with pathologic GS ≥ 8 infrequently achieved Trifecta due to a high rate of BR (33%) or a combined BR and ED (40%). In patients with pathologic Gleason 7 or less, the primary reason for not achieving Trifecta was due to ED.

We then performed univariate and multivariate analyses at the 2 year endpoint. In univariate analysis, the factors affecting the Trifecta was age, preoperative PSA, biopsy GS, NS procedure, specimen weight, pathologic GS and pathologic stage (all $p \leq 0.001$) (Table-3). Clinical stage and BMI did not achieve statistical significance in predicting Trifecta in a univariate analysis. In multivariate analysis, age, NS procedure, specimen weight, pathologic GS and pathologic stage were independent predictors of achieving the Trifecta. Individual preoperative variables such as PSA, biopsy GS and clinical stage did not predict Trifecta in our analysis (Table-3). However, when stratified according to the D'Amico classification, patients with low risk features were more likely to achieve Trifecta (all $p < 0.016$) (Table-2).

DISCUSSION

Since the advent of PSA, patients are more commonly diagnosed with low grade and low stage prostate cancer. Radical prostatectomy is associated with high long term survival rates with the ultimate goal to maximize QoL and eradicate cancer. UC and erectile function are the two most frequent QoL alterations associated with RP. Improvements in understanding anatomy and surgical technique have refined this procedure so that blood loss is now well controlled, and the surgeon can focus on aspects of surgery to maximize continence and potency. The primary objective of RP is to eradicate prostate cancer but success is dependent on tumor stage and grade. Once prostate cancer control is achieved, the patient will focus on UC and SP. Therefore, the Trifecta represents the optimal desired outcome. Investigations regarding each individual endpoint,have been reported but only few studies have addressed these together.

Table 2 - *Overall rates for BR, potency, continence and trifecta at median follow-up of 54 months according to the D'Amico preoperative risk group stratification.*

	D'Amico risk group stratification			
	Low (%)	**Intermediate (%)**	**High (%)**	P
BR	12.7	22.4	40.8	< 0.001
Potency	73.5	69.5	67.0	0.28
Continence	93.7	94.2	93.1	0.902
Trifecta				
Overall	62.4	52.4	43.0	< 0.001
2 year	67.9	60.1	55.1	0.016
5 year	65.4	56.9	49.5	0.004

Table 3 - *Univariate and multivariate analysis of clinical and pathologic factors affecting Trifecta.*

	Univariate	Multivariate		
Factor	**P**	**P**	**Odds ratio**	**95% CI**
Age	< 0.001		0.003	
		-	referent	
		0.008	0.593	0.402-0.875
Preop Biopsy GS	< 0.001			
6 or less(ref)		-	-	
7		NS	-	
8 or more		NS	-	
Clinical T stage				
T2a or less(ref)	0.67	-	-	
T2b				
T2C or more				
PSA	NS		NS	
Nerve sparing	< 0.001			
Bilateral		-	referent	
Unilateral		0.001	0.505	0.337-0.757
None		< 0.001	0.408	0.268-0.622
Wet weight of prostate	< 0.001			
< 50		-	referent	
50 or more		0.009	0.647	0.466-0.897
Pathologic stage	< 0.001			
T2		-	referent	
T3a		NS	0.936	0.566-1.549
T3b		< 0.001	0.208	0.096-0.453
Pathologic GS	< 0.001			
6 or less		-	referent	
7		0.009	0.644	0.462-0.897
8 or more		< 0.001	0.256	0.133-0.493

GS: Gleason sum; NS: Not significant

Our cohort included 831 men with a median follow-up of 52 months. Trifecta at 2 and 5 years was achieved in 64% and 61% of patients respectively. When stratifying patients in subgroups using the D'Amico classification (14), there was a significant decrease from the low risk to the high risk category in the achievement of Trifecta at 2 years (15%) and 5 years (16%) with a 15% and 16% difference respectively (Table-2). The postoperative SP affected the most for not achieving Trifecta in the low and intermediate risk groups (74% and 70% respectively). In the high risk group, failure of Trifecta was mainly due to BR (41%), while SP was similar across the risk groups (p = 0.28).

Patient and couple counseling needs to done according to evidenced-based facts using preoperative and postoperative parameters (15). In multivariate analysis, age, pathologic GS, pathologic stage, specimen weight and NS procedure were independent factors affecting Trifecta. Individual preoperative parameters were not significantly associated with achievement of Trifecta in

the multivariate analysis. However, stratification of patients into preoperative risk groups demonstrated that higher risk groups were less likely to achieve Trifecta at 2 and 5 years.

These results are comparable to the only other published reports on Trifecta. Bianco et al. (4) reported a Trifecta rate of 60% at 2 years in 758 men after open RP. Their patients responded a questionnaire reviewed with the physician. Eastham et al. (16) updated these results in 1577 men with a similar Trifecta rate of 62% at 23.5 months median follow-up. They then constructed a nomogram using preoperative variables. Pierorazio et al. (17) reported their Trifecta results in 314 patients after open RP. Their Trifecta rates were 72.6%, 56.2% and 40.0% in the low, intermediate and high risk categories at 1 year follow-up. Data collection relied on patient-physician interaction. Shikanov et al. (18) published their results in 380 patients after robotic assisted radical prostatectomy. Functional evaluations were based on subjective and objective UCLA-PCI index (19)) definitions for UC and SP. The Trifecta rates at 2 years were 72% - subjective data and 44% - objective data ($p < 0.0001$).

Specimen weight has been shown to have variable impact on SP and UC. In this analysis, specimen weight was recorded as <50 g or > 50 g. In our study, larger specimens (weight > 50 g) were associated with lower chance of achieving Trifecta (34% vs. 66%, $p < 0.001$) and specimen > 50g was an independent predictor of higher rate of UC and ED in multivariate analysis ($p < 0.001$). Pettus et al. (20) evaluated specimen size with functional outcomes in 3067 patients who underwent open RP. BR and functional results at 1 year were not affected by prostate size. Other studies of open RP have not demonstrated a correlation between prostate size and SP or UC (21,22). Frota et al. (23) reported their results of 193 laparoscopic radical prostatectomy. Prostate weight had no significant impact on BR and UC yet prostates $\leq$ 30 g were associated with lower potency. However, according to Ahlering et al. (24) in 139 men who underwent robotic assisted radical prostatectomy, smaller prostates were associated with faster recovery of potency and larger prostates correlated higher risk of delay in potency recovery.

There are several limitations in our study. A large number of patients were excluded due to lack of data or a follow-up less than 1 year. As a large referral and tertiary center, patients often have their procedure performed at our center and follow-up done by their local urologist. However, our cohort comprised of 831 patients which compares favorably with other reports on Trifecta. QoL outcomes represent subjective data that is converted to objective quantifiable variables. Data were collected through the review of medical records. UC as per our definition has its limitations but can be easily reported and quantified i.e. pads or no pads. However, quantifying erectile dysfunction remains a challenge since there maybe neurologic, vasculogenic and psychologic factors to consider. Rigidity of erection and ultimately the capacity to have satisfactory intercourse is the deisred endpoint. Patients' and surgeons' perceptions and expectations may have an impact on what is reported. Our results are tabulated from RPs performed by a single surgeon and caution should be used when extrapolating this data to a broader clinical setting.

CONCLUSIONS

Achievement of Trifecta represents the most desirable outcome after RP. Stratification of patients into preoperative risk categories may help clinicians discuss the many different options and the possible outcomes in the postoperative course. While patients often demand robotic prostatectomy, recent results have not shown any Trifecta advantages over the open RP. Adequate pre-operative counseling should focus on the probability of achieving the Trifecta in patients undergoing radical prostatectomy independent whether is done using open or other minimally invasive surgical approach.

ABBREVIATIONS

LTH = Lithotripsy Table Height; SWL = Shockwave Lithotripsy; KUB = Kidney, ureters, bladder X-ray study; BMI = Body Mass Index; SSD = Skin-to-Stone Distance; HU = Hounsfield Units

NCCT = Non Contrast-enhanced Computed Tomography; ROC = Receiver Operating Characteristic; SF = Stone Free; RF = Residual Fragments OR = Odds Ratio; SE = Standard Error; SD = Standard Deviation; CI = Confidence Interval

CONFLICT OF INTEREST

None declared.

ACKNOWLEDGEMENTS

"CURED" and Vincent A. Rodriguez

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Accepted after revision:
July 30, 2010

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EDITORIAL COMMENT

In this study Antebi et al. [ref] report on a single surgeon experience with radical prostatectomy in nearly a thousand patients and analyzed the factors contributing to achieve the "trifecta" of UC, SP and biochemical disease free survival following surgery for prostate cancer.

In the era of widespread diffusion of robot-assisted prostatectomy it is of utmost importance to report on the contemporary outcomes of the open approach to better counsel patients with regards to the outcomes of the treatment. It is likely that no oncologically superior approach exists and the outcomes of surgical treatment are strongly related to surgeon's skills.

In this series, 43-62% of men achieved the "trifecta". One should bear in mind that most if not all published reports on the outcomes of surgical treatment (both open, laparoscopic and robotic) for prostate cancer originate in high volume centers with highly experienced surgeons. These results therefore cannot be generalized. The outcomes of these reports are not a result of the approach to prostatectomy but of the surgeon performing it.

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Clinical Urology
International Braz J Urol
Vol 37 (3): 328-335, May - June, 2011

Biochemical Recurrence After Radical Prostatectomy: ıs the Dısease or the Surgeon to Blame?

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ABSTRACT

Purpose: The PSA recurrence develops in 27 to 53% within ten years after radical prostatectomy (RP). We investigated the factors (disease grade and stage or the surgeon's expertise,) more likely to influence biochemical recurrence in men post-radical prostatectomy for organ-confined prostate cancer by different surgeons in the same institution.
Materials and Methods: A total of 510 patients that underwent radical prostatectomy were investigated retrospectively. Biochemical recurrence was defined as detection of a PSA level of ≥ 0.20 ng/mL by two subsequent measurements. The causes, which are likely to influence the development of PSA recurrence, were separated into two groups as those related to the disease and those related to the surgical technique.
Results: Biochemical recurrence was detected in 23.5% (120 cases) of 510 cases. The parameters most likely to influence biochemical recurrence were: PSA level ($p < 0.0001$), T stage ($p < 0.0001$), the presence of extracapsular invasion prostate ($p < 0.0001$), Gleason scores ($p = 0.042$, $p < 0.0001$) and the presence of biopsy with perineural invasion ($p = 0.03$). The only surgical factor that demonstrated relevance was inadvertent capsular incision during the surgery that influenced the PSA recurrence ($p < 0.0001$).
Conclusion: The PSA recurrence was detected in 21.6% of patients who had been treated with radical prostatectomy within 5 years, which indicates that the parameters related to the disease and the patient have a pivotal role in the PSA recurrence.

Key words: *prostatectomy; prostate cancer; recurrence; prostate-specific antigen*
Int Braz J Urol. 2011; 37: 328-335

INTRODUCTION

Radical prostatectomy (RP) continues to be the "gold standard" in the treatment of localized prostate cancer for patients with a life expectancy of 10 years (1). However, biochemical recurrence may occur in 27 to 53% within ten years after radical prostatectomy (RP) (1-3) and additional treatment may be required in 35% of these patients (1,3). High pretreatment levels of PSA, high grade Gleason score, advanced clinical and pathological stage and positive surgical margin (PSM) have been proven to be independent predictors of biochemical recurrence post-prostatectomy (4,5). Most of these predictors are related with the disease characteristics. Thus, the PSA recurrence appears to be related to the disease itself rather than the surgery performed in patients who underwent RP. In the present study, we investigated possible causes that may influence biochemical recurrence in post RP men treated for localized prostate cancer performed by different surgeons in the same medical center.

MATERIALS AND METHODS

A total of 602 patients who were diagnosed with clinic localized prostate cancer and underwent retropubic RP between May 1998 and April 2009 were retrospectively studied. Ninety two patients were excluded from the study due to positive lymph

node metastases or lost follow-up. Following the EAU Guidelines on Prostate Cancer, the follow-up was conducted 3, 6 and 12 months post-prostatectomy during the first year, and every six months in the second year and thereafter with PSA level and digital rectal exam. PSA level ≥ 0.20 ng/mL by two subsequent measurements was defined as biochemical recurrence. We analyzed factors related to the disease or the surgery that may influence PSA recurrence (Table-1).

Ten different surgeons performed the operations in accordance with the technique described by Walsh (6). A modified pelvic lymph node dissection was performed in all patients. Surgical samples were stained with India ink in order to determine surgical margins and fixed with 10% formalin. Whole mount prostate and seminal vesicle examination was performed at intervals of 2-3mm.

PSM was defined as neoplastic cells in contact with inked surgical margin (7).

All statistical analysis was performed via SPSS 13 program and p value of ≤ 0.05 was considered statistically significant. Chi-square test, Student T-test, Logistic Regression and Multivariate analyses were used to examine correlation of variables and the PSA recurrence. Time of PSA free progression and its relationship with the variables were analyzed by Kaplan-Meier curve.

RESULTS

The mean follow-up was 89 months (12-114 months) and biochemical recurrence was detected in 120 (23.5%) of 510 patients. The time of the biochemical recurrence was observed to be 29.02 months (7-82 months) in average.

Group 1: The variables which are considered to be related to the disease and patient were investigated in this group.

Patients mean age was 67 years old (43-81 y.o.) and no statistically significant relationship was detected between this variable and biochemical recurrence by univariate analysis (p = 0.36).

The mean preoperative PSA level was 11.1 ng/dL (0.32-65 ng/dL) and a statistically significant relationship was observed between the PSA levels and biochemical recurrence. It was also observed that the rate of the recurrence was 14.9% in patients with a PSA level ≤ 11.1 ng/dL and 36% in those > 11.1 ng/dL (p < 0.0001).

Likewise, strong correlation between the pathological stage and progression of the disease was detected. The rate of the biochemical recurrence was 56.9% in 128 patients who were considered to be cT2 prostate cancer but then observed to be pT3a (extraprostatic extension) whereas 18.2% in 318 patients with organ-confined (pT2) disease (p < 0.0001).

The mean rate of PSA recurrence was 44.4% in patients with a Gleason score of 7 and above whereas 11.2% in those with a score of 6 and below (p = 0.042). Similarly, the rate of biochecmical recurrence in the surgical sample was 52.6% in patients with a Gleason > 7 , and 15.5% in those with Gleason < 6 (p < 0.0001).

The rate of PSA progression was 34.7% in 192 patients whose biopsy sample analysis revealed perineural invasion (PNI) whereas 19.4% in patients without PNI (p = 0.03). Additionally, significant correlations between the presence of PNI in biopsy and PSM (p < 0.001), pT stage (p < 0.001), extraprostatic tumor extension (p < 0.001), and preoperative PSA level (p < 0.014) were detected. Although PSA recurrence was observed in 29.6% of patients with PNI in surgical specimen (356 patients), the percentage was only 20.9 in patients without PNI (p = 0.092).

Similar results were obtained when we analyzed the PSA free progression 5 year-survival and parameters regarding the disease and patient using the Kaplan-Meier method (Table-2).

Group 2: The parameters related to the surgical treatment (surgeon's expertise).

It was observed that a PSM occurred due capsular incision during the dissection in 119 (23.3%) of 510 patients who underwent RP. The rate of biochemical recurrence was detected to be 56.6% in the patients of this group (p < 0.0001). It was observed that the mean blood loss was 420cc (50-2500cc) and there was no statistically significant finding between the blood loss and PSA recurrence (p = 0.24).

Walsh suggested to wait at least 6 weeks for tissue repair after the biopsy and then to perform RP (5). In the present study, we analyzed patients who had been operated before and after the 6 week period

Table 1 - *PSA recurrence groups.*

Group 1	Group 2
parameters related to the disease	parameters related to the surgical technique and/or patient
Age	Estimated Blood Loss
Pre operative PSA level	Positive surgical margin
Gleason Sum	Time between biopsy and RP
Extraprostatic extension	Surgical experience
Prostate weight	
Perineural invasion	
T stage	

post-biopsy, and the results did not attain statistical significance (p = 0.36).

Each of 10 surgeons operated on 51 patients (32-188 patients) in average whereas, no statistically significant relationship was observed between the surgeons and PSA progression (p = 0.18). Additionally, when number of procedures/surgeon and PSA progression was studied no statistically difference was observed (p = 0.16) even for the surgeon with the highest number of operations (188 cases). However, the rate of tumor incision by the surgeon with the highest number of operations was 17.02% whereas, the remaining nine surgeons was 27.01% (p = 0.026) (Table-3). On the other hand, the rate of EPE was 32.9% in patients operated on by one surgeon whereas it was 20.5% in those operated on by the remaining 9 surgeons (p = 0.032). Table-4 summarizes the rates of 5-year survival without PSA progression and their relationships with other parameters related to the surgery.

While multivariate analysis showed positive correlations between biochemical recurrence and PSM (p = 0.042), preoperative PSA level (p = 0.002), and pT stage (p = 0.002), the most significant predictor for the recurrence was found to be with PSM.

DISCUSSION

The most common predictors of biochemical recurrence after radical prostatectomy are high pre-treatment levels of PSA, Gleason score, clinical tumor stage, pathological stage, and PSM (8-10). In our study, pre-surgery PSA level, clinical and pathological T stage, PSM, biopsy and surgical specimen Gleason score and the presence of biopsy perineural invasion were determined to be factors that correlated with PSA recurrence.

PSM is directly associated with biochemical recurrence after RP. PSM is defined as tumor at the inked margin of the excised specimen (7,11-13). Wieder and Soloway reported that the rate of PSM was 22.5% (12) in organ-confined disease. In the present study, PSM is evident in 23.3% of patients with organ-confined disease.

The incision of the tumor in patients with organ-confined disease is undoubtedly an important parameter related to surgical experience, which correlates with PSA recurrence (9,14). Felix et al. compared the results of one surgeon with the highest number of RP operations with other 10 surgeons and found that rates of PSA recurrence and PSM of the surgeon with the highest number of operations were significantly lower (15). Similar results were obtained in other studies (16-19). In the present study, when the results of the surgeon with the highest number of operations (188 cases) were compared to the remaining 9 surgeons, the PSM rates were observed to be consistent with the literature. On the other hand, it was found that the rate of biochemical recurrence was not correlated with surgical experience. The effect of individual experience of the surgeon on the success of surgery is controversial. In the present study, the comparison between surgeons

Table 2 - *Association of Group 1* with the PSA recurrence.*

	Progression free survival rate**(%)	P value
Age		
< 70	38.4	
≥ 70	43.2	0.260
PSA (ng/dL)		
< 10	56.1	
≥ 10	12.8	< 0.0001
Gleason sum		
< 7	62.3	
≥ 7	12.0	< 0.0001
Extraprostatic extension		
Yes	12.7	
No	66.4	< 0.0001
Prostate weight (gr)		
< 50	36.4	
≥ 50	48.2	0.092
Presence of perineural invasion		
Yes	22.9	
No	44.1	0.043
pT stage		
T2	78.4	
T3	17.9	< 0.0001

* *The parameters related to the disease and patient.*
** *For five years, analyzed by Kaplan-Meier Method.*

(highest number of operations and other surgeons) revealed no significant differences. However, differences in EPE rates were noted. The capsular incision rate of the surgeon with the highest number of RP was significantly lower than other surgeons, whereas, EPE rates for the same surgeon were significantly higher, which may be explained by the selection bias of higher complexity and clinical stage patients for the most experienced surgeon.

The relation between PNI in biopsy specimen and biochemical recurrence is controversial. Although PNI in radical prostatectomy specimen is very common, there is no clear evidence between PNI and disease progression yet, which is also demonstrated in our study. However, the correlation between PNI in biopsy specimen and biochemical recurrence was detected, although the reasons are not known. The PNI in biopsy specimen could be a predictor to determine the tumor aggressiveness (20,21), since strong correlation between PNI in the biopsy specimen and PSM, pathological T stage, EPE, and preoperative PSA level were found in our study.

Table 3 - *Results Comparison between the surgeon with the highest number of radical prostatectomies and others.*

	The surgeon with the highest number of operations	Other surgeons	p
No. of patients	188	322	
Age	60.12	66.16	0.22
PSA(ng/dL)	16.02	08.02	0.03
Prostat weight (g)	57.49	50.76	0.83
Gleason Sum	7.29	7.02	0.61
T stage			
pT2a	18 (9.6%)	40 (12.4%)	0.82
pT2b	28 (15.5%)	64 (19.8%)	0.65
pT2c	60 (31.9%)	108 (33.5%)	0.54
pT3a	62 (32.9%)	66 (20.5%)	0.03
pT3b	20 (10.1%)	44 (13.8%)	0.19
PNI[1]	74 (39.3%)	118 (36.6%)	0.87
PSM[2]	32 (17.0%)	87 (27.0%)	0.02
EPE[3]	62 (32.9%)	66 (20.5%)	0.03
PSA recurrence[4]	36 (19.2%)	84 (26.0%)	0.17

Student T-Test and Pearson Chi square test used. / 1:Perineural invasion in biopsy; 2:Positive surgery margin; 3:Extraprostatic extension; 4:Number of patients with PSA recurrence

Table 4 - *The association of Group 2* with the PSA recurrence.*

	Progression free survival rate**(%)	P value
Estimated Blood Loss (cc)		
< 1000	74.2	
≥ 1000	70.1	0.890
Capsular incision		
Yes	14.3	
No	73.1	< 0.0001
Time between biopsy & RP (weeks)		
< 6	50.1	
≥ 6	62.7	0.590
Surgical Experience		
The surgeon with the highest number of operations	68.1	
Other Surgeons	46.2	0.091

** The parameters related to the surgical technique./ ** For five years, analyzed by Kaplan-Meier Method.*

CONCLUSIONS

Among the causes related to the surgical technique, which influence the biochemical recurrence, only PSM due to capsular incision is of importance. Although the surgeon's "factor" did not attain statistical significance, the significant relationship between the number of patients the surgeon operated on and rates of capsular incision indicates the importance of surgical experience. However, the clinical outcome after surgery for the treatment of clinically localized prostate cancer appears to be more related to the aggressiveness of the disease than surgeon's expertise alone.

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
September 19, 2010

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EDITORIAL COMMENT

Biochemical recurrence (BR) after radical prostatectomy has been described up to 50% after 10 years of follow up. The problem is to identify which parameters are important in the determination of the recurrence in order to introduce adjuvant therapies for better overall survival rate. PSA levels, Gleason score and tumor stage are the main factors, but in times of prostate cancer screening most patients have clinically localized tumors, PSA lower than 10 and intermediate Gleason score. Among these patients positive surgical margins is the main factor related to BR as illustrated in this paper. But even in this specific situation some studies have demonstrated 70% of recurrence free survival. Who is the patient that deserves to be treated with adjuvant therapy? Some specific aspects have been considered as positive surgical margins and the Gleason score (1,2). This is an open field to better understand the behavior of prostate cancer and certainly, it deserves attention from the scientific community. The pivotal question is how to determine the patients taht derserve treatment versus overtreatment.

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Clinical Urology
International Braz J Urol
Vol 37 (3): 336-346, May - June, 2011

Tadalafil Rehabilitation Therapy Preserves Penile Size After Bilateral Nerve Sparing Radical Retropubic Prostatectomy

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ABSTRACT

Objective: To evaluate the change in penile size r bilateral nerve sparing retropubic radical prostatectomy (BNSRRP) and possible effect of Tadalafil.
Materials and Methods: A total of 65 patients underwent BNSRRP and they were evaluated prospectively for a whole year of follow-up . The patients were randomized to control without rehabilitation (Group 1) or Tadalafil rehabilitation group (Group 2). The patients were evaluated at months 3, 6 and 12 postoperatively for erectile function, penile measurements (flaccid penile length, penile length at maximum erection, penile circumference at flaccid status, and penile circumference at maximum erection), penile abnormalities and general health status. Statistical analysis was performed by Chi-Square test and significance was defined as p value < 0.05.
Results: In Group 1 there was significant decrease in penile measurements at month 3 compared to preoperative measurements. There was decrease in all parameters at month 6 compared to month 3 but only the decrease in penile length at maximum erection was significant. There were no significant differences between postoperative months 6 and 12 for all measurements. In Group 2 there was a tendency to decrease in all measurements at month 3 compared to baseline. There was no significant difference for penile measurements between postoperative 3rd and 6th months and between 6th month and the first year.
Conclusion: Although further large sampled trials are needed to describe the possible positive effect of tadalafil or other PDE5-I's on penile size after BNSRRP, tadalafil rehabilitation is effective in preserving penile size especially in the early postoperative period after BNSRRP.

Key words: *Penile: erectile; prostatectomy; erectile dysfunction; tadalafil*
Int Braz J Urol. 2011; 37: 336-346

INTRODUCTION

In recent years especially with the advent of serum prostate specific antigen (PSA) prostate cancer has been frequently detected in relatively young men (1). Besides other treatment modalities radical prostatectomy (RP) is generally used for patients with clinically localized prostate cancer (2). The goal of the surgical intervention is to eradicate the disease with minimal possible morbidity. Erectile dysfunction (ED) and urinary incontinence are the two main potential problems that may adversely affect the patients' quality of life postoperatively (3).

In different series ED was reported in 14-84% of the men who underwent RP (4-6). Men suffering from postoperative ED may also complain from loss of penile length (7). Additionally some patients without postoperative ED may not have desirable sexual intercourse because of penile shortening (8). Some studies in the literature prospectively tested the use of phosphodiesterase 5 inhibitors (PDE5-I) and their potential effect on postoperative erectile function after RP (9,10).

Few trials studied the possible effect of PDE5-I's specifically on penile length in the postoperative period (8).

In this prospective study we aimed to evaluate the change in penile size after bilateral nerve sparing retropubic radical prostatectomy (BNSRRP) and possible effect of tadalafil treatment in a relatively young population with prostate cancer. We hypothesized that presence of postoperative ED and the protocol of postoperative tadalafil administration as rehabilitation therapy might affect the penile length.

MATERIALS AND METHODS

Between October 2006 and February 2008, 85 patients with full preoperative potency underwent BNSRRP in our institution. Data of 65 of these patients were evaluated in this prospective trial and flow chart for the patient enrollment is summarized in Figure-1. Inclusion criteria were as follows: age < 65 years, preoperative full potency, no history of penile plaques or previous penile surgery, clinical stage T1c or lower, PSA < 10ng/mL and a biopsy Gleason score < 8. All patients were preoperatively evaluated by International Index of Erectile Function (IIEF-EF) and Sexual Encounter Profile (SEP) diary questions 2 and 3 to determine the erectile function status of the patient. All patients had preoperative IIEF-EF scores > 25 and answered SEP questions 2-3 'yes'. General health status was questioned on co-morbidities involving hyperlipidemia, diabetes and hypertension. Also all patients were evaluated for metabolic syndrome based on the guidelines from the 2001 National Cholesterol Education Program Adult Treatment Panel (ATP III) (11). Physical examination and penile ultrasound scan were performed preoperatively to detect any penile plaque or abnormality. Penile length and circumference were measured both in flaccid and at maximum erection with a paper ruler as reported by Munding et al. (12), by a single physician. Penile length was measured from the tip of the glans to the pubopenile skin junction; penile circumference was measured at the most distal part of the shaft, just proximal to the glans penis. Measurements were repeated twice to optimize the reliability of the results obtained. To obtain maximum erection, 30 mg of papaverine was injected to each corpus cavernosa and patients were required to do manual genital stimulation.

All patients underwent BNSRRP by the technique previously described by Montorsi et al. (6) that is famous for permitting efficient dissec-

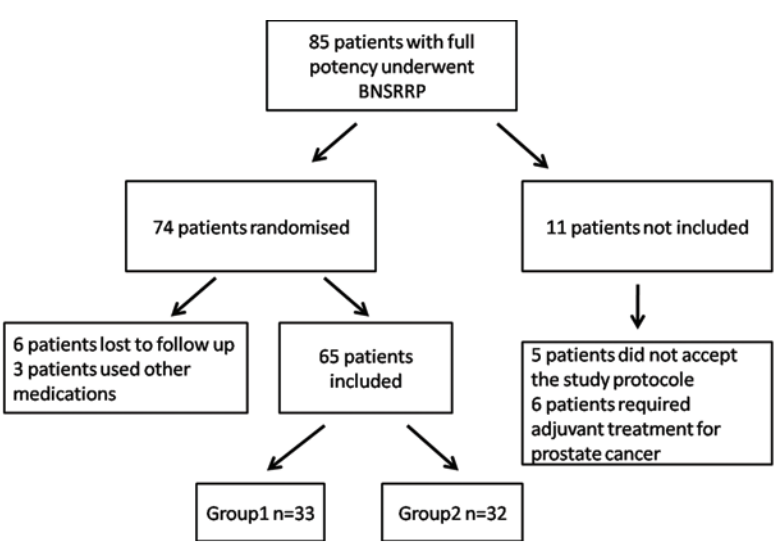


Figure 1 - *Flow chart for the inclusion of the patients.*

tion of the neurovascular bundles at the level of the membranous urethra and prostate apex, which significantly reduces the risk of cavernous nerve injury. The urethral catheter was removed 14-20 days after the surgery and the patients were encouraged to attempt sexual intercourse 1 week after the catheter removal. The patients were randomized to two groups; no use of tadalafil (Group 1) and 3 days/week tadalafil (20mg/day) protocols (Group 2) on the day of surgery. For randomization NCSS (Number Cruncher Statistical System) 2007 program was used. Patients in Group 1 and Group 2 received the protocols for 6 months following the removal of urethral catheter.

The patients were evaluated at months 3, 6 and 12 following the surgery for erectile function, penile measurements, penile abnormalities and general health status with the same protocol used preoperatively. Penile size measurements were performed blindly by the same physician preoperatively and postoperatively. None of the patients received any adjuvant or neoadjuvant treatment for prostate cancer.

Statistical evaluations were performed with Chi-Square test. Two-sided tests with significance at 0.05 were used. An independent sample t test was used to evaluate differences in penile measurements and erectile function between the pre and postoperative periods. All patients signed a written informed consent before the randomization in the study.

RESULTS

Patients mean age was 57.2 years old (50 to 65 years old). Mean preoperative PSA was 6, 1ng/mL (3.6-9.6ng/mL). Prostate biopsy Gleason score was < 6 in 14 patients, 6 in 56 patients and 7 in the remaining 35 patients. The three groups did not show statistical differences in preoperative factors regarding to age, PSA, IIEF-EF, hypertension, Diabetes Mellitus, hyperlipidemia and metabolic syndromes, and the values are summarized in Table-1.

The two groups did not show significant difference for the preoperative measurements. The average of pre-operative and postoperative (months 3, 6 and 12) penile measurements for both groups are shown in Figure-2. Individual penile measurements average changes for the same time periods is demonstrated in Table-2.

In Group 1 there was significant decrease in penile length and circumference measurements in both flaccid state and at maximum erection at month 3 compared to preoperative measurements ($p < 0.05$). Also there was a decrease in all parameters at month 6 compared to month 3 but the only statistically significant decrease was in penile length at maximum erection ($p < 0.05$). No statistical differences were noted between postoperative month 6 and 12 for all measurements ($p > 0.05$).

In Group 2 there was a tendency to decrease in all measurements at month 3 compared to baseline but this decrease was not statistically significant. Also there was no statistically significant difference for any of the penile measurements between postoperative 3rd and 6th months as well as between postoperative 6th month and the first year.

The comparison of the means of individual differences for penile measurements in both groups, which were performed to omit the effect of some outliers, revealed similar results with the comparison of means of each group.

Concerning erectile function status, 24 patients (72.7%) in Group 1 and 25 in Group 2 (78.1%) were found to have IIEF-EF > 25 at the end of 1 year follow-up. In patients with a postoperative IIEF-EF score > 25, the mean of individual changes of penile measurements at both flaccid status and maximum erection, between the preoperative and postoperative first year, were compared for both groups. There was no significant difference in these parameters. Although there was a prominent tendency of decrease in penile measurements for patients in both groups with a postoperative IIEF-EF score < 25, statistical significance could not be tested due to the low number of patients. The number of patients for each group in each time period for erectile function status is given in Table-3. During the follow-up 2 patients in Group 1 developed penile plaque that were also detected by ultrasound scan.

Table 1 - *Preoperative data of both groups.*

Parameter	Group 1 (n = 33)	Group 2 (n = 32)	P value
Age (year)	58.1	56.2	
PSA (ng/mL)	5.8	6.3	
IIEF	26.5	26.2	
Hypertension (n)	12	14	P > 0.05
Hyperlipidemia (n)	6	4	
Diabetes mellitus (n)	4	5	
Metabolic syndrome (n)	6	5	

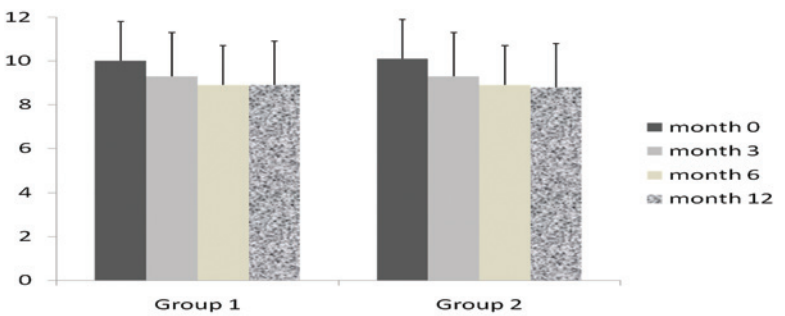
DISCUSSION

Potential pathophysiology of ED that may occur after RP has been widely discussed in several studies (13-15) and there are studies evaluating the penile length changes after RP (7,12,16). The mechanism responsible for the reduction in penile length after RP has not been elucidated. Ciancio and Kim reported that 41% of patients with ED after RP had penile fibrotic changes (17). McCullough and Lepor speculated that the loss of penile size in impotent patients after nerve sparing RRP was due to postoperative denervation atrophy and/or fibrosis of the corpora cavernosa smooth muscle (18). Iacono et al. evaluated histomorphological alterations in cavernous smooth muscle and collagen content after radical prostatectomy. Similarly to other studies, they concluded that progressive fibrosis in the corpora cavernosa after radical prostatectomy resulted from denervation and/or an ischemic process (19). Several human and animal studies support the hypothesis of maintaining adequate penile oxygenation by preserving neurovascular bundles and thus erectile function, may play an important role in preventing irreversible penile fibrotic changes (8,14,15). User et al. performed a study on postpubertal rats and grouped them according to bilateral or unilateral cavernous nerve transection versus a sham operation (14). They suggested the hypothesis that bilateral injury to the cavernous nerves may induce significant apoptosis of smooth muscle cells particularly in the subtunical area which causes penile fibrosis and abnormality of the veno-occlusive mechanism of the corpus cavernosum. Leungwattanakij et al. showed that cavernosal neurotomy was associated with an up regulation of fibrogenic cytokines and collagenization of the corporoa smooth muscle in animal model (15). In many studies it has been postulated that a chronic absence of postoperative erections might lead to cavernosal hypoxia (7,12,16). Finally, significant tissue damage and increased corpora fibrosis occur and may cause postoperative shortening of the penis.

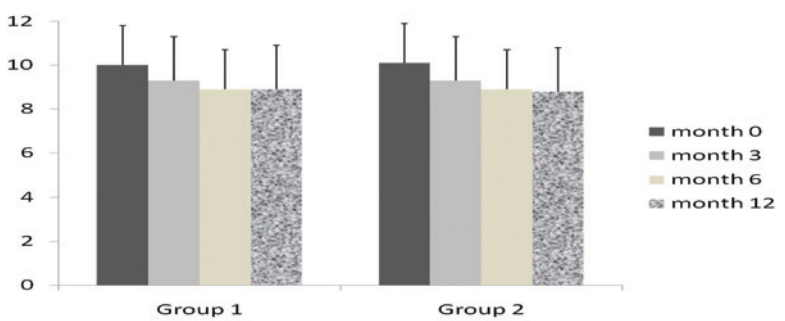
Schwarts et al. found an association between early use of high doses of sildenafil after RP and preservation of smooth muscle content within human corpus cavernosum (20). Bianco et al. speculated that the surgeon plays the most important role in determining the patients' postoperative outcome (21).

In our trial, operations were performed by two high volume surgeons. The mean preoperative flaccid penile dimensions in our series were similar to those reported before (16,22). Although the mechanisms were not well understood it's clear that a decrease in penile length may occur after RP. Our outcomes for both groups were similar to past trials suggesting a decrease in penile length postoperatively (7,12,16). Briganti et al. found no difference in penile size between pre and postoperative measurements with the use of full dose PDE5-I on demand (8). We found a significant decrease in all penile measurements in control patients (not using Tadalafil) at 3rd postoperative month when compared with preoperative measurements (p = 0.001). There was also a significant decrease in penile length measured at maxi-

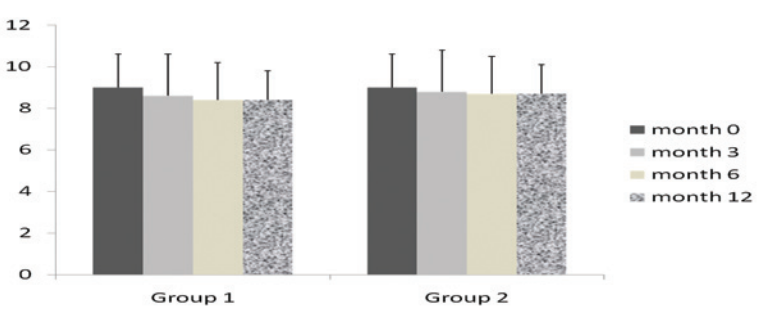
Figure 2 - *The means and standard deviations (SD) of penile measurements preoperatively and at months 3, 6 and 12 postoperatively for both groups.*



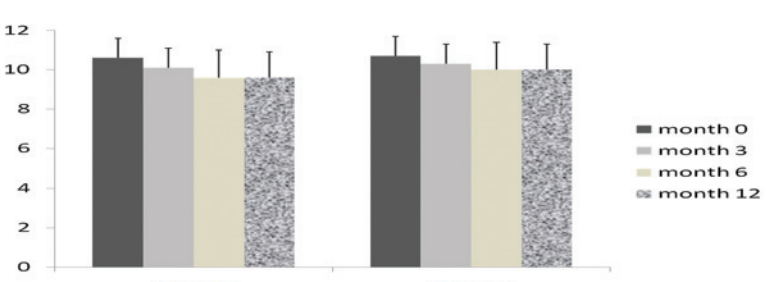
a - *Flaccid penile length (cm).*



b - *Penile length at maximum erection (cm).*



c - *Penile circumference at flaccid status (cm).*



d - *Penile circumference at maximum erection (cm).*

***Table 2 - Follow-up of** changes of penile measurements (mean) of groups 1 and 2*

	Group 1 (Mean)	Group 2 (Mean)
Change in flaccid penile length (cm)		
0-3 Months	0.8*	0.5
3-6 Months	0.3	0.2
6-12 Months	0.1	0.1
Change in penile length at maximum erection (cm)		
0-3 Months	0.9*	0.6
3-6 Months	0.7*	0.4
6-12 Months	0.2	0.1
Change in penile circumference at flaccid status (cm)		
0-3 Months	0.5*	0.3
3-6 Months	0.2	0.1
6-12 Months	0.1	0.1
Change in penile circumference at maximum erection (cm)		
0-3 Months	0.4*	0.3
3-6 Months	0.1	0.1
6-12 Months	0.1	0.1

** mean $p < 0.05$*

mum erection at 6 months compared to 3 months postop for the first group. In patients who used Tadalafil regularly as a rehabilitation protocol in Group 2, there was no statistically significant penile shortening at 3 months postop when compared to preoperative measures ($p = 0.07$). Regular use of Tadalafil revealed similar results as Briganti's stduy (8). Despite the limited number of patients in our series, we believe that early use of Tadalafil as a rehabilitation therapy may have positive effects on penile length after RP.

Although Savoie et al. (16) reported penile shortening in 68% of their patients following RP; they concluded that there was no difference between patients with or without postoperative ED in terms of penile measurements. However Briganti et al. showed that postoperative preservation of erectile function is positively correlated with the maintenance of penile length following BNSRRP (8). Likewise to their results our patients who had an IIEF-EF score > 25, had preservation of penile size following surgery. However, we could not verify meaningful results in patients with IEF-EF score < 25 postoperatively, probably due to the low number of patients. Therefore, we can not conclude an association between preservation of postoperative erectile function and penile length.

There is a lack of consensus on penile measurements and the use of PDE5-I's following RP and presence (unilateral or bilateral) or absence of nerve sparing surgery and the type of protocol of PDE5-I (on demand/or no use vs. rehabilitation). Although we did not evaluate the effect of nerve sparing surgery on penile measurements, we compared pre and postoperative penile measurements in both 'penile rehabilitation' and 'control' groups.

Sildenafil has been previously shown to be associated with maintenance of postoperative penile structures in patients undergoing RP (20). However it was reported in a recent study that

Table 3 - Erectile function status of patients in both groups.

	Group1 (n=33)			
IIEF	**Month 0 (baseline)**	**Month 3**	**Month 6**	**Month 12**
6 – 10	-•	-	1	1•
11 – 16	-•	5	5	4•
17 - 25	-•	9	8	9•
26 - 30	33†	19	19	19†
SEP 2				
Yes	33	22	22	21
No	-	11	11	12
SEP 3				
Yes	33	23	22	22
No	-	10	11	11
	Group 2 (n=32)			
IIEF	**Month 0 (baseline)**	**Month 3**	**Month 6**	**Month 12**
6-10	-•	1	-	-•
11-16	-•	3	4	3•
17-25	-•	7	7	8•
26-30	32†	21	21	21†
SEP 2				
Yes	32	23	23	24
No	-	9	9	8
SEP 3				
Yes	32	25	26	26
No	-	7	6	6

• = Although there was a prominent tendency of decrease in penile measurements for patients in both groups with a postoperative IIEF-EF score < 25, statistical significance could not be demonstrated probably due to the low number of patients.
† = In patients with a postoperative IIEF-EF score > 25, there was no significant difference in the means of individual changes of penile measurements at both flaccid status and maximum erection, between the preoperative and postoperative 1st year for both groups.

the duration of action of sildenafil and vardenafil is about 4 hours, whereas Tadalafil action is approximately 36 hours, and the overall safety of the treatment is good (23). In another study by Doggrell S (24) it was concluded that Tadalafil is similarly effective as Sildenafil in the treatment of ED and in comparison studies; Tadalafil is preferred to Sildenafil (50/100mg) by men with ED, possibly because of its longer duration of action.

Our study represents a prospective study including relatively young and preoperatively potent patients who underwent BNSRRP and postoperatively underwent 'Tadalafil rehabilitation' or 'no rehabilitation-control' groups. The duration of action of Tadalafil which is 36 hours provided a PDE5 inhibition in the rehabilitation group.

Preservation of penile size in a man with ED may be crucial to be potential candidates for penile implantation. In addition, we question whether ED may be the result of decreased self-esteem due to shortened penile size following surgery.

We observed a significant decrease in all penile measurements of the control patients in the early postoperative period (3rd month) when com-

pared to baseline. However, this decrease was not statistically significant when early and late postoperative penile measurements were compared. There was no significant decrease in both early and late postoperative measurements when compared to preoperative penile length measurements in the rehabilitation group. These findings can also be interpreted as, postoperative Tadalafil penile rehabilitation as effective therapy in the early postoperative period, decreasing the rate of penile length shortening in patients undergoing BNSRRP in the first postoperative year.

Despite our findings, the study is limited by a relatively small sample size and there is no evaluation regarding the effect of nerve sparing (unilateral vs. bilateral) surgical technique. Although all patients were encouraged to have sexual intercourse after the removal of the urethral catheter, not all men were motivated do to so after surgery.

CONCLUSIONS

Tadalafil penile rehabilitation is an effective therapy in preserving penile size especially in the early postoperative period after BNSRRP. Future clinical trials with larger population of patients may better define the possible positive effects of PDE5-I's on penile size after BNSRRP, including Tadalafil.

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
October 25, 2010

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EDITORIAL COMMENT

The study is very interesting. From this experiment, there are many important points for achievement of proper quality of life for men who underwent retropubic radical prostatectomy and prevention of post operative ED and loss of penile length:

The role of rehabilitation therapy by tadalafil early after BNSRP and its possible effect on the penile size and erectile function, could be due to the superiority of tadalafil over sildenafil and vardenafil by its longer duration (36 hours) and its overall safety of the treatment.

The patients were encouraged to perform sexual intercourse 1 week after catheter removal. This early performance might prevent cavernosal hypoxia.

Although the study did not evaluate the effect of surgical technique on penile measurements, the surgeon's skill is a major factor. The bilateral nerve sparing radical retropubic pros-

tatectomy and the efficient dissection of the membranous urethra and prostatic apex reduce significant risk of cavernous nerve injury which prevents penile fibrotic changes.

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EDITORIAL COMMENT

The microarchitecture of erectile tissue is closely related to erectile function (1-3). As previously assumed (4), the microstructural alterations inside the corpus cavernosum are likely to have an impact on its function becoming the cause, or at least a concomitant cause, of erectile deficiency. In patients who underwent radical prostatectomy, the quantitative and qualitative decrease in elastic fibers and smooth muscle fibers, along with a progressive increase in collagen fibers deposition, leads the corpus cavernosum to a fibrotic tissue (5). Similar microstructural alterations of the erectile tissue had already been detected by other authors in patients with severe arterial insufficiency (6).

This phenomenon may affect not only the quality of erection of the operated patients but also the next options of treatment of the erectile deficiency.

The administration of Sildenafil soon after radical prostatectomy appears to exert an antifibrotic effect in the corpora cavernosa of prostate cancer patients with a consequent recovery of erectile function (7).

The fibrotic process following a radical prostatectomy (5) could be the cause of a changing in the corpora cavernosa structure, with their retraction and a consequent shortening in penile lenght.

The authors concluded that the well-timed assumption of tadalafil in patient underwent radical prostatectomy, could inhibit, as it has been shown with the post-operative administration of sildenafil (7), the fibrotic process, avoiding the corpora cavernosa retraction, the conseguent penile shortening leading to a significant improvement in the recovery of erectile function.

Lately, the use of a new natural compound (Tradamix®) containing potent antioxidant (8-10) is giving encouraging good result (data not published) on the prevention of the corpora cavernosa fibrosis in patients that underwent RP and in the treatment of Peyronie's disease.

In the treatment of mild, moderate ED and of the degenerative, dysfunctional process of the corpora cavernosa, the assumption of natural compound shows clear advantages compared to the several side effects and the many pharmacological incompatibilities observed with the use of 5PDE inhibitors (11).

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International Braz J Urol Vol 37 (3): 347-354, May - June, 2011

Clamp Ablation of the Testes Compared to Bilateral Orchiectomy as Androgen Deprivation Therapy for Advanced Prostate Cancer

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ABSTRACT

Purpose: Burdizzo clamp ablation of the testes (CAT) may provide an incisionless, cost-effective form of androgen deprivation therapy (ADT) in men with adenocarcinoma of the prostate (ACP) who find bilateral orchiectomy (BO) unacceptable or can not afford medical ADT. The aim of this study was to compare CAT with BO as primary ADT in men with ACP.

Materials and Methods: Written, informed consent was obtained from men with locally advanced or metastatic ACP. Patients were prospectively randomized to BO (n = 9) or CAT (n = 10) under local anaesthesia, and were evaluated 3 and 7 days, 6 weeks and 3 months post-procedure. The protocol was approved by the local institutional ethics committee. Statistical analysis was performed using Student's, Mann-Whitney's and Fisher's tests.

Results: Mean duration of the procedure was significantly longer for BO than CAT (16.9 vs. 10.9 minutes). Mean pain scores during and after the procedure did not differ significantly. Serum testosterone decreased significantly on days 3 and 7 after CAT, but increased at 6 weeks, and was significantly higher than after BO. Serum luteinizing hormone increased significantly from day 3 after BO and from day 7 after CAT. Serum prostate specific antigen decreased significantly after BO, but not after CAT. Minor complications were more common after BO (89%) than CAT (40%). In the 9 men who did not achieve castrate levels of testosterone after CAT, BO was performed.

Conclusions: CAT was quicker to perform and had a lower complication rate, but was not as effective as BO in achieving castrate serum testosterone levels.

Key words: *Prostate Cancer; orchiectomy; androgens; castration.*

Int Braz J Urol. 2011; 37: 347-354

INTRODUCTION

Androgen deprivation therapy (ADT) is the most effective treatment for locally advanced or metastatic adenocarcinoma of the prostate (ACP). Surgical ADT consists of bilateral orchiectomy (BO) whereas medical ADT can be achieved by means of luteinizing hormone releasing hormone agonists (LHRHa), anti-androgens or estrogens (1,2).

BO requires surgical facilities, complications are quite common (although usually minor) and removal of the testes (castration) is psychologically unacceptable to many men, although it is less expensive than LHRHa (3). Medical ADT is psychologically more acceptable, but requires strict patient compliance with regular follow-up. LHRHa therapy is extremely expensive and therefore, unavailable to many patients in developing countries (3). Anti-androgen monotherapy is also expensive, and not as effective as BO or LHRHa. Estrogen therapy is inexpensive, but causes mastalgia and gynecomastia and may cause fatal thrombo-embolism (1,2).

The Burdizzo clamp is widely used in veterinary practice as an incisionless method of castration (4). It consists of pincers with a compound leverage action which crushes the spermatic cord, resulting in testicular infarction (Figure-1) (5). Skin damage or bruising is reported to be minimal (6,7).

Scientific literature with regard to its use in humans is scant. Zufall reported in 1958 on 200 patients who had vasectomy performed using the clamp (5). Herzog and Santucci reported in 2002 a case of gender reassignment where the clamp was used at the patient's insistence (8).

The aim of this study was to evaluate the feasibility, safety and efficacy of clamp ablation of the testes (CAT) using the Burdizzo clamp in men with ACP.

MATERIALS AND METHODS

The protocol was approved by the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Stellenbosch.

The inclusion criteria were (1) histologically confirmed ACP, (2) locally advanced or metastatic cancer requiring ADT, (3) patient of sound mental status and willing to give written, informed consent.

The exclusion criteria were (1) serious or life-threatening complications requiring immediate ADT (e.g. severe bone pain, impending or established paralysis, renal failure, brain metastases) and (2) local testicular or scrotal abnormalities.

Evaluation at randomization, during the procedure, and at 3 days, 7 days, 6 weeks and 3 months post-procedure included pain assessment using a visual analog scale (VAS) with range 0-100, analgesic use, complications, serum testosterone (TT), luteinizing hormone (LH) and prostate specific antigen (PSA) levels, and testicular volume measured by ultrasound.

Group 1, patients underwent surgical BO under aseptic conditions in an operating room as a day case. Bilateral spermatic cord blocks and midline scrotal skin infiltration were performed using a mixture of 10 mL lignocaine Lidocaine 1% and 10 mL bupivacaine Bupivacaine 0.5% (9). In accordance with the guidelines of the European Association of Urology, it is not our practice to administer routine peri-operative antibiotic prophylaxis for so called "clean operations" where the urinary tract is not opened (10).

Group 2 patients underwent CAT (Figure-1). Bilateral spermatic cord blocks, as well as, a scrotal block were performed using 20 mL bupivacaine Bupivacaine 0.5%. The scrotal block entailed circumferential infiltration of the scrotal skin at the narrowest part of its attachment to the perineum, which effectively anaesthetized the entire scrotal skin (11). Using the thumb and forefinger of the non-dominant hand, the testis was grasped and the jaws of the Burdizzo clamp positioned over the spermatic cord. The spermatic cord on each side was then clamped twice; - cranially and caudally - for 60 seconds.

Prophylactic antibiotics were not given. For post-procedure analgesia, all patients received oral paracetamol Paracetamol and ibuprofen Ibuprofen tablets to be taken as needed for pain. The protocol provided for patients with uncontrolled pain to be hospitalized for treatment with opiates and regional anaesthesiaanesthesia if necessary. Group 2, patients with

Figure 1 - *The Burdizzo clamp (A) positioned to crush the spermatic cord (B).*

serum TT above castration level (< (> 1.7 nmol/L) at week 6 were offered salvage BO.

Statistical analysis was performed using GraphPad Instat® software with Student's t-test for parametric data, Mann-Whitney test for nonparametric data and Fisher's exact test for contingency tables. A two-tailed p-value < 0.05 was accepted as statistically significant (SS). All data are shown as mean ± standard error of the mean (SE).

RESULTS

From November 2007 to November 2008, 19 patients were randomized to group 1 (n = 9) or group 2 (n = 10). Mean patient age and serum TT, LH, PSA and testis volume at randomization were not significantly different between the two groups (Table-1). Mean duration of the procedure was significantly longer for BO than CAT (Table-1).

Table 1 - *Study data (mean ± SE and range).*

	Group 1 (Bilateral orchidectomy)	**Group 2 (Clamp ablation of the testes)**
Number of patients	9	10
Baseline data		
Age (years)	64.7 ± 2.6 (57-77.8)	66.1 ± 2.0 (57-78.6)
Testosterone (TT) (nmol/L)	12.4 ± 2.6 (1.7-27.6)	13.9 ± 2.9 (4.7-33.1)
Luteinizing hormone (LH) (IU/L)	4.3 ± 1.2 (0.1-10.4)	8.1 ± 3.1 (1.8-34.8)
Prostate specific antigen (PSA) (µg/L)	108.6 ± 36.8 (3.2-311.0)	160.8 ± 89.0 (4.4-869.0)
Testis volume (cc)	14.6 ± 1.5 (6.9-28.2)	15.2 ± 1.5 (5.8-26.9)
Duration of procedure (minutes)	16.9 ± 0.9 (13-20)	10.9 ± 1.1 (6-17)**
Castrate serum TT (< 1.7 nmol/L) (%)		
3 days	9 (100%)	3 (30%)**
7 days	9 (100%)	4 (40%)**
6 weeks	8 (89%)	1 (10%)**
Complications (%)		
Any complication	8/9 (89%)	4/10 (40%)
Haematoma of scrotum	4	2
Oedema of scrotum/penis	0	2
Infection / abscess	4	0
Sinus	6	0
Antibiotics given	4	0
Sutures removed	3	0
Surgery (excision of sinus)	1	0

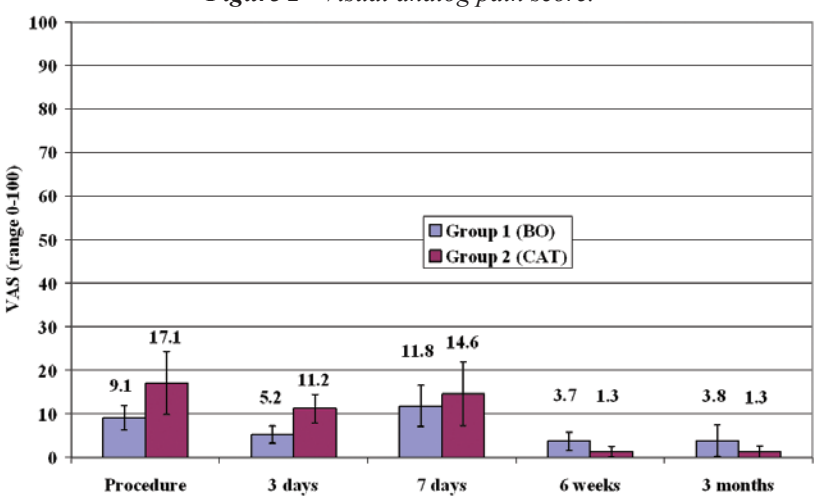
** *statistically significant difference compared to group 1*

There were no statistically significant differences in pain scores (Figure-2) or analgesic use between the groups. No patient had severe pain requiring opiates or regional anaesthesia.

Mean serum TT decreased significantly from day 3 in group 1 (BO) and was significantly lower than in group 2 (CAT) on days 3 and 7 and at 6 weeks (Figure-3). Mean serum TT in group 2 was significantly lower than baseline on days 3 and 7, but not at 6 weeks. Serum TT was below castration level (< 1.7 nmol/L) in all patients in group 1 from day 3 onwards, but in only 3/10 patients at 3 days, 4/10 at 7 days and 1/10 at 6 weeks in group 2 (Table-1).

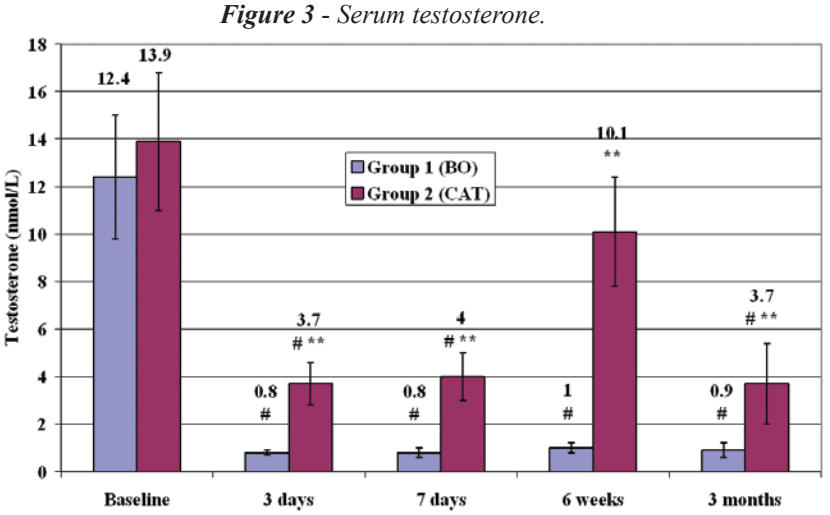
In group 2, tThe 9 patients above castration level not castrate at 6 weeks after CAT were offered BO. This was performed within 3 months in 8 of these patients. The remaining patients initially refused BO, but later consented and the procedure was performed 7 months after the initial CAT. Histological examination of the testes removed after CAT

Figure 2 *- Visual analog pain score.*



*** statistically significant difference compared to group 1 at corresponding time.*

Figure 3 *- Serum testosterone.*



 # statistically significant difference compared to value at randomization in same group.

showed blood vessels that were thickened but patent, with areas of fibrosis. The lumen of the vas deferens was obliterated.

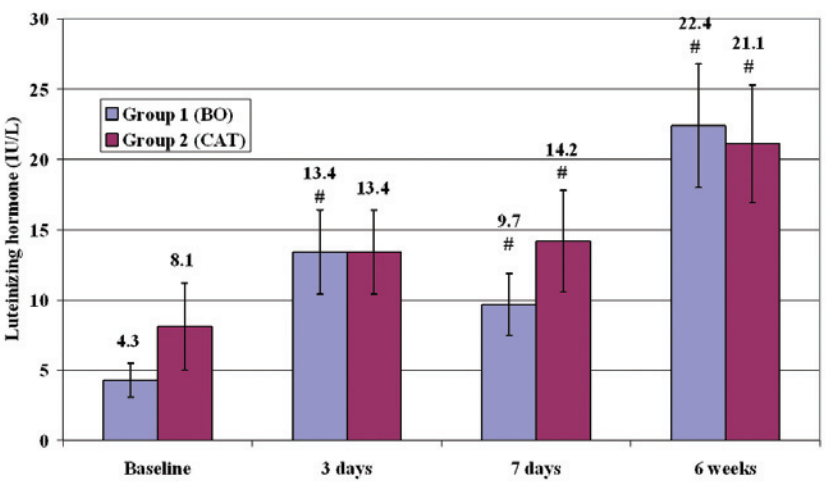
Mean serum LH increased significantly compared to baseline in group 1 from day 3, and in group 2 from day 7 onwards (Figure-4).

Mean serum PSA was significantly lower than baseline at 6 weeks and 3 months in group 1, but did not decrease significantly in group 2 (Figure-5).

Mean testis volume increased significantly on day 7 and decreased significantly at 6 weeks in group 2 (Figure-6).

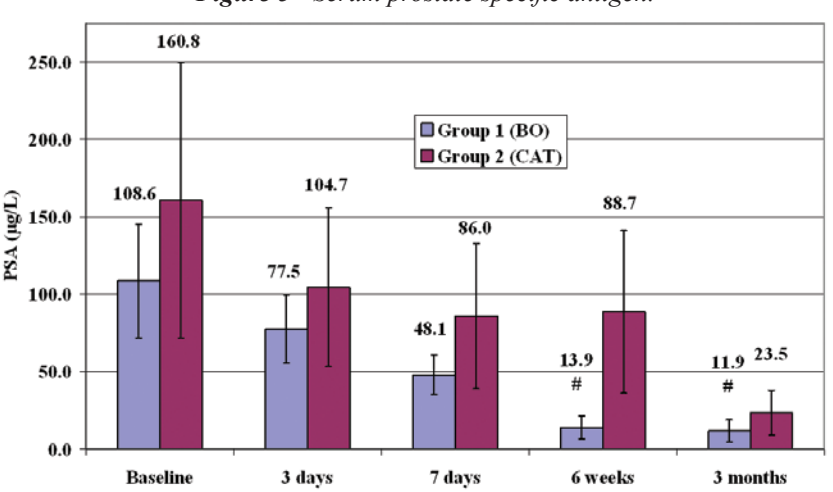
No vaso-vagal attacks crisis or other adverse events occurred during any of the procedures. In group 2, linear bruising of the scrotal skin in the areas where the clamp was applied occurred in all patients, but had completely disappeared by 6 weeks in all cases. Overall, complications were more common

Figure 4 *- Serum luteinizing hormone.*



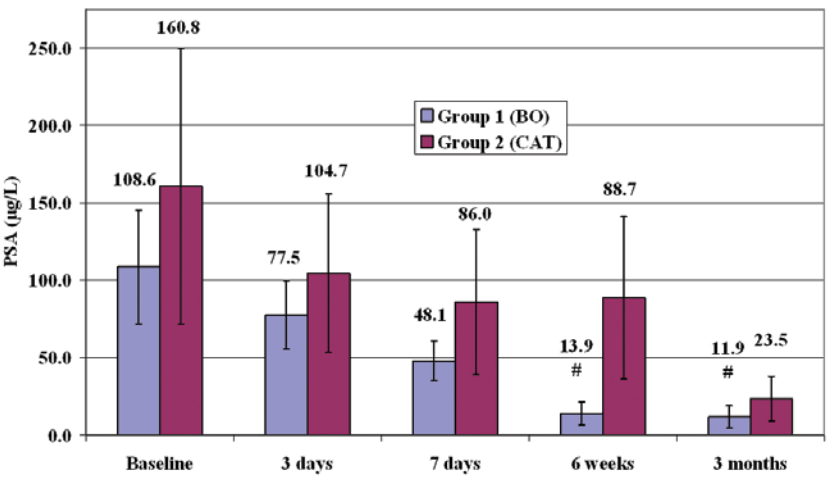
 # statistically significant difference compared to value at randomization in same group.

Figure 5 *- Serum prostate specific antigen.*



 # statistically significant difference compared to value at randomization in same group.

Figure 6 *- Testicular volume.*



 # statistically significant difference compared to value at randomization in same group.

in group 1 (89%) than group 2 (40%) (p = 0.057) and 4/9 patients required antibiotics for wound infection after BO (Table-1).

DISCUSSION

The ethical aspects of this study were thoroughly reviewed and discussed before approval of the protocol by the institutional review board. Numerous surgical techniques and medicines that are used in veterinary practice are also used in humans, and vice versa. Therefore, the fact that the Burdizzo clamp is used in veterinary practice should not, in itself, preclude its use in humans. Performing an animal study to evaluate testosterone and PSA levels after clamp ablation would not provide an answer to the question whether this technique is feasible in humans or would produce the same effect as in veterinary practice, where it is well established as an effective form of incisionless castration. Parental consent for neonatal circumcision under local anesthesia is generally accepted from an ethical point of view,view; therefore, CAT under local anesthesia in adult men with advanced ACP who have given written, informed consent should also be ethically acceptable.

Theoretically, CAT has several potential advantages. It is incisionless, does not require aseptic technique, sterilized surgical instruments, electrocautery or suture materials, and it avoids the risks of postoperative hematoma formation, wound infection with abscess formation or wound dehiscence. It can be performed more rapidly and at much lower cost than BO. In men who find surgical castration unacceptable, it may be psychologically and cosmetically more acceptable than BO, because it does not involve removal of the testes.

In the present study CAT was performed in an operating room because of initial concern about the risk of a vaso-vagal reaction requiring the availability of resuscitation facilitiesadequate treatment. However, CAT can be easily performed outside an operating room, because aseptic technique is not necessary.

The probable mechanism of action of CAT is damage to the blood vessels, presumably intimal injury, leading to subsequent thrombosis, therefore testicular infarction should not be dependent on the duration of clamping. The literature describes successful outcomes in veterinary practice after clamp application times varying from less than 5 seconds to 60 seconds. Up to 70% of practitioners apply the clamp twice or more to each cord (6,7,10,12).

The results of this study indicate that CAT delivered a significant injury to the testes, causing a statistically significant but transient decrease in the mean serum TT level and a sustained increase in mean serum LH. However, CAT was not as effective

as BO in decreasing the serum TT level. The mean TT level by 6 weeks after CAT had increased compared with the mean value at 7 days, possibly because there was a concomitant increase in LH level. Mean testicular volume increased significantly at 7 days, probably due to an inflammatory response resulting from ischaemiaischemia-reperfusion injury, and decreased significantly at 6 weeks.

The histological findings in the testes removed 6 weeks after CAT showed that, although the lumen of the vas deferens was obliterated, there were still some patent blood vessels. This indicates that CAT, as performed in this study, was not sufficiently effective in causing arterial vessel injury leading to complete obliteration of testicular blood supply. However, if the technique can be modified to achieve complete ischaemicischemic infarction of the testes, CAT may offer a rapid, low-cost form of incisionless surgical ADT in men with advanced ACP who do not have access to medical ADT and who find BO psychologically or cosmetically unacceptable.

CONCLUSIONS

In this study CAT was quicker to perform and had a lower complication rate compared with BO under local anaesthesia. CAT caused significant testicular ischaemic injury, but was not as effective as BO in achieving castrate serum TT levels. However, if the technique of CAT can be adapted to achieve complete infarction of the testes, it may become a cost-effective and appealing form of ADT in men who find BO unacceptable and do not have access to expensive LHRHa therapy.

ABBREVIATIONS

ACP adenocarcinoma of the prostate; ADT androgen deprivation therapy; BO bilateral orchiectomy; CAT clamp ablation of the testes; LH luteinizing hormone; LHRH luteinizing hormone releasing hormone; PSA prostate specific antigen; TT testosterone; VAS visual analog scale;

CONFLICT OF INTEREST

None declared.

ACKNOWLEDGEMENT

This study was funded by a research grant from the Urological Association of South Africa.

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Accepted after revision:
November 29, 2010

EDITORIAL COMMENT

The basis of androgen deprivation (AD) in prostate cancer was established, back in 1941, by Huggins and Hodges (1). The dramatic clinical regression of advanced disease with the surgical or medical hormonal blockade was awarded by a Nobel Prize in 1967. In 1971, Schally et al., discovered and developed an analogue of luteinizing hormone releasing hormone (LH-RH), as effective as orchiectomy, which also rendered a Nobel Prize (2). All AD modalities may have negative or adverse events, such as depression due to the empty scrotum, high costs (analogues of LH-RH), gynecomastia and cardiovascular toxicity (estrogens) (3). The present article aimed to test a new, less-invasive, low-cost and incisionless approach to achieve hormonal blockade. The authors used a veterinary instrument (Burdizzo clamp) applied to the scrotum, in order to cause testes infarction by crushing the gonadal vessels. The major objective was to compare orchiectomy with this novel method, but the vascular damage caused by the clamp was not severe enough to sustain low testosterone levels. Almost seventy years have gone since Huggins and Hodges published the benefits of orchiectomy. Despite few modifications in the original technique were presented (subcapsular orchiectomy), up to date, no other surgical or medical castration method showed to be more efficient, rapid, low cost and less complicated treatment for advanced prostate cancer. It really deserved a Nobel Prize!

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Clinical Urology
International Braz J Urol
Vol 37 (3): 355-361, May - June, 2011

The Lithotripsy Table Height: a Novel Predictor of Outcome in Shockwave Lithotripsy

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ABSTRACT

Background: Outcome of Extracorporeal Shockwave Lithotripsy (SWL) is determined by physical factors that affect stone fragmentation and clearance.
Purpose: To evaluate the predictive value of the Lithotripsy Table Height (LTH) in SWL outcome. Lithotripsy Table Height (LTH) is a variable that represents skin to therapy head distance, and it is proportional to the energy that reaches the stone.
Materials and Methods: A prospective study enrolled patients undergoing SWL for radiopaque urinary stones. All procedures were performed using a Modulith SLX (Karl Storz, Germany) Lithotripter. Patient weight, height and age; stone location and size; number of shock waves delivered, and LTH were recorded. One month post-procedure a KUB was obtained. Logistic regression analysis was used to evaluate the effects of these variables on stone-free outcome. A ROC curve was plotted.
Results: Fifty-six patients were enrolled. After one month follow-up, overall success rate (Stone Free) was 83.9% (n = 47). LTH was the only independent predictor of outcome in both univariate and multivariate analysis ($p = 0.029$). Stone size ($p = 0.45$) and BMI ($p = 0.32$) were not significant. In the ROC curve, LTH showed an Area under the Curve = 0.791. Patients with LTH < 218 (n = 8) had relative risk of residual stones = 7.5, odds Ratio: 6.6 (Stone free rate 37.5% vs. 91.5%).
Conclusion: LTH appears to be an independent predictor of SWL outcome. High success rates can be expected if LTH > 218. Patients with lower LTH had a less effective therapy, therefore, worse stone fragmentation and clearance. These findings may help improve patient selection for SWL therapy.

Key words: *extracorporeal shockwave lithotripsy; high-energy shock waves; treatment outcome; calculi.*
Int Braz J Urol. 2011; 37: 355-361

INTRODUCTION

Extracorporeal Shockwave Lithotripsy (SWL) represents a major technological breakthrough in the management of patients with stone disease. Since its introduction in the early eighties, millions of patients have benefited by this kind of therapy. In 1989, a report by Chaussy (1), estimated that 70% of non selected urinary stone patients could be treated with SWL monotherapy, with an additional 25% able to be treated by SWL in combination with endourologic procedures. Differences between reported overall success rates for SWL range from 50 to 95% (2,3). Key factors that determine the outcome of patients undergoing SWL have been subject of intense research in recent years, the objective being a better selection of patients for this kind of therapy.

In this study, the predictive value of the Lithotripsy Table Height (LTH) in SWL outcome is evaluated. This variable is determined individually

by the amount of tissue between the stone and the therapy head. Because both focal distance (distance from therapy head to the focal point; where pressure is maximum) and therapy head are fixed, to locate the stone in the focal point of the lithotripter, LTH is set by the operator for each patient before SWL begins, by moving the lithotripsy table along the z axis (up and down), using fluoroscopy at 30º, until the sum of Skin-to-Stone Distance (SSD) and Skin-to-Therapy Head Distance equal the focal distance. Since only Skin-to-Therapy Head Distance head is modifiable, LTH is directly proportional to the Skin-to-Therapy Head distance, and inversely proportional to SSD. Stones located deep within a patient's body (large skin-to-stone distance), require the table to be lower (i.e. closer to the therapy head) than superficial stones (small skin-to-stone distance; high table). It's important to note that this depends not only on the amount of fat, but also any other tissue interposed between the stone and the lithotripter, such as bone; connective tissue; renal parenchyma; etc., and location of the stone within the urinary system (for example, stones located in a calyx may be closer to the skin than one in the pelvis or ureter). The table's exact coordinate in the z axis is measured (in mm) by a sensor in the SWL table, and displayed in real time in a digital screen, located on the control panel of the SWL machine. To provide appropriate conduction of the shock waves from the therapy head to human tissue, a cylindrical water cushion is interposed to fill the gap between the skin and the therapy head. This cushion is deflated to lower the table and inflated to elevate it. The LTH is proportional to the ratio of water (cushion) to tissue in the media where the shock waves are propagated, within a conical area with the focal distance as its height. If the table is high, the cushion is inflated and a large proportion of the conical area is water; if it's low, shockwaves are conducted mainly through human tissue (Figure-1). Our objective was to evaluate this variable as a predictor of stone fragmentation and clearance.

MATERIALS AND METHODS

A prospective cohort study to assess predictive value of LTH in SWL therapy was designed and

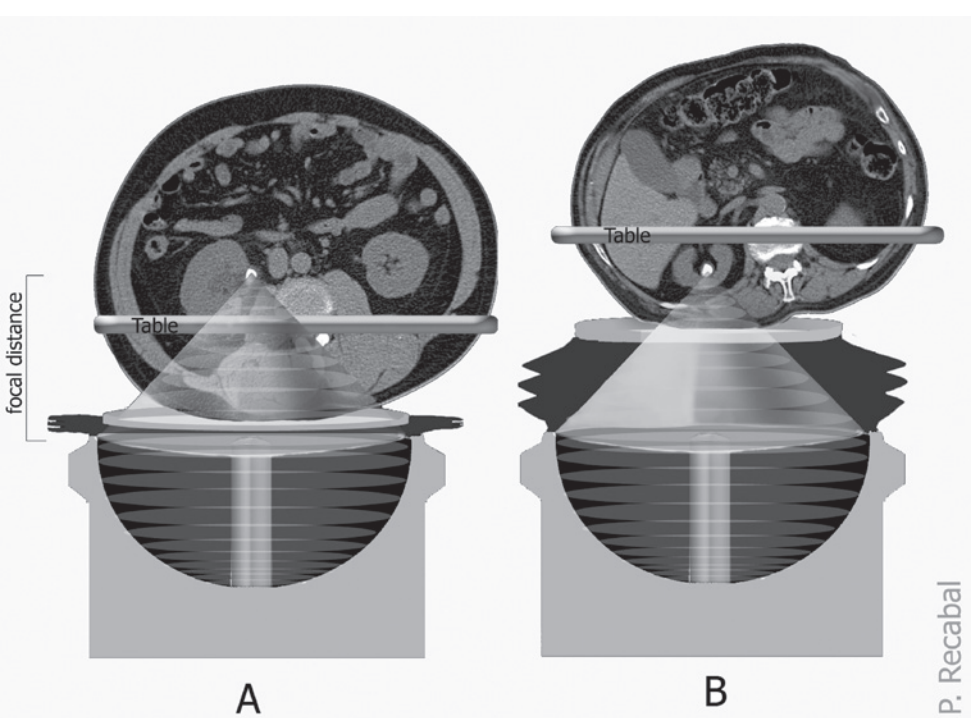

Figure 1 - *If the table is low (A), tissue represents a large proportion of the media where shockwaves are being propagated, whereas when* ***it is high (B), shockwaves are conducted mainly through water.***

conducted at Hospital Clínico Universidad de Chile. Calculated sample size was 50 patients, considering α = 0.01 power 0.9, and Relative Risk = 5. After approval by the review board, fifty-six untreated patients undergoing SWL at our institution were enrolled between October 2007 and July 2008. Inclusion criteria were having a solitary radiopaque urinary stone larger than 5 mm in its longest dimension as measured by non-contrast-enhanced computed tomography (NCCT) and SWL as the initial stone treatment. Written informed consent was obtained from each subject. SWL was done using a Modulith SLX (Karl Storz, Germany) Lithotripter in all procedures. This system unit is provided with a cylindrical electromagnetic shock wave source, X-ray C-arm for stone localization and patient table with floating table-top. By moving the patient table within a three dimensional Cartesian coordinate system under fluoroscopic guidance, stones were located on the focal point, 165 mm above the therapy head (focal distance for this lithotripter). LTH was set for each procedure by moving the table in along the z axis to locate the stone in the focal point, with an image intensifier at 30° relative to the vertical. Each procedure was performed with the table at one particular coordinate in the z axis (Figure-1), which was recorded as each individual patient's LTH. Shock waves are delivered by means of externally-applied, high-intensity acoustic pulses, reflected off a parabolic reflector and focused above the therapy head at a fixed distance. All procedures were performed under conscious sedation. A maximum of 3000 shocks were delivered to kidney stones and 4000 shocks to ureteral stones or until the stone was completely fragmented. Shockwave frequency was 60 min-1. Clinical data recorded included patient weight, height and age; stone location and size; number of shock waves delivered; and the LTH. A follow-up KUB was obtained at four weeks, and reviewed by a staff radiologist at our institution who was blinded to patient's body habitus and LTH. Stone free status was defined as absence of visible fragments on the KUB. Logistic regression multivariate analysis was used to evaluate the effect of several variables (LTH, BMI, stone size, number of shocks and age) on SWL outcome. A Receiver-Operating-Characteristic (ROC) curve was constructed to assess LTH test accuracy. A p-value of 0.01 or less was considered significant. Statistical analysis was performed using SPSS v15.0 and STATA 9.

RESULTS

Of the 56 patients, 39 were male and 17 female. Stones were in the kidney in 25 (44.5%) patients (of which 2 were lower pole stones) and in the ureter in 31 (55.5%) patients. At one month follow-up, 47 (83.9%) patients were stone free (absence of residual fragments); five had incomplete stone clearance, and four patients had no stone clearance (7.1%) and had subsequent retreatment. The LTH ranged from 184 to 277. Eight out of nine patients with residual fragments had an LTH under the mean (235). The mean LTH in the stone free group was 239 ± 17 vs. 216 ± 25 in patients with residual fragments (p = 0.001). Results are presented in Tables-1 and 2. In comparison of means

Table 1 - *Clinical and demographic characteristics.*

	Overall Mean (SD)	**Stone Free Mean (SD)**	**Residual Fragments Mean (SD)**	***p*-value**
n	56	47	9	
Stone size (mm)	10.5 (4.9)	10.2 (4.7)	11.6 (6.2)	0.330
BMI	25.6 (4.5)	25.3 (4.6)	27.1 (3.6)	0.327
LTH (mm)	235 (20.8)	239.8 (17.3)	216.0 (25.5)	0.001*
Number of Shocks	2499 (1015)	2375.5 (1002)	3144.4 (864)	0.003*
Age	42.2 (14.6)	41.5 (14.4)	46.7 (15.9)	0.380

Data for the entire group is presented as mean (standard deviation) in the second column. Data for Stone Free and Residual Fragment patients was analyzed by comparing means using t-test.
*Patients with residual fragments present a lower mean LTH, and a higher BMI, stone size and Number of shocks. / SD = Standard Deviation. BMI = Body Mass Index. LTH = Lithotripsy Table Height. / * statistically significant (p < 0.05).*

Table 2. *Univariate and multivariate analysis of factors predicting residual fragments.*

	Univariate Logistic regression			**Multivariate Logistic regression**		
Variable	OR (95% CI)	SE	p-value	OR (95% CI)	SE	p-value
Stone size	0.95 (0.84-1.08)	0.06	0.451	0.96 (0.81-1.15)	0.03	0.663
BMI	0.93 (0.81-1.07)	0.07	0.324	1.02 (0.84-1.23)	0.10	0.880
LTH	1.06 (1.02-1.11)	0.02	0.002*	1.06 (1.01-1.12)	0.03	0.031*
Age	0.97 (0.92-1.03)	0.03	0.380	0.97 (0.91-1.05)	0.04	0.464
N° of Shocks	0.99 (0.998-0.999)	0.00	0.032*	0.99 (0.998-1.000)	0.00	0.277

In the univariate analysis OR: Odds Ratios (95% confidence intervals).
*SE = standard error. BMI = Body Mass Index. LTH = Lithotripsy Table Height. / * statistically significant.*

using t-student, LTH and Number of shocks waves delivered were associated with outcome, where patients with residual fragments showed lower LTH and higher number of shocks delivered. No significant difference was found in LTH of patients in the supine vs. prone position (p = 0.20), or if compared by side (p = 0.24) or location (kidney vs. ureter; p = 0.26). No significant difference in outcome was noted when analyzed by stone location separating upper, mid and lower calyx, pelvis and upper mid and lower ureter (p = 0.59), although X2 may be not be meaningful due to the low count in some cells. No significant difference in outcome was observed if analyzed by location as kidney vs. ureter, using Fisher exact test (p = 0.49). LTH was the only independent predictor of outcome in the multivariate analysis (p = 0.02). A significant correlation was found between patient weight and LTH (Pearson -0.41; p = 0.002), and between BMI and LTH (Pearson -0.34; p = 0.010). In the ROC curve, the area under the curve was 0.79 for LTH (Figure-2). A cut-off LTH value of 218 yielded a sensitivity of 93.6%, specificity of 55.5% and positive predictive value (PPV) of 91.5% for success. Patients with very low LTH (i.e. < 218; n = 8; 14.2% of the sample) had a SWL success rate of 37.5% for LTH < 218 vs. 91.5% for LTH > 218, and a Relative Risk of residual fragments = 7.5.

DISCUSSION

In this study LTH appears as an independent predictor of outcome in SWL, showing statistical significance in both univariate and multivariate analysis. This is, to our knowledge, the first report that addresses LTH as a predictor of outcome. Interestingly, the marked increase of residual fragments in patients with very low LTH (i.e < 218), is noted in statistical analysis as the only variable with significant correlation to outcome, despite patients with residual fragments having received more shocks. BMI showed a significant correlation with LTH, but didn't reach statistical significance in the regression analysis. Accordingly, a study by Mensentzev (4) presented good SWL outcomes in morbidly obese patients, except when the stone was > 1 cm from the focal point. A tendency towards stone size was also noted. In our institution, patients with stones larger than 20 mm are primarily treated by endourological techniques, which explains the low number of stones larger than 20 mm in the cohort. For stones 20 mm or more (n = 4), both patients that were stone free had LTH above the media, whereas both patients with residual fragments had a LTH under the media. Apparently, this variable comes into consideration at the lower end of the distribution, as the energy delivered to the stone by means of the shockwave, is dissipated by reflection of part of the energy due to impedance mismatch in the media where it is being propagated (5), occurring not only when the shock wave propagates from water to tissue, but also within human tissue, due to different densities amongst different tissues such as skin, muscle, fat, kidney, etc... Thereby reducing the amount of energy that actually reaches the stone. This finding is a potential explanation to high SWL success rates in paediatric

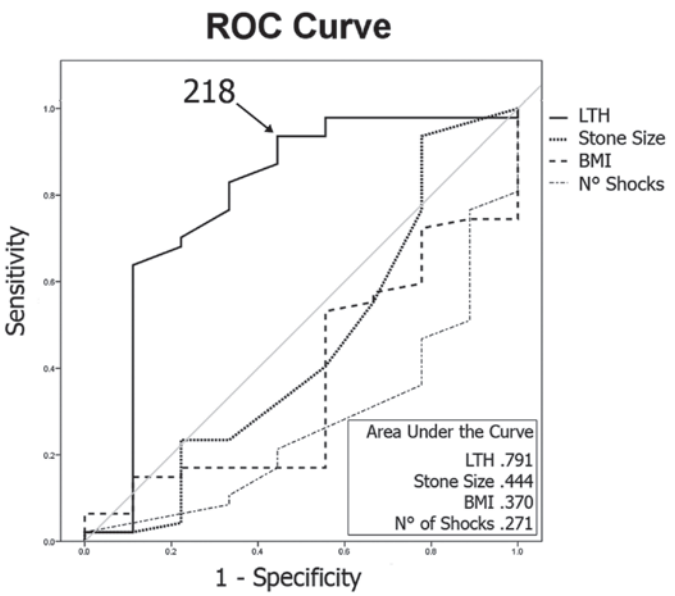

Figure 2 - *Receiver operating characteristic curve.*

patients (6-8), in which very high LTHs are to be expected. One drawback of this study is cohort size, as it was designed considering a large difference in means between groups, low statistical α value = 0.01, and potency 90%, and is thereby underpowered to rule them out as predictors; if a smaller difference is to be detected, a larger cohort is required. Cohort size also impairs further analysis considering specific stone location within the urinary tract. Our study supports the hypothesis that LTH predicts outcome, because it is proportional to the energy that actually reaches the stone. As the intracorporeal portion of distance to the focal point increases, stone fragmentation and clearance is reduced. Other important drawback is that other variables that have been related to outcome, such as stone location and composition (9,10), and data obtained from a NCCT such as radiographic density measured in Hounsfield Units (HU) (11-13), anatomical findings and SSD (4,14) were not included in the analysis. A special consideration should be made regarding SSD, a test addresses the same issue as the Lithotripsy table height. Apparently shockwaves aren't conducted perfectly in human tissue, and if more tissue is interposed between the shockwave generator, less energy is likely to reach the stone and cause its fragmentation. Unfortunatel,y most patients in our study were preoperatively evaluated with KUB / US and in those who had a NCCT, SSD was not available, so it remains to be determined which test is more reliable as an outcome predictor as these haven't yet been compared. Theoretically, LTH could be more accurate because it is inversely proportional the distance from the stone to the skin where the shockwaves are actually entering the body -this distance is not fixed as human tissue is lax and can be compressed differently in the CT-scan table than when the therapy head is attached for SWL- whereas SSD on the CT-scan is an average of three arbitrary measurements from the stone to the skin at 0, 45 and 90 degrees and does not necessarily represent the area where the shockwaves are being conducted, for example for SWL in the prone position. Having this information preoperatively in clinic is certainly more ideal than obtaining it right before the procedure, but this issue can be discussed preoperatively and a different procedure (such as Retrograde Intra-Renal Surgery) could be performed in the same table if expected SWL success is very low. A question that arises from our study is if it's the ratio of tissue to water, or only the total amount of tissue within the conical area where the shockwaves are conducted -analogue to the SSD- that determines the amount of energy actually delivered to the stone. Lithotripters

with a larger and broader parabola have larger focal distances, which varies the ratio of tissue to water without modifying the SSD. Unfortunately it is not possible to extrapolate the impact of different focal distances for different lithotripters, because our results were obtained using only one lithotripter, so the focal distance was the same for every procedure in this study. The comparison of lithotripters with different focal distances will help understand better the way shockwaves are conducted in the human tissue. We believe that even though a larger focal distance allows reaching 'deeper' stones, this patients will still present poorer outcomes than those with more superficial stones, meaning that the LTH effect will be present in every lithotripter but exact numbers may differ. Numerical data shown is only valid for the lithotripter used (Modulith SLX, Karl Storz, Germany), and, these findings need to be validated in studies comparing different machines.

CONCLUSIONS

SWL continues to be standard of care for many patients with stone disease, having satisfactory overall success rates. In this study, patients with residual fragments presented a significantly lower LTH than stone free patients. These findings could aid in patient selection, as an endourologic procedure might be performed instead, even in the same setting, for patients with very low LTH along with other variables predicting poor outcomes for SWL, and SWL could be considered for larger stones in patients with high LTH. Further studies are warranted to assess this variable in other lithotripters and consider other variables.

ABBREVIATIONS USED

LTH = Lithotripsy Table Height; SWL = Shockwave Lithotripsy; KUB = Kidney, ureters, bladder X-ray study; BMI = Body Mass Index; SSD = Skin-to-Stone Distance; HU = Hounsfield Units; NCCT = Non Contrast-enhanced Computed Tomography; ROC = Receiver Operating Characteristic; SF = Stone Free; RF = Residual Fragments; OR = Odds Ratio; SE = Standard Error; SD = Standard Deviation; CI = Confidence Interval

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
October 17, 2010

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EDITORIAL COMMENT

Extracorporeal shock wave lithotripsy (SWL) has remained the preferred treatment for small to moderate sized kidney stones. Stone size, location, composition as well as patient characteristics (e.g. body mass index, BMI) all influence outcome. Sampaio and Aragao (1) first described three anatomical factors that influence the success of fragment clearance after ESWL, including an infundibulopelvic angle of > 90°, an infundibular width of > 4 mm and special arrangement of the lower pole calyceal group. Pareek et al. (2) evaluated 64 patients with stones of 5-15 mm and found a statistically significant association between the stone-free rate, stone density and BMI (measured as skin-to-stone distance on CT) The most powerful predictor of failure was a skin-to-stone distance of > 8 cm.

In this study the authors analysed stone size, BMI and lithotripsy table height (LTH) as independent predictors of outcome following SWL. All procedures were performed with the Modulith SLX lithotripter. 56 patients were prospectively analysed. The main endpoint of this manuscript was that LTH was the only independent predictor of treatment results. Patients with LTH < 218 had much higher risk of residual stones than patients with LTH > 218.

The aperture focus distance varies with different types of lithotripter. The European Guidelines on Urolithiasis (3) recommends calculating the optimal (or maximal) skin-to-stone distance for each type of lithotripter. To my knowledge, this was the first report that offered LTH to help improve patient selection for SWL. The results were encouraging. I feel LTH calculation prior SWL could be recommended in obese patients.

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Clinical Urology
International Braz J Urol
Vol 37 (3): 362-370, May - June, 2011

Comprehensive Analysis of Etiology on the Prognosis of Urethral Strictures

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ABSTRACT

Introduction: Urethral strictures remain a reconstructive dilemma, due to high incidence of recurrence and less than satisfactory outcomes. Even experienced surgeons following strict surgical principles have not achieved optimal results, leading us to think whether
the etiology of strictures dictate the outcome . We evaluated this "cause-effect" relationship highlighting the significance of the etiology on the overall prognosis of urethral strictures.
Materials and Methods: A total of 302 males with urethral strictures were assessed (both retrospectively and prospectively) over a period of ten years. The preoperative evaluation was performed by retrograde urethrogram, urethrosonogram, and uroflowmetry and categorized, based on etiology: a) as post traumatic, b) post infective, c) iatrogenic or d) unknown. Traumatic strictures were subjected to pelvic X-ray and sub-categorized into grades A, B and C, following the TILE classification. Patients were operated; with tunica albuginea urethroplasty for anterior strictures and U shape prostato-bulbar anastomosis for posterior strictures.
Results: Traumatic strictures accounted for 54% of cases. 127 of the 302 patients were treated using Tunica Albuginea Urethroplasty, while U shaped Prostatobulbar Anastomosis was performed on others. Post traumatic strictures had best outcome whereas post infective strictures had the worse outcome. Among strictures following pelvic fractures, TILE grades A and B had a better post operative course as compared to TILE C. Overall complication rate was 13.24%.
Conclusion: Our study demonstrated that etiology of urethral strictures may play a vital role for the overall prognosis of urethral strictures.

Key words: *Prognosis; urethral stricture; treatment outcome; etiology.*
Int Braz J Urol. 2011; 37: 362-370

INTRODUCTION

Urethral Stricture Disease encompasses a spectrum of divergent ailments that cause obliteration of the urethral lumen and slowing or blocking urinary flow, secondary to fibrosis and healing of the urethral mucosa and surrounding tissues.

Urethral strictures have been a reconstructive dilemma for many years due to the high incidence of recurrence and less than satisfactory outcomes. A thorough preoperative evaluation, appropriate surgical planning, and adherence to basic surgical principles, even in the hands of the most experienced surgeon, have failed to achieve the desired results.

This has shifted the entire onus on the impact of a yet unexplored entity- the etiology.

Moreover, a stricture is a stricture, be it anterior or posterior and any etiology responsible for its causation, may lead to either an anterior or posterior variety of stricture.

Strictures are a common iatrogenic sequel to urethral instrumentation and catheterization. Infective strictures have taken a back seat when compared with the rate of pelvic trauma and urethral manipulation, as well as with the advent of newer antibiotics and increasing public awareness as regards to sexually transmitted diseases (1).

Despite advancements in the field of reconstructive urology, there is no consensus as the best mode of treating this complex entity, in order to optimize the results.

We evaluated the "cause- effect" relationship between etiology of urethral stricture and outcome post-urethroplasty.

MATERIALS AND METHODS

This study included 302 male patients presenting with signs and symptoms of urethral stricture, for the first time, over a period of ten years, both retrospectively as well as prospectively, from 1999 to 2009 [RKM, GA, BS, FK, SO]. Congenital strictures, as well as, patients managed without surgical reconstruction were excluded from the study.

A detailed preoperative assessment included careful history-taking and physical examination; followed by stricture evaluation via retrograde urethrogram, urethrosonogram, and uroflowmetry. Patients were categorized, based on their stricture etiologies, as post traumatic, post infective, iatrogenic (post catheterization and post instrumentation), or unknown.

Patients with traumatic urethral strictures were then subjected to pelvic X-rays in both anteroposterior and lateral views, to identify the presence, as well as, type of pelvic fracture, and further subcategorize them into grades A, B and C, of the TILE classification (Table-1).

Irrespective of the etiology, if any patient had chronic retention of urine or complete outflow obstruction not amenable to urethral drainage, a urinary diversion in the form of suprapubic cystostomy was done.

A minimum wait of 6 weeks was allowed before urethroplasty to patients that required suprapubic cystostomy. Tunica albuginea urethroplasty (TAU) was the procedure of choice for anterior urethral strictures and U shaped prostato-bulbar anastomosis (USPBA) for posterior urethral strictures, in order to minimize the influence of the surgical procedure on the outcome (2,3). No modifications were performed as regards to the surgical techniques, over the course of the study.

Post urethroplasty, a silicon catheter was kept for three weeks in case of simple strictures and for six weeks in complex strictures. Complex cases included the combined strictures of both the anterior and posterior urethra and the posterior urethral strictures with false passages resulting from multiple attempts of urethral instrumentation before the patients were referred to our center.

Table 1 - *TILE Classification of Pelvic Fractures.*

Tile Grade	**Fracture Type**	**Fractures Included**	**Fracture Management**
A	Stable, Minimally displaced.	Avulsion pelvis, Iliac wing, Isolated pubic rami, Undisplaced acetabular.	Conservative.
B	Rotationally unstable, Vertically stable.	Open book, Ipsilateral pubic rami with posterior complex injury, Bucket handle.	Conservative, occasionally require traction.
C	Rotationally unstable, Vertically unstable.	Unilateral pelvic, Bilateral pelvic [anterior & posterior], Acetabular with unilateral or bilateral pelvic.	Always require traction and/ or fixation.

Patients were scheduled for an initial postoperative assessment at the end of 3 months, with contrast urethrogram, urethrosonogram, and uroflometry. Post operative results were assessed by comparing pre and postoperative investigations and patient satisfaction (Table-2) and similarly at subsequent follow ups, at 6, 12 and 24 months to evaluate the long term results and complications.

RESULTS

The results are exemplified both descriptively and statistically. Most of our patients were young with a mean age of 35.5 years old (range: 15-65 years).

Prostatobulbar Anastomosis was performed in 175 patients (48%).

Results were quantified at regular intervals on the basis of the criteria enlisted in Table-1, evaluating patient's satisfaction.

Loss of follow-up is a well recognized challenge in any study but we collected data in 82% of our patients for two years.

A comparison of the etiology regarding to success rates depicted that post traumatic strictures had the best overall outcome. Whereas, post infective variety had the poorest results (Figure-1).

Among the strictures following pelvic fractures, those in TILE grades A and B had a better post operative course as compared to TILE C variety (Figure-2).

Table 2 - *Postoperative Result Assessment Criteria.*

	GOOD	FAIR	POOR
Retrograde Urethrogram	Good caliber.	Partial narrowing at stricture site.	Persistent stricture.
Urethrosonogram	Patent and distensible lumen.	Patent lumen with decreased distensibility	Stricture present.
Uroflowmetry	Qmax > 20 mL/sec	Qmax: 15- 20 mL/sec	Qmax < 15 mL/sec
Patient Satisfaction	Satisfactory voiding, No instrumentation needed.	Satisfactory voiding but required dilatations.	Not satisfied, not voiding or voiding with thin stream, need multiple dilatations or repeat surgery.

Traumatic strictures were the most common etiology found, accounting for 54% of all cases (Table-3). Although the most common stricture location was the membranous urethra (35%), the bulbar (30%) and penile (27.5%) urethra were equally affected and 7.5% patients had multiple urethral strictures.

Preoperative maximum flow rate (Qmax) analysis showed a range of 3.0 to 12.5 mL/s, the mean flow rate was 7.6 mL/s, which improved to 32 mL/s post operatively, ranging from 18 mL/s to 46 mL/s.

Average stricture length measured intraoperatively was 3.2 cm, ranging from 2.5 to 12.5 cm. A total of 127 patients (42%) were treated using Tunica Albuginea Urethroplasty, while U shape

Overall complication rate in our study was 13.24% (40 patients). Re-stenosis occurred in 4.6% patients second only to post operative infection (6.9%). Analyses of complications based on the primary cause are shown in Table-4.

DISCUSSION

Various studies have been done to identify the major etiologies for stricture formation, notwithstanding their actual impact on the long term outcome post surgical intervention.

In 1981, a review of 20 articles between 1961 and 1981, regarding the etiology of strictures,

Table 3 - *Various etiologies encountered.*

S. No.	Etiology	Number of cases	
		Number	% of cases
1.	Pelvic trauma	163	54%
2.	Post instrumentation	17	5.6%
3.	Post catheterization	64	21.1%
4.	Infection	46	15.2%
5.	Unknown	12	3.9 %

was published, with urethritis being the most common cause at that time, in 40% of the cases (4). Other major series in the developed world, also report a 32% to 79% rate of iatrogenic causes (5,6). Jordan and Schlossberg, in 2002, suggested that most strictures in the recent era are a result of external trauma (7). Our study also observed such transition to the etiology of strictures, with 54% incidence of urethral strictures occurring post trauma.

Traumatic strictures most frequently involve the posterior urethra. Pelvic fracture causing disruption at the bulbo-membranous junction. Studies have reported an incidence of such strictures up to 31%, in countries with poor road conditions, as well as, inadequate traffic regulations (8). Casselman and Schillinger hypothesized that the mechanism of injury to the urethra in major pelvic fracture cases involves compression of the pelvic ring laterally, resulting in an increase in the antero-posterior diameter, leading to superior bladder displacement and consequent urethral stretching and avulsion (9). In our study, 54% of strictures encountered were of the traumatic etiology, with 84% of these patients having radiological evidence of pelvic fractures. Various types of pelvic fractures were seen, majority of injuries classified as grades A and B (83.2%) of the TILE classification system (10), with involvement of the inferior pubic rami being the most common type.

The TILE classification of pelvic fractures is based on progressive instability of the pelvis (10). Type A fractures are stable with respect to rotation and vertical displacement, whereas type B fractures are rotationally unstable and vertically stable. Type C fractures are both vertically and rotationally unstable. Classifying by level of instability is valuable in predicting morbidity and mortality, as the pattern of urethral injury can be predicted on the basis of the type of pelvic fracture. The highest risk of urethral injury is found in a straddle fracture combined with diastasis of the sacroiliac joint (11). For every 1 mm increase of the pubic symphyseal diastasis, or displacement of the infero-medial pubic bone fracture fragments, the risk of urethral injury increases by 10% (12).

Post traumatic strictures tend to be short, occurring exclusively in the bulbar (5) and membranous urethra 87.73% of traumatic strictures in our study were seen to involve these sites, and 85% of these were less than 4 cm in length.

Management of post traumatic strictures usually involves preliminary diversion by suprapubic cystostomy, followed by definitive repair several weeks later. The delayed urethroplasty after 3 months after initial trauma reduces complications of impotence and incontinence. In addition, the major advantage of delayed urethral reconstruction is that it can be done under controlled conditions when the patient has recovered from major associated injuries (13).

In our study, 6 weeks post suprapubic cystostomy, these patients were taken up for surgery; with tunica albuginea urethroplasty (TAU) being our procedure of choice for anterior urethral strictures and U shaped prostato-bulbar anastomosis (USPBA) for posterior urethral strictures (2,3).

Postoperatively, periodic evaluation revealed a decline in the success rate over a period of time as depicted in our previous studies (2,3). A

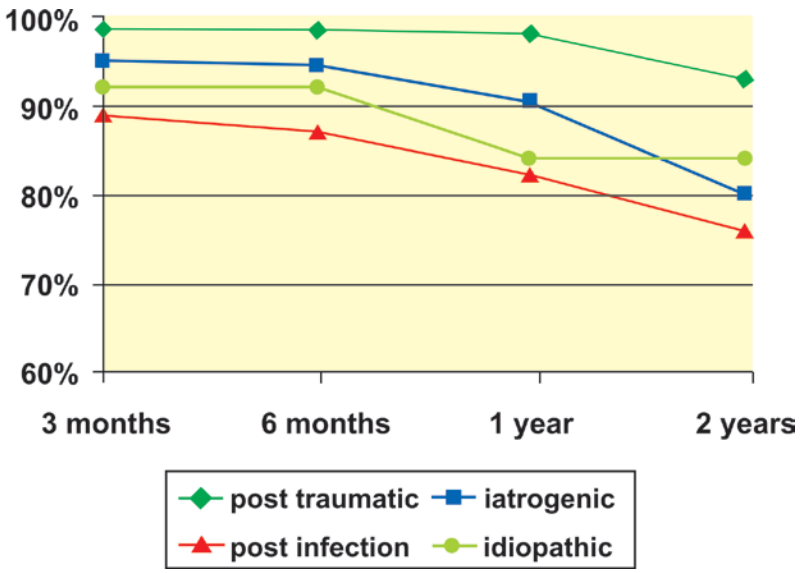

Figure 1 - *Etiology and success rates.*

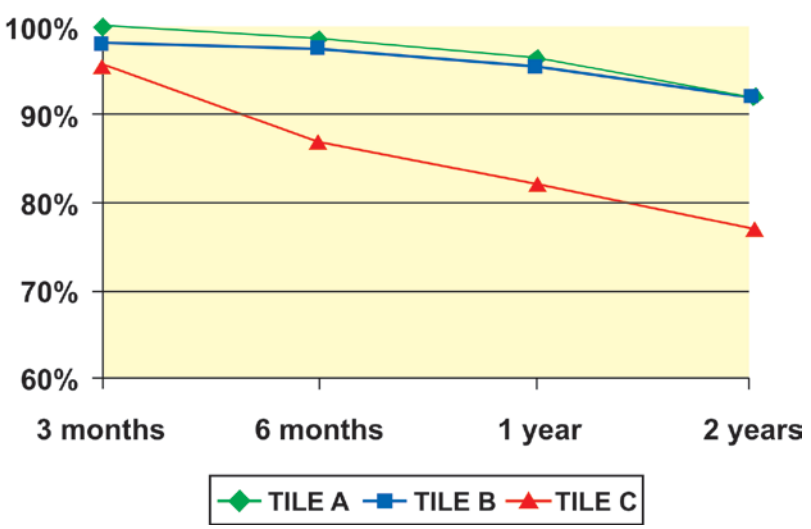

Figure 2 - *Success rates based on TILE grading.*

similar trend was evident in post traumatic strictures in the present study. Furthermore, the results were much better in patients falling in TILE category A, with 92% success rate at 2 years follow-up, when compared with 91.5% for TILE grade B and 77% in cases of TILE C, at the same time.

Numerous studies support the occurrence of complications after urethral injury following a pelvic fracture, due to the injury itself rather than the surgical technique (14-16). We encountered complications in 26 patients with post traumatic strictures: infection, re-stenosis, impotence, urinary incontinence, urethra-cutaneous fistulae, wound dehiscence and ejaculatory disturbances, with rates acceptable in comparison to other studies (17,18).

Iatrogenic urethral injuries producing urethral strictures result from urethral instrumentation, urethral catheterization, and rarely following

Table 4 - *Complication rates based on stricture etiologies.*

S.No.	Complication	Infection	Restenosis	Impotence	Incontinence	UCF	Wound Dehiscence	Ejaculatory problems
	Etiology	[6.9%]	[4.6%]	[1.6%]	[2.6%]	[1%]	[2.6%]	[1%]
1.	Pelvic trauma	6 [3.6%]	6 [3.6%]	3 [1.8%]	5 [3%]	1 [0.6%]	4 [2.4%]	1 [0.6%]
2.	Iatrogenic	7 [8.6%]	5 [6.1%]	1 [1.2%]	2 [2.4%]	1 [1.2%]	1 [1.2%]	2 [2.4%]
3.	Infection	7 [15.2%]	3 [6.5%]	1 [2.1%]	1 [2.1%]	1 [2.1%]	2 [4.3%]	0
4.	Unknown	1 [8.3%]	0	0	0	0	1 [8.3%]	0

abdomino-perineal resection for carcinoma of the rectum (19). Prolonged catheterization and transurethral surgery are the main reasons for the ischemic urethral insult. A rate of 32% to 79% of iatrogenic causes has been reported in different studies (5,6). We recorded a 26.8% incidence of iatrogenic urethral strictures.

Urethral stricture is a major late complication of TUR (2.2% to 9.8% of cases) (20, 21), as well as, radical (8.4%) (22) and simple (1.9%) (23) prostatectomy. Numerous causes of stricture formation post-TUR have been suggested, such as improper traumatic insertion of the resectoscope with perforation of the bulbous urethra and instrument friction at the penoscrotal angle, eventually exacerbated by the narrow urethral caliber as well as monopolar current "leak" due to insufficient resectoscope isolation (20). Moreover, patients undergoing such urological procedures are also catheterized in the post operative period. The exact cause, however, remains undetermined to date.

Prolonged catheterization, as in multiple trauma or burn patients, leads to urethral inflammation and ischemia, and ultimately stricture formation (5). Moreover, improper urethral catheter insertion is a preventable source of injury, with a recent report suggesting that 3.2 urethral injuries per 1000 inpatients occurred due to improper urethral catheterization (24).

Post instrumentation strictures are usually short and well defined, commonly located in the bulbomembranous urethra, whereas those occurring post catheterization tend to be long and irregular, and more common at the penoscrotal junction (19), correlating well with our findings. A total of 60% of post instrumentation strictures encountered by us were at the membranous and bulbar urethra, while 48% of post catheterization strictures were located at the penoscrotal junction.

Iatrogenic strictures frequently require elaborate reconstructive procedures (25). Repeated urethral dilatation exacerbates short strictures, making them longer (26). The reconstructive urologist must consider the etiology, as well as, the prior treatments when planning whether to excise or graft the stenotic urethral segment.

Post operative short term follow-up results were encouraging for post traumatic strictures but the long term results were not so good.

Infection and re-stenosis were the most frequent complications encountered s, more so in the case of post catheterization strictures, whereas impotence, incontinence, urethra-cutaneous fistulae, wound dehiscence and ejaculatory disturbances were also seen.

Nevertheless, adequate and strict indications for urinary catheterization, skilled urethral catheter insertion and consideration of suprapubic catheter placement whenever prolonged catheterization is anticipated, should decrease the incidence of these iatrogenic strictures, which often tend to be multifocal or panurethral (27), and thus more difficult to treat.

Inflammatory strictures may be seen with gonorrheal infection, nonspecific infections by chlamydia and ureaplasma urealyticum, as well as, lichen sclerosus, usually beginning with inflammation of glans and inevitably leading to meatal stenosis. Progression of stricture may involve the anterior and posterior urethra (28).

We encountered 46 patients (15.2%) with post infective strictures, with 66% of these located in the penile and bulbar urethra. Escherichia Coli was the most common isolate from the urine culture in these patients, suggesting that urethral obstruction may induce organisms which are cleared rapidly from the normal urinary tract, to cause bacteruria, bacteremia and even pyelonephritis (29).

Post urethroplasty evaluation at 6 months showed 86.95% success rate, which reduced to 75.67% at 2 years. A high rate of infection (15.2%) and re-stenosis (6.5%) was seen in the follow-up of inflammatory strictures, correlating with other similar studies. None of the patients, however, faced any ejaculatory problems. Post infective strictures was the worst in terms of overall prognosis.

Idiopathic strictures or strictures without any apparent reason have been observed in different studies (5,7,29). 3.9% of our patients fell into this category.

Although several theories have formulated, its mechanism remains unknown. But it may occur as a delayed manifestation of unrecognized childhood trauma, even presenting as long as 18 years after perineal trauma (1). Many idiopathic strictures may develop as a consequence of inadequate canalization, when the part of the urethra derived from the urogenital sinus joins the part derived from the urogenital folds, becoming symptomatic with growth (30). In elderly men, another explanation postulated is that idiopathic strictures are mainly ischemic in origin (29).

These strictures are significantly more prevalent in the bulbar area and more common in the younger age group (31). A total of 59% of idiopathic strictures in our study involved the bulbar urethra.

Our study demonstrates that post traumatic urethral strictures, secondary to pelvic fractures of the TILE category A, are shorter; mainly involve the bulbar and membranous urethra, post surgical intervention have the best long term outcome, as well as, the lowest complication rate, and the best prognosis.

CONCLUSIONS

Post urethroplasty success has been attributed to sevral factors,i.e.; location and length of the stricture, degree of spongiofibrosis, the choice of surgical procedure and surgical expertise. However, the impact of etiology regarding to outcome has remained unexplored. Our study demonstrated that the etiology may playsa vital role to the overall prognosis of urethral strictures treatment.

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
November 16, 2010

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EDITORIAL COMMENT

Mathur and co-workers present a very extensive series on urethral stricture disease and its management, as well as, prognostic factors. In their analysis they found that more than 54% of the strictures were posttraumatic. Moreover they are able to even correlate pelvic fracture patterns with individual outcome. Overall complication rate with less than 15% is remarkably low in such a complex cohort of patients. In addition to the well-known technique of prostato-bulbar anastomosis, the authors employed their own technique of for anterior reconstruction. The so-called tunica albuginea ure-

throplasty offers the advantage of locally available substitute tissue even in case of oral disease precluding the use of buccal mucosa (1). As such we do require alternative graft sources in patients with oral disease allowing for comparable complication rates (2). Genital skin remains such an alternative donor site being important for the reconstructive armamentarium. The authors clearly demonstrate that post-inflammatory strictures yielded a poor outcome as compared to the posttraumatic ones. In fact this observation is most likely due to underestimating the degree and extension of spongiofibrosis. Ultrasound has been shown to be a valuable tool for this task before urethroplasty (3).

Nevertheless, Mathur et al remain to be congratulated for the comprehensive analysis of stricture etiology, pelvic fracture pattern and individual surgical outcome. Being aware of the relation between these features and surgical success allows us for a more accurate preoperative counseling in our patients.

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Clinical Urology
International Braz J Urol
Vol 37 (3): 371-379, May - June, 2011

Patient Positioning During Digital Rectal Examination of the Prostate: Preferences, Tolerability, and Results

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ABSTRACT

Purpose: To evaluate the preferred position used by Brazilian Urologists to perform DRE, the position that Brazilian patients prefer or think it is less embarrassing to have a DRE, and to evaluate the results of DRE with patients in left lateral decubitus, modified lithotomy, standing-up, or the physician will have them place their elbows on the table and squat down slightly.
Materials and Methods: Brazilian Urologists were contacted by e-mail, and 200 patients answered a questionnaire while undergoing prostate cancer screening.
Results: The preferred position was modified lithotomy position reported by 63.4% of Urologists, and left lateral position reported by 42.7% of the patients. Total DRE time was lower in the standing-up position. Pain and urinary urgency scores were similar regardless of the position used, and bowel urgency score was higher in patients squatting down. Patients were similar in terms of age and PSA level, but there was a significant difference between the standard deviations of estimated prostate weight in left lateral position. There were no differences in prostate asymmetry, positive DRE, or incomplete palpation of the prostate rates among different examination positions.
Conclusions: Despite individual subjective preferences, a faster examination time in the standing-up position, and higher bowel urgency scores in patients with their elbows placed on the table and squatting down slightly, there were similar rates of prostate asymmetry, positive DRE, and incomplete palpation of the prostate, and comparable patient tolerability among different examination techniques.

Key words: *patient positioning; prostate; diagnosis; pain; digital rectal examination*
Int Braz J Urol. 2011; 37: 371-379

INTRODUCTION

Digital rectal examination (DRE) was the only diagnostic test for prostate cancer before 1920, and although diagnostic procedures have increased in number, complexity, and expense (1), DRE is still an important part of prostate cancer screening because of its simplicity, limited time and expenses, and relative little discomfort involved. Furthermore, DRE may detect more clinically significant prostate cancers, decreasing rates of overdiagnosis and overtreatment of potentially indolent prostate cancers.

Several positions have been recommended over the years to allow a thorough DRE, from the exaggerated knee-chest position and bimanual sitting-rectal position commonly used in the past (2,3), which are frequently uncomfortable, complicated and time-consuming, to the straightforward and most

frequently used positions (lateral position, modified lithotomy position, and standing-up position) (4-6).

Although positioning preferences are individual and, there is little published information comparing different position techniques during prostate cancer screening (4-6). The purpose of this study is to evaluate the preferred position used by Brazilian Urologists to perform DRE, in which position Brazilian patients prefer or perceived as less embarrassing to undergo DRE.

MATERIALS AND METHODS

Urologists' preferences

Urologists from 4 Brazilian States (PR, RS, SC, and SP) were contacted by e-mail regarding their preferences on patient positioning during DRE. Three e-mails were sent for all members of Brazilian Society of Urology in each State. The first email was entitled "Research on prostate cancer screening", and it had one question regarding in which position he/she usually performed DRE when screening for prostate cancer. The second and third emails were entitled "SECOND CALL" and "LAST CALL", respectively, and they were sent with 14 and 30 days delay between communications only for Urologists that did not answer the preceding e-mail. In the body of the e-mail, there was a figure illustrating the different positions, and a description of each possible alternative (Figure-1).

Patients' preferences

Two hundred patients undergoing prostate cancer screening answered if they had received DRE in the past. If 'yes', they answered, based on Figure-1, in which position they were examined previously, and in which position they preferred - or they perceived as less embarrassing - to undergo DRE. Patients who had no preference were examined in the same position they underwent DRE previously. If 'no', they responded in which position they preferred undergoing DRE for the first time. When no preference was stated, they were positioned at the discretion of the examiner.

Tolerability

Immediately after DRE, patients quantified the intensity of pain, urinary urgency, and urge to defecate felt during examination using a 0-to-10 visual analog scale (VAS).

Results

Total DRE time (in seconds) was recorded starting after patient instructions were given, including removing the pants down to patient's knees level, patient positioning, DRE, and clothing. Time using the toilet after examination was not included.

Estimated prostate weight (in grams), prostate asymmetry, positive DRE (presence of hard nodules), and incomplete palpation of the prostate rates were calculated for each position.

All patients were examined by a single examiner with 5 years of clinical experience after a 4-year Residency in Urology.

Statistics

Categorical variables were analyzed using Fisher Exact Test. Continuous data were evaluated using t-Student Test. Statistical significance in this study was set as $p < 0.05$.

RESULTS

Urologists' preferences

We received 506 (27.7%) answers from a total 1,827 e-mail contacts to Urologists from one Southeastern and three Southern Brazilian States; 193 (10.6%) e-mails were undeliverable, and 1,128 (61.7%) did not answer . The preferred position reported by 321 Urologists was modified lithotomy position (63.4%), followed by left (or right) lateral position (17.0%), standing-up position (14.2%), squatting down with elbows on the table (3.4%), and other position (1.0%).

Patients' preferences

From a total 200 patients, 111 (55.5%) had already received DRE in the past. In this group, when asked in which position they preferred - or

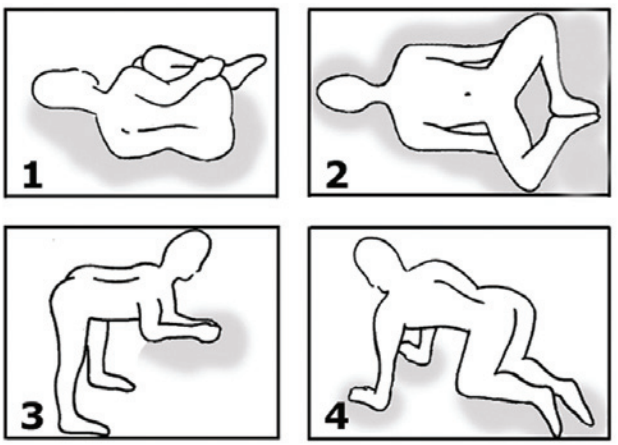


Figure 1 - *The Burdizzo clamp (A) positioned to crush the spermatic cord (B).*

thought it was less embarrassing - to undergo DRE, 69 (62.2%) patients chose the same position used previously, 24 (21.6%) chose a different position than in past DRE, and 18 (16.2%) patients had no preference (Table-1). Thirty-eight (55.9%) patients that had DRE in modified lithotomy position chose a different position in current DRE, and 2 patients who underwent examination in left lateral position or standing-up position chose a different position in current DRE (8.3% and 13.3%, respectively).

Eighty-nine (44.5%) patients underwent DRE for the first time. The preferred position chosen by these patients was left lateral position (42.7%), and 15 (16.9%) patients had no preference (Table-1). Overall, the preferred position was left lateral decubitus (37%), followed by standing-up (20.5%), modified lithotomy (19.5%), and squatting down with elbows on the table (6.5%).

Tolerability

The four groups of patients undergoing one of each position illustrated in Figure-1 were similar in terms of age and PSA level (Table-2). Pain, urinary urgency, and urge to defecate scores are summarized in Table-3. Urge to defecate score was higher in the squatting down position with elbows on the table, in comparison with the standing-up position. All other scores were comparable regardless of the position used.

Results

Total DRE time was lower for the standing-up position compared to all other groups. Timing among modified lithotomy position, left lateral position, and squatting down with elbows on the table was similar. Estimated prostate weight was different in the left lateral position when compared to modified lithotomy position, and to squatting down with elbows on the table. There was no difference in prostate asymmetry, positive DRE, or incomplete palpation of the prostate rates among the different posi-

Table 1 - *Patient positioning in past DRE, and patients' preferences in current DRE.*

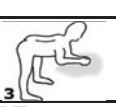
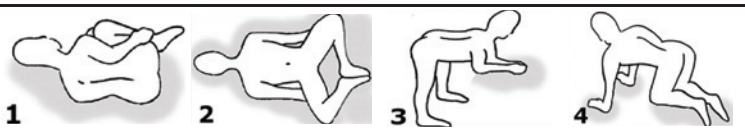
Preferred patient position for DRE	1	2	 3	4	**No preference**
Positive past history of DRE					
Position in past DRE	24 (21.6)	68 (61.3)	15 (13.5)	4 (3.6)	-
Same position chosen in current DRE	22 (31.9)	30 (43.5)	13 (18.8)	4 (5.8)	18 (16.2)
Different position chosen in current DRE	14 (58.3)	0 (0.0)	7 (29.2)	3 (12.5)	
Preferred position	36 (32.4)	30 (27.0)	20 (18.0)	7 (6.3)	18 (16.2)
Negative past history of DRE					
Preferred position	38 (42.7)	9 (10.1)	21 (23.6)	6 (6.7)	15 (16.9)
TOTAL	**74 (37.0)**	**39 (19.5)**	**41 (20.5)**	**13 (6.5)**	**33 (16.5)**

Table 2 - *Age and PSA level of the patients.*

Pain/discomfort					p value
	1	2	3	4	
Age (years)	50.0 ± 8.3	51.0 ± 7.3	52.5 ± 7.3	55.0 ± 8.7	> 0.05
	(39 – 77)	(40 – 72)	(41 – 71)	(43 – 68)	
PSA (mg/dL)	0.97 ± 1.7	1.18 ± 2.9	1.20 ± 2.6	0.87 ± 1.5	> 0.05
	(0.1 – 7.4)	(0.1 – 17.1)	(0.2 – 13.0)	(0.3 – 5.0)	

tions (Table-4). The number of patients in each group was not large enough to allow comparison between rates of prostate cancer detection in each position. Two (1.0%) patients had prostate cancer overall, both in the left lateral position group.

DISCUSSION

Positioning preference for examining the prostate varies from one country to another (4), from one examiner to another (5), and even from one patient to another (6). In the US, DRE is more often performed in the standing-up position, while in UK patients are usually examined in the lateral position (4). In Brazil, Messina et al. reported that the preferred position for DRE reported by 846 Urologists is the dorsal decubitus position (57.9%) (5), similar to the modified lithotomy position reported in the present study, which was the preferred position claimed by 63.4% of responders.

Furlan et al. reported that 53.9% of 269 patients preferred DRE in supine position (similar to modified lithotomy position) (6). A potential bias in this study was that patients answered the question regarding their preference after receiving DRE in supine position. In the present study, we observed that patients' preferences are influenced by past experience, given that 62.2% of patients chose the same position used in past DRE. Therefore, patient preference may be to some degree related to examiner preference. The preferred position reported by Brazilian Urologists (modified lithotomy position) was validated by the fact that 61.3% patients receiving DRE in the past were examined in this position. Previous experience certainly influenced patients' preferences, since all

Table 3 - *Patient tolerability of DRE.*

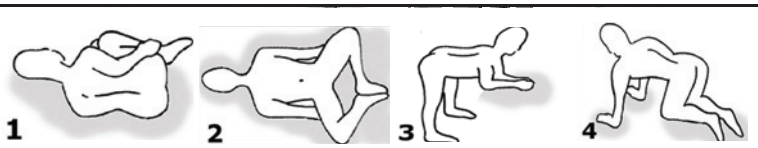
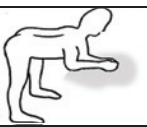
Pain/discomfort median ± SD (range)					p value
	1	2	3	4	
Pain score	5.0 ± 2.2	4.5 ± 2.2	5.0 ± 2.4	5.0 ± 2.1	> 0.05
	(0.5 – 9.5)	(0 – 10)	(0 – 10)	(0 – 7)	
Urinary urgency score	2.2 ± 3.1	2.0 ± 3.0	4.0 ± 3.7	2.0 ± 3.5	> 0.05
	(0 – 10)	(0 – 10)	(0 – 10)	(0 – 10)	
Bowel urgency score	0.0 ± 2.6	0.0 ± 2.2	0.0 ± 2.2	1.5 ± 3.4	*
	(0 – 10)	(0 – 8)	(0 – 10)	(0 – 8)	

Table 4 - *Results of DRE.*

Results	1	2	 3	4	p value
Total DRE times ± SD (range)	140.5 ± 27.6 (93 – 241)	142.0 ± 23.8 (104 – 202)	111.0 ± 18.6 (86 – 168)	148.0 ± 20.0 (124 – 188)	*
Estimated prostate weigth g ± SD (range)	40 ± 10.6 (20 – 80)	40 ± 12.6 (20 – 80)	40 ± 11.2 (20 – 70)	45 ± 8.1 (35 – 60)	**
Prostate asymmetry rate No. (%)	19 (21.1)	10 (21.3)	10 (19.2)	3 (30.0)	> 0.05
Nodularity rate No. (%)	2 (2.2)	2 (4.2)	2 (3.8)	0 (0.0)	> 0.05
Incomplete palpation of the prostate rate No. (%)	2 (2.2)	2 (4.2)	2 (3.8)	0 (0.0)	> 0.05

** p < 0.001 in total DRE time for all groups compared to standing-up position*
*** p < 0.05 in estimated prostate weigth between modified lithotomy position, and kneeling while resting on the table with the hands compared to left-lateral position*

patients that chose modified lithotomy position in current DRE were positioned in the same way in previous DRE examinations. In Furlan's study, if patients were able to choose a different position than supine, most patients would have preferred the standing-up position, followed by left lateral position (6). In the present study, patients undergoing DRE for the first time picked left lateral position first and standing-up position second. In the group of patients that had received DRE in the past, the preferred position was, again, left lateral position, followed by modified lithotomy position and standing-up position. Based on these results, most patients prefer or perceive as less embarrassing to undergo DRE in the left lateral position or the standing-up position. In addition, we observed that the majority of patients that had DRE in the past have a tendency to be positioned in the same way, and that 16.5% of patients have no preference, or they believe the selection of positioning is up to the examiner. Only one study compared patient preference between standing-up position and left lateral position, and found better acceptance of the standing-up position (7).

Despite individual subjective preferences, there is little objective information to suggest that positioning of the patient makes much difference in the results of DRE. In the present study, we found that total DRE time was lower for the standing-up position. Since DRE was performed in all patients by one examiner in the same medical office, the single difference in total DRE time between each position was patient positioning itself. Lower DRE time in standing-up position may be due to needless laying on the examining table, and speedier clothing after examination. Although time should not be a major issue while evaluating patients' health, faster examination may be valuable if standing-up position prove to be as effective as other positions, particularly when examining large number of patients in prostate cancer screening programs.

Early in the past century, Frank Hinman stated that the exaggerated knee-chest position (on the knees with hips to heels and chest to knees) was the only position that allowed a thorough palpation of the prostate and seminal vesicles (2). Although some conditions such as obesity, hip

osteoarthritis, bedridden patients, or extremely large prostates may require special positioning or bimanual examination to allow for complete palpation of the prostate (3), currently, the majority of patients may be satisfactorily examined in one of the four positions. Overall, we found a 0% to 4.2% rate of incomplete palpation of the prostate, similar between the different positions studied. When the prostate cannot be completely palpated, additional flexion of the hips and knees is a simple method that frequently allows a complete examination.

Subtle findings such as asymmetry between prostate lobes may be suggestive of the presence of prostate cancer, and considered by some to be an indication for prostate biopsy (8). Empirically, when prostate asymmetry is acknowledged in left lateral position, patients should be examined again in a different position to confirm asymmetry. This was not confirmed in the present study, since prostate asymmetry rate was similar between the different positioning techniques.

Romero et al. reported that pain and discomfort during DRE are not negligible, and that measures to decrease patient distress should be evaluated (9). In their study, in which all patients were positioned in modified lithotomy, 61% reported moderate to unbearable pain, and 22% reported moderate to unbearable urinary urgency or urge to defecate during DRE (9). Using a VAS, Furlan et al. reported a mean pain score of 1.68 for DRE in supine position (6), and Kaygisiz et al. found a mean pain score of 2.59 in left lateral position (10). In our study, mean and median pain scores were respectively 4.63 and 5.00 ± 2.3 for the entire cohort, similar among the different positions evaluated. Patients in standing-up position, however, had a tendency to higher urinary urgency score (median 4.00 ± 3.7). Urge to defecate score was higher in patients positioned squatting down with elbows on the table (median 1.50 ± 3.4) in comparison with the standing-up position (0.00 ± 2.2). These results should be interpreted with caution due to the small number of patients.

Patients in the different subgroups of our study were similar in terms of age and PSA level, and although median estimated prostate weight was identical in left lateral position (40g ± 10.6), modified lithotomy position (40g ± 12.6), and standing-up position (40g ± 11.2), there was a significant difference between the standard deviations of estimate prostate weight in left lateral position, modified lithotomy position, and squatting down with elbows on the table (45 ± 8.1). Since the degree of prostatic enlargement is of more practical interest than the precise estimate of prostate volume (11), small differences between the groups may not be clinically significant.

Strengths of our study include that a single examiner performed all DRE per site. Patients were questioned about their preferences before examination, avoiding bias, and they were divided in groups according to their choices. Limitations to this study include a small survey response rate (27.7%). However, the proportion between the different positioning preferences remained fairly the same throughout data collection. Randomization through patients' and examiners' preferences is not a recommended method for research purposes. Standard methods of randomization should be used in future studies. Another limitation was the relatively small sample size in each subgroup, especially for the squatting down with elbows on the table. A significantly larger sample of patients would be necessary to evaluate the rate of prostate cancer detection.

CONCLUSIONS

The preferred position reported by Brazilian Urologists to perform DRE of the prostate is the modified lithotomy position, while our patients prefer or think it is less embarrassing to receive DRE in left lateral position.

Results of DRE in the different positions evaluated demonstrate a faster examination time in the standing-up position, and similar prostate asymmetry rate, positive DRE rate, and incomplete palpation of the prostate rate. Pain, urinary urgency, and bowel urgency scores are also comparable between each position, except for squatting down with elbows on the table, which may show increased bowel urgency score.

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
October 18, 2010

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EDITORIAL COMMENT

The need to undergo a Digital rectal examination (DRE) as part of the Prostate cancer screening continues to torment many patients. Despite many articles suggesting that it is unnecessary, DRE continues to have a role in the diagnosis and management of prostate cancer as the search for the perfect marker continues.

Romero et al. have reported on patient positioning during DRE of the prostate. They have analysed both the clinicians' and the patients' preference about undertaking/undergoing a DRE. It is no surprise that most patients prefer the left lateral position which is my experience in the United Kingdom as well as the Far East. This could be attributed to the ability to avoid eye contact in this position. Also, the foetal position is somewhat comforting. On the other hand, The North American Urologists tend to prefer the knee-elbow/bent over position which is quicker and less taxing on the mobility-challenged.

An important finding in the study is the total completeness of the examination in the knee-elbow position. This suggests in a select group of

patients such as the markedly obese, this position would be appropriate.

This article suggests findings which should enable urologist to undertake a better quality DRE especially from the patient perspective.

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EDITORIAL COMMENT

Digital rectal examination (DRE) is done for various complaints. The patient's position should adopt according to their desire, comfort, physical condition and the indication concerned. The purpose of the study was to evaluate the preferred DRE position by the urologists and their patients, a comparison between four typical positions. The exam is important to the diagnosis of anorectal disorders and prostate palpation. It is considered as one of the physician basic skills (1). Without a DRE, patients would have their disease detected only by the presence as urinary symptoms and cancer would be more likely to have higher stage and less potentially curable (2). The quality and degree of the pain and discomfort is debatable among studies, encourage us to find the best clinical set up for patients acceptance and cooperation even in their inexperienced first visit (3-5). A previous attempt to investigate the tolerability and acceptance of the patients have been presented by Furlan et al., yet this new study sheds more light and adequate statistical power (3). As for this manuscript, one can consider retrieving data regarding doctor's finger diameter and length; it might influence the patients discomfort in specific positions.

Left or right lateral position seems to be mostly preferred by the patients while the modified lithotomy position is mostly preferred by the urologists. The main argument for the patients prefaration is decreased embarrassment. In our every day practice we attempt to adopt to our patients needs and comfort in order to keep their compliance and cooperation, therefore the lateral position seems to be more popular while doing full abdomino-pelvic examination. However it is common to use a standing up position for annual prostate screening and therefore this data should be correlated to the status of the visit (first, routine annual or part of other urological investigated issues) and be explained to the examinee beforehead. One should realize that even a small, simple clinical issue might be so important for the well being of the patients, for his further cooperation that eventually will lead to a better diagnosis and early detection of treatable disease.

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EDITORIAL COMMENT

The authors evaluated the preferred position for digital rectal examination (DRE) used by Brazilian Urologists and patients. They also analyzed results and tolerability of different positions. DRE should be part of urological evaluation; PSA does not reduce the value of DRE. This kind of papers emphasizes the importance of DRE.

In this study preferred position is written and discussed well, study gives information about pain score and even urinary and bowel urgency score. However modified lithotomy position was preferred by Brazilian Urologists, different positions could be selected in different country with the similar pain and discomfort rate. This study could guide the clinician to select the position; for example standing-up position could be selected in busy clinics with lower total DRE time.

Mean pain score of DRE is 5.0, this high pain score should not discourage the urologist to perform DRE since pain score was lower in previous literatures (1,2) as written in discussion.

Limited patients' number of group 4 and position selection criteria with examiners' and patients' preferences are deficiency for comparing the DRE pain and tolerability between groups as written in discussion. This analyze could not give us definite judgment however it is well written paper for patient and urologist selection with pain and tolerability for whole groups and it should have been the essence of the study.

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International Braz J Urol
Vol 37 (3): 380-387, May - June, 2011

Urinary Incontinence Following Surgery for BPH: the Role of Aging on the Incidence of Bladder Dysfunction

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ABSTRACT

Purpose: The reported incidence of urinary incontinence (UI) due to bladder dysfunction following surgery of BPH is variable. We described the causes of incontinence in a large group of men that developed this unsual complication and analyzed the influence of age on the prevalence of bladder dysfunction.
Materials and Methods: We wvaluated a total of 125 patients with urinary incontinence following surgical treatment for BPH : Transurethral resection of the prostate (81men) and open prostatectomy (44 men). A third group of 21 patients with incontinence following radical prostatectomy was used for comparison. All patients underwent urodynamic analysis. Urethral Sphincter Insufficiency (USI)was defined as involuntary loss of urine induced by Valsalva maneuver in the absence of a detrusor contraction. Bladder dysfunction was defined as detrusor overactivity and/or decreased compliance.
Results: Urethral sphincter insufficiency was the most common etiology of urinary incontinence in the three groups of patients. However, bladder dysfunction was observed in 59.3%, 56.8% and 57.1% of patients who underwent transurethral resection, open prostatectomy and radical prostatectomy, respectively. Median patient age was 69 and 75 years for patients with and without bladder dysfunction, respectively. A logistic regression model for the presence of bladder dysfunction showed that age was a statistically significant predictor.
Conclusions: Urethral Sphincter insufficiency is the main cause of incontinence following surgery for BPH. Bladder dysfunction may be the isolated cause of incontinence in approximately 25% of patients. The chances of bladder dysfunction rises 5.3% for each year added to patient age. Patients older than 70 years have twice the probablility of post procedural incontinence.

Key words: *Prostate; benign prostatic hyperplasia; urinary incontinence; surgery*
Int Braz J Urol. 2011; 37: 380-387

INTRODUCTION

BPH is the most common benign neoplasm in men (1) and contemporary data shows that about 10% of these patients will need some form of surgical treatment (2). UI following surgery for BPH is a rare complication. While early incontinence may occur in up to 30-40% of patients, late incontinence occurs in fewer than 1% of cases (3,4).

The etiology of post-prostatectomy incontinence can be multifactorial, including USI and/or Bladder dysfunction (BD) defined as Decreased compliance (DC), or Detrusor Overactivity (DO) (5). USI occurs as a result of injury to the sphincter mechanism and incontinence is usually associated with increase in. BD, which includes detrusor overactivity and/or DC. Moreover, DC is associated with increase in detrusor pressure with storage of urine, which can result in urinary incontinence.

However, while UI following RP, is mainly attributed to SI, (5,6) the prevalence of BD among patients with UI following surgery for BPH may

be significantly higher (7). Some studies have reported that more than 60% of these cases are attributed to BD, probably as a result of the long-lasting obstructive process (8).

Due to the inconsistent reports linking BD to post-prostatectomy incontinence, (7-9) and the impact of BD on the outcome of treatment, we reported the causes of UI in a relatively large group of men with this rare complication following surgery for BPH and compared them to a group of patients with UI following RP. We also analyzed the influence of age on the prevalence of BD.

MATERIALS AND METHODS

A total of 125 patients referred from various centers with UI following surgical treatment for BPH (TURP in 81 and OP in 44) were evaluated at our Urodynamics laboratory during the last 19 years. A third group of 21 patients with UI following RP for treatment of prostate cancer was used for comparison. Mean elapsed time between prostatectomy and urodynamics evaluation was 21 months (range 6 to 168 months).

All patients provided a detailed clinical history which included age, time interval since the prostatectomy, presence of urgency or stress incontinence and concurrent medications. Severity of incontinence varied from use of one pad per day to constant leakage and all men were disappointed with the complication. A focused neurological examination was performed at presentation and no patient presented a potential neurological cause for their urinary dysfunction.

All patients underwent urodynamic analysis as previously described (10). Uroflowmetry was performed when possible. Peak flow rate, voiding time and volume were recorded. The patients were then catheterized and post-void residual volume was measured. Cystometrogram comprised multichannel water cystometry with simultaneous measurement of vesical and abdominal pressure. Intravesical, intra-abdominal and detrusor pressures, filling and volume voided, were measured.. International Continence Society recommended definitions were applied (11). DO was defined as any involuntary bladder contraction occurred during filling with a pressure rise of 15 cmH2O or more, or involuntary contraction of any magnitude associated with urgency. Bladder compliance was calculated by dividing the bladder capacity in cc by detrusor pressure in cmH2O at cystometric capacity. A value of less than 12.5 cc/cmH2O was considered DC (12). USI was defined as involuntary loss of urine induced by Valsalva maneuver in the absence of a detrusor contraction. BD was defined as DO and/or DC.

Urinary incontinence was defined as an involuntary loss of urine passively or stress induced during the urodynamic evaluation. With the patient in the supine position, the bladder was filled to 200-250 mL (Filling rate of 50 mL per minute) and various provocative maneuvers were performed. If no leakage occurred, stress test was repeated at 50 mL increments until maximum capacity. During the filling any overactivity or DC was noted. If no leakage was detected, the urethral catheter was removed and the patient was asked to perform Valsalva maneuver in the standing position. All urodynamic studies were performed by the same physician. Review of each study was done by independent third party, to eliminate any artifacts and to determine accurately the urodynamic diagnosis.

For statistical analysis patients were divided into groups based on type of surgery and urodynamic diagnosis. Analysis of patients characteristics according to the type of surgery were performed through the ANOVA, Kruskal Wallis and Fisher's exact tests. Relationships between patient age and urodynamic variables were calculated through the Pearson's correlation coefficient. For analysis of patient age according to the presence of BD we also used the Student's T test. Finally, the influence of age on urodynamic findings was analyzed using a logistic regression model. Statistical significance was defined as a $p < 0.05$.

RESULTS

Patients age ranged from 45 to 88 years old (mean 69 y.o.). Analysis of patient's characteristics according to the type of surgery showed that patients with UI who underwent OP tended to be

older and had greater rates of compliants related to stress UI. Median urinary flow rates were greater among patient who underwent RP, but these results were only marginally significant. Median urethral functional length was shorter among patients who underwent RP (Table-1). Other variables were not statistically different between the three groups.

tion with USI in 20 patients (13.7%). DC was the sole cause of incontinence in 13 patients (8.9%) and occurred in combination with SUI in 30 patients (20.5%). While almost 14% of patients who underwent TURP presented DC as the sole cause of UI, no patient who underwent RP had this finding; however this difference was only marginally

Table 1 *- Characteristics of the patients according to the type of surgery.*

	TURP (n=81)	OP (n=44)	RRP (n=21)	p
Mean age (years)	69.0 (± 9.1)	72.0 (± 6.9)	67.0 (± 6.3)	0.07*
(min – max)				
Complaint				
Stress UI	43.2%	72.7%	52.4%	0.004**
Urgency UI	16.0%	2.3%	2.3%	
Total UI	39.5%	25.0%	47.6%	
Median urinary flow (mL/s)	9.0	10.0	12.0	0.087***
(min – max)	(3 – 24)	(2 – 35)	(8 – 16)	
Median bladder capacity (mL)	350	350	350	0.608***
(min – max)	(50 – 900)	(50 – 600)	(100 – 500)	
Urethral leak point pressure	42	37.5	40	
(cm H2O)	(10 – 200)	(0 – 200)	(2 – 90)	
Median urethral functional length (cm) (min – max)	3 (1 – 6.5)	3 (1 – 6)	2 (1 – 3.5)	0.006***

**ANOVA / **Fisher exact test / ***Kruskal Wallis test*

The etiology of post-prostatectomy incontinence according to urodynamic analysis was unrelated to the type of surgery. USI was the most common etiology of urinary incontinence in the three groups, and was observed in 66.7%, 79.6% and 85.7% of patients who underwent TURP, OP and RP respectively (p = 0.126). USI alone was found in 56 patients (38.4%) and was present in combination with BD in additional 51 patients (34.9%). USI was considered the main cause of UI in those patients with associated BD because of their clinical complains (stress urinary incontinence without symptoms of urgency). BD consisting of DO and/or DC was detected in a total of 85 patients (58.2%). DO was the isolated cause in 21 patients (14.4%) and was found in combina-

significant. One patient presented poor compliance and DO in combination with SUI. One patient had bladder outlet obstruction and overflow incontinence. In three patients incontinence was not demonstrated on urodynamic evaluation (Table-2).

Analysis of patient age according to the presence of BD showed that median patient age was 72 and 68 years old among patients with and without BD respectively (p = 0.020) (Figure-1). Correlation of patient age and complaint of stress or total UI demonstrated that median patient age was 69 and 75 years old for patients with and without incontinence issues, respectively (p = 0.031). The median patients age was 68 and 73 years old for patients with USI and without USI documented with uodynamic studies, respectively (p < 0.001)

Table 2 - *Cause of UI according to the type of surgery.*

Cause	TURP	OP	RP	p
DC	13.6%	4.5%	0	0.086
DO	16.0%	13.6%	9.5%	0.848
DO + SI	9.9%	20.5%	14.3%	0.242
SI	37.0%	40.9%	38.1%	0.943
SI + DC	18.5%	18.2%	33.3%	0.304
SI + DO + DC	1.2%	0	0	> 0.999
Normal	2.5%	0	4.8%	0.253
Obstruction	1.2%	2.3%	0	> 0.999

(Figure-2). Associations of age with urodynamic parameters through the Pearson correlation test only showed that age was inversely associated with urinary flow. The other parameters presented lower correlation coefficients (Table-3).

A logistic regression model for the presence of BD considering patients age and type of surgery revealed that age was a statistically significant predictor of outcome. (Table-4). These results demonstrate that each additional year of age increases BD by about 5.3%. Likewise, when patients with a 10 year difference in age are compared, the chances of BD increases by 67%. BD was 2.3 times more likely to occur in older patients > 70 years old (p = 0.017; OR = 2.326). The type of the surgery had no significance in these results. In fact, the proportion of patients with BD was 59.3%, 56.8% and 57.1% among patients who underwent TURP, OP and RP respectively (p = 0.960).

DISCUSSION

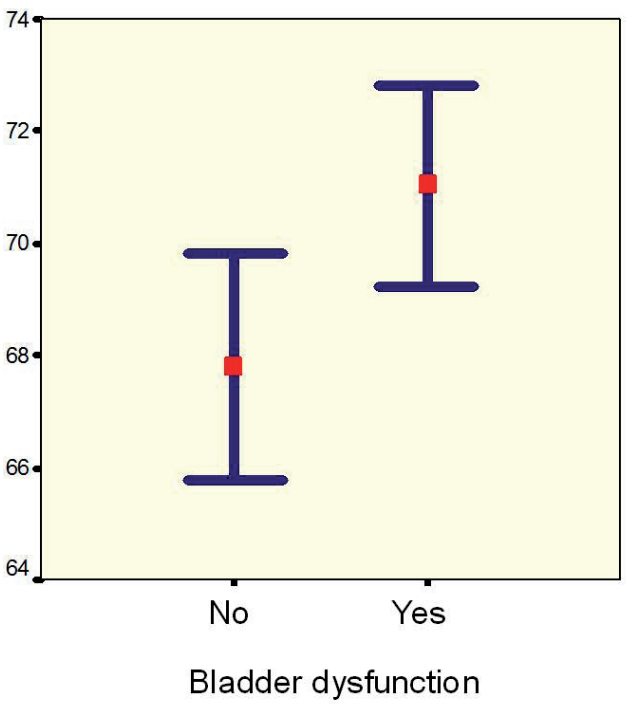
Post-prostatectomy urinary incontinence, although often temporary, is a devastating complication with a major impact on quality of life. In the present study we demonstrated that despite patients who underwent OP presented greater rates of incontinence related to stress UI, the etiology of UI according to urodynamic findings were statistically similar between the three groups of patients. Patients who underwent TURP presented higher rates of UI due to DC when compared to patients who underwent OP or RP, but this figure was only marginally significant.

Post-prostatectomy incontinence may be a temporary impairment which may spontaneously resolve. Most patients recover urinary continence within the first 6 months following surgery. Early incontinence is usually related to urge incontinence, either because of irritative symptoms due to the prostatic fossa healing and associated urinary tract infections or detrusor overactivity caused by long-lasting BPH (3). In the present series, urodynamic studies were performed after the 6th postoperative month.

Incontinence that persists longer than six months may require complete investigation including an urodynamic evaluation. Many factors have been implicated in the etiology of post-prostatectomy incontinence. They include BD, such as DC and/or DO and damaged sphincter mechanism. In the present study more than 70% of cases of UI were attributed to USI. These cases are usually caused by iatrogenic trauma of the external sphincter. Particularly, in cases that undergo TURP, which were the majority in our series, the lesion usually occurs ventrally (at 12 o'clock), where the Verumontanum is not visible. Also, there is an increased risk of sphincter injury if the Verumontanum has already been resected (3).

Conflicting reports in the literature make it difficult to confirm the importance of BD on the pathogenesis of UI. In our series, BD was detected in 58.2% of the patients and was the isolated cause

Figure 1 - *Mean patients age according to the prevalence of bladder dysfunction (p = 0.020).*



of UI in approximately 25% of patients. Although only 9.5% of patients who underwent RP had UI due to BD, these figures were only marginally significant (Table-2). Similarly to our results, a study of 60 men with a mean age of 64.8 years who underwent RP and acquired post-prostatectomy UI, USI was demonstrated in 90% of cases. A component of BD was seen 45% of cases (mainly due to DO), but incontinence was actually a result of BD in only 27% of patients (5).

Other series have analyzed patients who underwent surgery for BPH regarding post-operative continence rates. An analysis of 56 incontinent patients, 31 who had undergone TURP and 25 who had undergone RP, showed that patients in the TURP group were older and had higher incidence of DO. Interestingly, the most common etiology for UI, was DO alone. DO was present in 61% of cases, including 77% after TURP and 40% after RP. Stress incontinence alone was present in only 5% of patients, including 3% after TURP and 8% after RP, and DO with stress incontinence was present in 34% of cases, including 19% after TURP and 52% after RP (8). Another retrospective review of the records of 56 patients with post-prostatectomy incontinence after surgery for BPH showed that 43% were found to have complex incontinence (either mixed or associated with bladder outlet stenosis), requiring combined treatment. Forty one percent had a simple type of incontinence, i.e., pure USI or DO. Three patients had residual adenoma and 1 had a urethral stricture, while 9% remained unclassified (9). Higher rates of USI were found by Winters et al., (7) who analyzed 92 patients with UI (65 after RP and 27 after TURP) with multichannel videourodynamic testing performed at least 1 year after prostatectomy. USI was detected in 92% of cases and despite DO was a common finding, occurring in 37% of patients, it was found to be the sole cause of UI in only 3.3% of cases. There was no statistically significance in the incidence of USI after RP or TURP; however, TURP patients had a significantly higher incidence of DO.

In the present study we also analyzed the influence of patient age on the etiology of UI. The influence of age on recovery of urinary continence

Figure 2 - *Mean patients age according to the presence of urinary sphincter insufficiency (p < 0.001).*

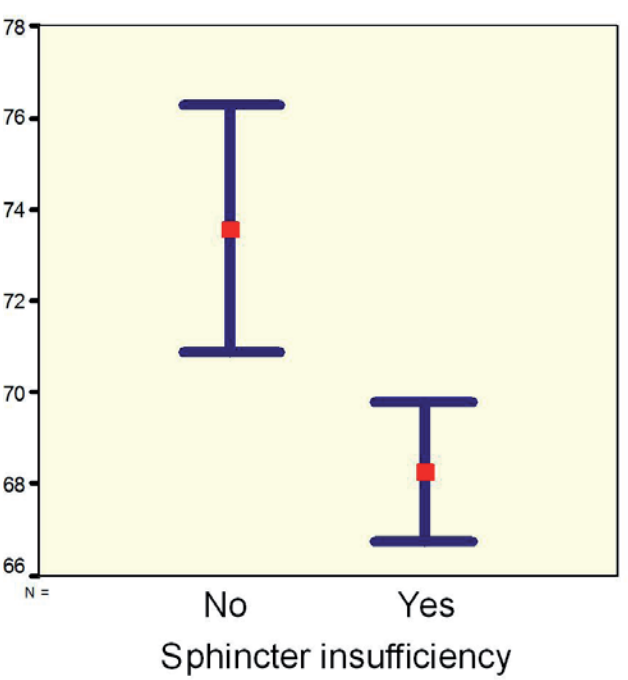


Table 3 - *Correlation coefficients of patient age with urodynamic parameters.*

Variable	Pearson´s correlation	p
Flow rate	-0.184	0.037
Urethral leak point pressure	0.128	0.127
Functional lengh	0.045	0.603
Post-void residual volume	0.132	0.112
Bladder capacity	-0.124	0.137

Table 4 - *Logistic regression model for the presence of UI.*

Variable	p	Odds ratio	CI (95%)
Age	0.018	1.053	[1.009 ; 1.099]
OP / TURP	0.534	0.784	[0.364 ; 1.689]
RP / TURP	0.779	1.013	[0.377 ; 2.724]

has been studied mainly among patients who underwent RP, and conflicting results have been shown in the literature. Eastham et al. (13) studied risk factors for UI following RP in 581 patients who were previously continent. They concluded in a multivariate analysis that the factors that were independently associated with increased chance of regaining continence were decreasing age, a modification in the technique of anastomosis (introduced in 1990), preservation of both neurovascular bundles and absence of an anastomotic stricture. Conversely, in the study of Catalona and Basler (14) who analyzed 784 patients that underwent RP, continence was regained in 94% of cases and did not correlate with patient age.

The present study analyzed the influence of age on the etiology of UI among patients who underwent surgery for BPH showed that despite age had low correlation coefficient rates with urodynamic parameters, patients who presented BD were 3.2 years older than the ones who did not present this abnormality. Furthermore, the chances of presenting BD rises 5.3% for each year of age and patients older than 70 years old had twice the chance of presenting BD, no matter which type of surgery they had. These figures could explain why older patients may sometimes present greater rates of UI, or longer periods for recovery of UI. The association of aging and BD in men is well known, and studies have shown similar occurence in elderly women.

Limitations of the present study include the retrospective nature of this report and the relatively small number of patients with UI following RP precluded an accurate comparison of urodynamic parameters. Preoperative urodynamic data were not available, since most patients were referred from other medical centers. Some patients were submitted to urodynamic testing six months after surgery, and as reported by Giannantoni et al. (15), improvement in compliance and contractility may occur after this period in patients submitted to radical prostatectomy. However, to our knowledge, this is the largest study to analyze patients with late UI following surgery for BPH.

CONCLUSIONS

Urinary Stress Incontinence is the main cause of post-prostatectomy incontinence following surgery for BPH. However, BD may be the isolated cause of UI in approximately 25% of patients and coexist with USI in 30% of cases. Older patients have greater rates of BD and patients older than 70

years of age may be considered a high risk group. Urodynamic evaluation is essential to identify the etiology of post-prostatectomy incontinence and to optimize the outcome of treatment.

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Accepted after revision:
July 30, 2010

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EDITORIAL COMMENT

The purpose of the study is to assess the relative role of bladder dysfunction and urinary sphincter deficiency following prostate surgery. This interesting subject is difficult and articles have already been published on it. However many

factors may be involved in incontinence following surgery for BPH. The role of age is one of them, but age may be a cause of sphincter deficiency as well as bladder dysfunction or both. The analysis is complex and conclusions difficult to draw. The limit of this study was to be a retrospective analysis, and to have been carried out only after surgery without comparative data before surgery. Concerning the follow-up period, a minimal 6 months interval between surgery and urodynamics was probably not enough in some patients, usually a 12 months was reported. However the authors presented an interesting study and have to be encouraged to initiate a prospective study.

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Basic and Translational Urology
International Braz J Urol
Vol 37 (3): 388-394, May - June, 2011

New Ex-vivo Organ Model for Percutaneous Renal Surgery

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ABSTRACT

Objectives: Percutaneous Renal Surgery (PRS) is a demanding procedure and success is mostly hampered by the lacking of training facilities. Thus, the purpose of the study was to evaluate a significantly improved pre-existing porcine kidney-training model for percutaneous renal access and PRS.
Materials and Methods: A biologic training model using porcine kidneys coated by a full-thickness porcine skin flap was prepared. The ureter was dissected, stones were placed into the collecting system using an 18F amplatz sheath, and a catheter was placed in the ureter for further irrigation with saline or contrast medium. For initial training with an easy access, a standard guide-wire was inserted in the ureter through the renal parenchyma. The kidney was punctured with radiographic or ultrasound guidance. Minimally invasive percutaneous nephrolithotomy (MIP) was then tested using the model under radiographic or ultrasound guidance. The model was then evaluated in MIP training courses, which are regularly held at The Hannover Medical School.
Results: All trainees were urologists with experience in endourologic surgery but lacked practice in PRS. In conclusion, all 36 participants attained access to the collecting system using models with readily placed guide-wires. Subsequently, PRS was successful in all cases. Percutaneous puncture under ultrasound guidance and following intrarenal surgery was successful in 30 (83.3%) cases. Therefore, all participants rated the model useful for simulating percutaneous renal surgery.
Conclusions: This new porcine kidney model is easy to build and is made cost effective by using readily available material. Moreover, it provides realistic and reproducible training model for PRS. The "organ" model mimics the retroperitoneum by having a full-thickness skin flap with a layer of subcutaneous fatty tissue.

Key words: *kidney; minimally invasive surgical procedures; percutaneous nephrolithotomy animal models; kidney calculi*
Int Braz J Urol. 2011; 37: 388-394

INTRODUCTION

The increasing incidence and prevalence of urolithiasis in Germany throughout the last decades (1) grew to be a socioeconomic burden with regard to diagnostics and treatment. Thus, new challenges in diagnostic and therapy have to be addressed. A modern treatment of a stone disease has to meet several requirements: It has to be fast and effective, providing a high stone free rate with minimal perioperative morbidity along with a low re-intervention rate. Due to diameter, the number and location of urinary tract stones, mostly ESWL, ureterorenoscopy and percutaneous nephrolithotomy (PCNL) are recommended in the current urologic guidelines (e.g. EAU, AUA Guidelines). The use of percutaneous nephrolithotomy was developed in the 1970s as an alternative to open surgery, but with the introduction of the ESWL in the early 80s PCNL became less popular. This technical evolution, as well as, the improvement in the field of semirigid and flexible ureterorenoscopy during the following three decades, has dramatically changed the operative management of urolithiasis. Nevertheless, PCNL was recommended for large renal calculi. Although, PCNL has been accepted

to be safe and effective, it also has significant perioperative morbidity (2,3). Therefore, urologist minimized their PCNL instruments in the past decade so to be less invasive and moreover reduce therapy-associated morbidity. This led to the development of new minimized instruments, where less invasive procedures such as Mini-PCNL (miniaturized PCNL) (4) and MIP (minimally invasive percutaneous nephrolithotomy) (5,6) take part. These techniques showed advantages in terms of shorter hospital stay and reduced postoperative pain while maintaining the high stone free rates of former PCNL (7). These improvements in the field of percutaneous surgery and the critical evaluation and discussion of the results of ESWL and ureterorensocopy with respect to stone free rates and complications led to a rising acceptance of minimally invasive percutaneous procedures throughout the previous years. Therefore, an increasing number of these procedures require sufficient structured training opportunities to maintain surgical effectiveness, with respect to stone free rates and patient safety.

Although miniaturization decreased the perioperative morbidity, percutaneous renal surgery is still one of the most advanced techniques in modern endourology. Frequently, urologists complain of lack of training experience due to scarce training facilities and high cost organ models. Consequently, operative expertise is mostly acquired in the operating theatre. Analysis of structured learning curve of percutaneous nephrolithotomy suggested that basic skills are achieved after > 20 procedures, surgical competence is achieved after 60 cases and surgical excellence after > 100 cases (8-10).

An ex-vivo PCNL organ training model described by Zhang et al. (11) was modified in significant aspects. It was then evaluated during MIP training courses at The Hannover Medical School, and has proven efficiency in various teaching sessions taken place in our own department, in addition to the training courses held for urologists. The model allows training of multiple steps of percutaneous renal surgery such as; renal puncture, tract dilation, access sheath introduction, intrarenal endoscopic exploration and further intrarenal surgery. It also provides a sufficient tool to overcome the initial learning curve of the first 10 procedures.

MATERIAL AND METHODS

The PCNL kidney model was built using a porcine kidney, a porcine full thickness skin flap with subcutaneous tissue, an indwelling catheter, artificial renal calculi with a maximum diameter of 5 millimeters and a standard plastic tray.

The kidneys and skin flaps were obtained from freshly slaughtered adult pigs. For ureter preparation and catheterization, a minimum length of 10 cm ureter was preserved during kidney extraction (Figure-1). The full-thickness skin flap with subcutaneous tissue, in which was harvested from the abdominal wall of adult pigs, was approximately 5-6 cm in thickness and 40-50 cm in diameter, enough to cover the entire kidney (Figure-2).

First, the ureter was dissected and intubated with an 18F amplatz sheath (Karl Storz, Tuttlingen, Germany). Afterwards, multiple artificial calculi were placed in the collecting system through the amplatz sheath (Figure-3). The ureter was catheterized for further irrigation with saline or contrast medium using a 12F indwelling catheter and then ligated with commercially available sewing material (Figure-4). For the initial training experience, a standard guide wire was inserted through the ureter and diverted bluntly through renal parenchyma providing an easy access to the collecting system with the single-step dilatation system (Karl Storz, Tuttlingen, Germany). The kidney was placed in the center of the skin flap, ensuring that the convex part of the kidney was attached to the fold of the skin flap (Figure-2). Next, the optional guide wire was placed through the skin flap. The kidney was coated with ultrasound gel, to assure sufficient ultrasound visualization during puncture. Finally, the skin wrap was sealed with a running suture of cotton sewing material, and placed into the plastic trays. It is important to note that point out, prepared organ model was not frozen in order to maintain the natural characteristics of the tissue during the surgical training sessions, in contrast to previous descriptions (11).

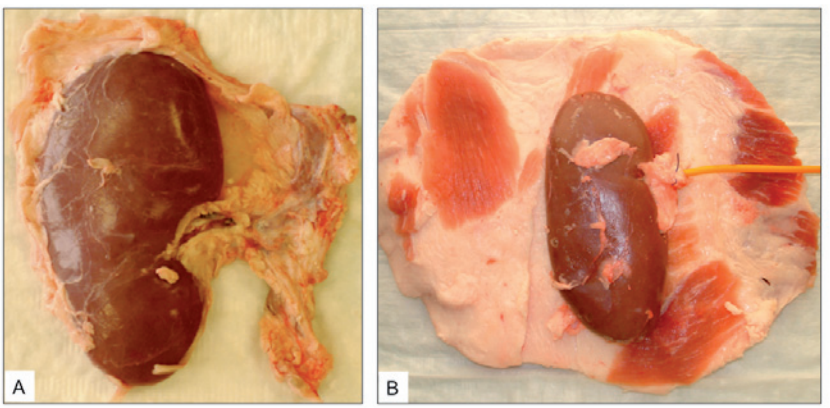

Figure 1 - *Freshly harvested porcine kidney (A) and full thickness skin flap used to cover the kidney (B).*

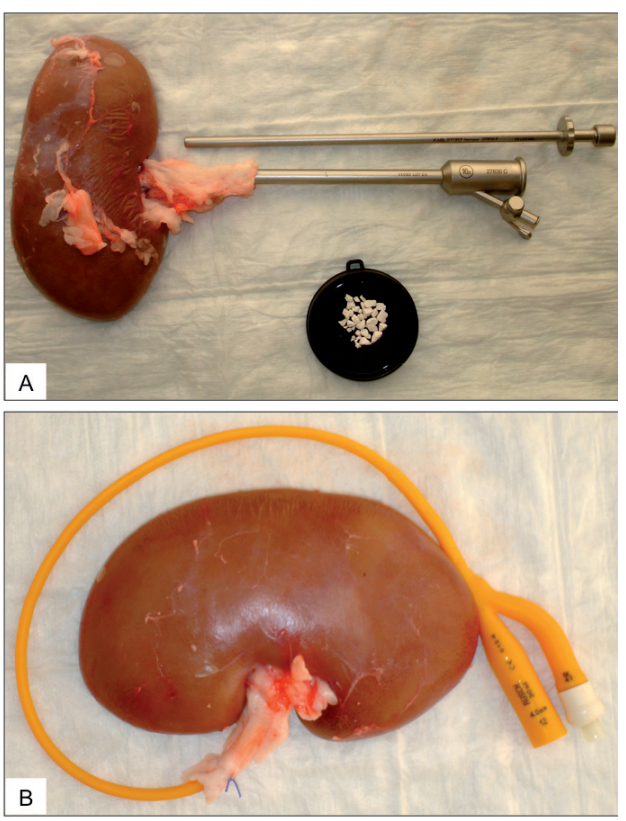

Figure 2 - *Placement of artificial calculi into the renal pelvis (A) and catheterized renal pelvis for saline or dye irrigation (B).*

The model was applied to percutaneous renal surgery training under radiologic or ultrasound guidance. Either the X-ray unit (Philips Uro Diagnost MRF, Netherlands) or the ultrasound unit (BK Medical, Falcon Ultrasound Scanner Type 2101, Copenhagen, Denmark) with a 3-6 MHz probe (BK Medical Type 8803, Copenhagen, Denmark) was used during the procedure. Also, a radiologic contrast medium or normal saline was injected through the indwelling catheter to produce visual images, in order to achieve sufficient artificial hydronephrosis for percutaneous renal puncture. Next, various surgical steps of PRS were performed such as; puncturing, guide-wire placement, single step dilation, insertion of the miniaturized 18F Amplatz sheath (Karl Storz, Tuttlingen, Germany), introduction of a 12F nephroscope (Karl Storz, Tuttlingen, Germany), intrarenal exploration, and minimally invasive percutaneous nephrolithotomy (MIP). The organ model was than evaluated in MIP training courses, which are held in our department with basic questionnaire in terms of successful puncture of the collecting system, access to the renal pelvis and subsequent intrarenal surgery. Moreover, the preexisting surgical experience in the field of percutaneous renal surgery of the participating trainees and the personal perception of this model were also evaluated as not useful, undetermined or helpful.

RESULTS

Based on the previously described organ model (11) a total number of 6 porcine kidneys were necessary to improve and modify this model for percutaneous renal surgery. The preparation of one single organ model acquired 10-15 minutes time, until it was ready for a percutaneous training session.

Altogether, 36 urologists attended 6 urologic training courses for percutaneous renal surgery at the affiliated hospitals. All 36 participants were known to have experience in urologic endoscopic surgery (defined as ureteroscopy, renoscopy) yet no experience in the field of percutaneous renal surgery (defined as minimally invasive percutaneous nephrolithotomy (MIP), percutaneous

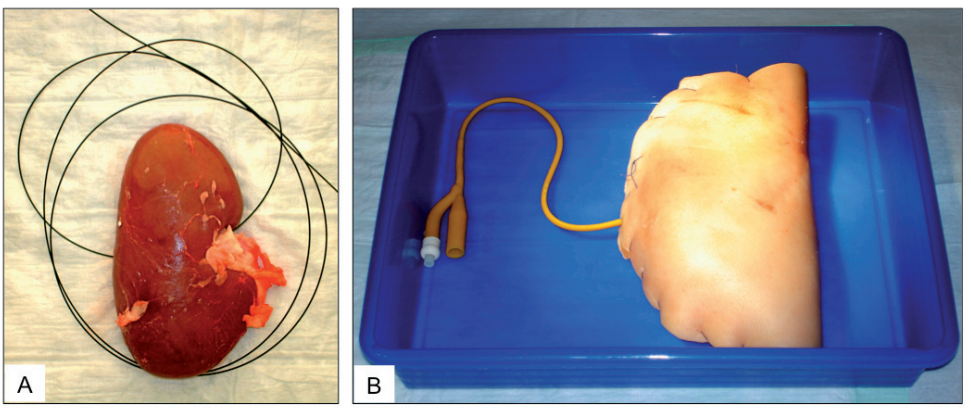

Figure 3 - *Guide-wire for easy access to the renal pelvis (A) and wrapped organ model, closed by running sutures, in the plastic tray for subsequent training (B).*

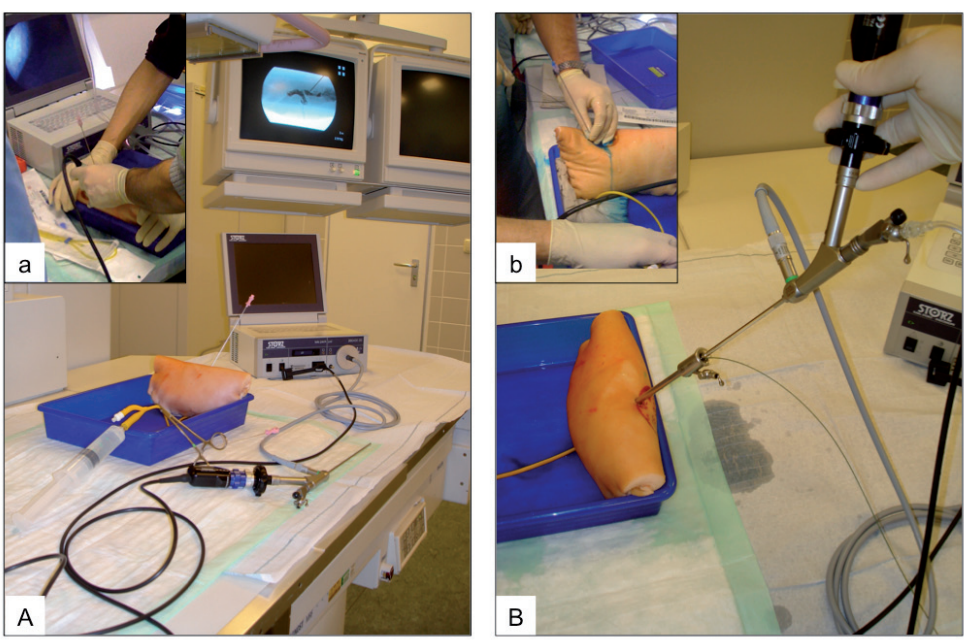

Figure 4 - *Puncture of the renal pelvis (A) and subsequent intrarenal surgery (B). Alternate ultrasound guided puncture (a) and verification of successful access to the renal pelvis by blue dye irrigation is depicted (b).*

nephrolithotomy (PCNL)). All 36 (100%) trainees were able to access the renal pelvis using the designed model, readily prepared with a guide wire. Furthermore, percutaneous surgery (MIP) was successful in all cases through this predefined access. 30 (83.3%) participants managed to achieve access to the collecting system by ultrasound or radiographic guidance. If surgical access was achieved, subsequent percutaneous transrenal surgery (MIP) was successful in 30 cases (100%). All participants practiced the percutaneous hands-on manipulations on this model under the direct guidance and surveillance of three experienced endourologists. By the end of this course, all attendants rated the porcine kidney model for simulation of percutaneous renal surgery as “helpful”.

The low cost for this organ model was the result of use of inexpensive ureteral catheters for irrigation of the renal pelvis during percutaneous surgery, as well as, the use of standard sewing material. The use of reusable material and instruments improved the cost-value relation of this model. In summary, the total cost accounted approximately 10€ for each prepared organ model. Nonetheless to be considered, that initial cost for the described reusable instruments in animal use only may occur establishing an organ model training program for percutaneous renal surgery.

In conclusion, this percutaneous renal access and other intrarenal procedures proved feasible and practical under radiographic or ultrasound guidance.

DISCUSSION

Learning percutaneous renal surgery is still demanding, although several virtual and biologic models have been published. But only virtual or laboratory training of percutaneous renal surgery provides the opportunity to overcome the initial learning curve. Thus, training models have to meet several requirements. These models must be cost effective, easy and fast to prepare with commonly available material and organs. They need to be realistic, provide the feeling of human tissue and simulate the retroperitoneal anatomy. Finally, they should provide easy access to the renal pelvis for subsequent renal surgery, along with a high success rate under training conditions. To address these challenging requirements, several training models have been published to date, consisting of virtual computer-based non-biologic training and organ-based models using porcine kidneys.

A nonbiologic computer-based simulator PERCMentor (Simbionix, Lod, Israel) has been published by Knudsen et al. in 2006, providing virtual reality skills. This might allow trainees to develop the basic skills necessary to perform percutaneous access to the renal collecting system (12). However, expenses of this sort of training system are unclear for software and hardware costs, addition to time-consuming labor-intensive training of urologists. The advantage of biologic models is the “tissue feeling”, an imitation of human tissue while allowing a great variety of procedures of intrarenal surgery (13). To date 6 reports have been published providing feasible biologic models using porcine kidneys for percutaneous renal surgery training. Porcine kidneys have been wrapped in a foam layer, embedded in silicon, enclosed in chicken carcasses and in porcine thoracic/abdominal walls. Radiologic and ultrasound guidance were applied for percutaneous renal access guidance (13-17).

A model published by Zhang et al. in 2008 was primarily the inspiration of building our own (11). This ex-vivo porcine kidney training model was significantly improved in meeting criterions of cost effectiveness, preparation, and simplified access to the collecting system in the initial training phase and therefore, concluding success rates in percutaneous renal surgery. Not to mention, improved cost effectiveness was achieved by diminishing the use of expensive disposable materials. Moreover, the ureteral catheter was replaced by a 12F indwelling catheter and reusable plastic trays were used instead of wooden boards. The use of these plastic trays not only improves the hygiene, but it allows the collection of the saline irrigation during the procedures. The full-thickness skin was replaced by porcine entire abdominal wall of adult pigs including the subcutaneous tissue, providing enhanced ultrasound visualization for subsequent puncture, as well as improvement in realistic retroperitoneal circumstances with regard to consistency and resistance of the skin. This setting allows a realistic training of puncturing, single step tract dilatation, amplatz sheath introduction and subsequent intrarenal surgery. The porcine kidney anatomy is similar to that of humans, facilitating intrarenal endoscopic practice. The transureteral introduction of renal calculi through the 18F amplatz sheath into the renal pelvis significantly eased the preparation of the organ model.

Although the described organ model is cost-effective, other issues must be considered such as hygiene standards and policies, instrument sterilization and use of disposables during training.

In contrast to previous descriptions, our experience using the depicted organ model supports that neither an immediate irrigation following the kidney harvest (15), nor the refrigeration of the organ model (11) is required to maintain the rigidity of the kidney tissue. It was demonstrated high success rates for optimal puncture of the collecting system, subsequent tract dilatation followed by intrarenal surgery. Thus, this organ model can easily be prepared hours before a training session, reducing labor and preparation while retaining realistic scenario for training.

In contrast to other models (13,14), the kidney is not fixed to the surrounding structures in the skin-flap compartment, providing a sufficient and realistic mobility of the kidney, mimicking in-vivo circumstances. Comparing to organ models with porcine kidneys embedded in chicken carcasses (15), this model sufficiently avoids interferences in x-ray or ultrasound based puncture, usually caused by the chicken skeleton. Thus, improvement of success level in the initial training period was up to 10 percutaneous interventions in particular. This ex-vivo model lacks the simulation of ribs, simulating realistic conditions as in human anatomy. This could be developed to some extent by using part of the thoracic wall and superficial soft tissue to give an even better practice environment (17). Such model might improve the training results creating further advanced urologic surgeons with basic skills in percutaneous surgery.

All attending trainees were urologists (36/100%) without experience in percutaneous renal surgery while previously experienced in transurethral endourology. It is intriguing, whether the reported high success rate accessing the renal pelvis was due to the easy surgical access by a readily placed guide wire, or by pre-existing surgical skills in minimally invasive endourology. This organ model was used in 6 training sessions with 6 participants. An initial 90 minute didatic lesson with basic knowledge of percutaneous renal surgery was followed by a 3-hour hands-on-training at 3 training venues simultaneously. All trainees were personally instructed by three certified urologists with the opportunity of puncture practice, tract dilatation and percutaneous surgery at their own organ models. This setting allowed individual instructions given to all trainees, to guarantee the reported high success rate. Moreover, the individual training with personal porcine organ models led to the acceptance of the model, in which was demonstrated by the evaluations.

CONCLUSIONS

This porcine kidney model previously described is simple, cost effective and easy to prepare with reusable material and instruments. It mimics the natural circumstance, and provides realistic and reproducible practice for percutaneous renal surgery in the training laboratory. Furthermore, it provides incremental training opportunities for trainees with various skills in the field of percutaneous surgery with an easier wired access to the renal pelvis for the initial training period. The majority of the participating trainees evaluated this organ model as “helpful”. Hence, it is believed that this model will become an integral part of structured training for minimally invasive percutaneous nephrolithomy (MIP) “in the near future”.

ABBREVIATIONS

PRS Percutaneous renal surgery
MIP Minimally invasive percutaneous nephrolithotomy
ESWL Extracorporal shockwave lithotripsy
PCNL Percutaneous nephrolithotomy
EAU European Association of Urology
AUA American Association of Urology
F French

CONFLICT OF INTEREST

None declared.

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Accepted after revision:
December 15, 2010

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Radiology Page
International Braz J Urol
Vol 37 (3): 395-396, May - June, 2011

The Elusive Renal Cell Carcinoma: Reversal Imaging of Arterial Phase to Improve Acuity

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On routine physical examination the patient's physician noted microscopic hematuria The finding was reconfirmed by 2 Dipsticks over an interval of 4 months. The patient was a known diabetic, controlled by diet. Otherwise the patient was asymptomatic, without significant past medical history at the time of this work-up, the 47 year old Caucasian male appeared to be in good general health. Laboratory data showed Hb of 15.1gm/dL, HCT 45%, RBC 4.8 million/uL, WBC 6200,Neu 62%, BUN 18 mg/dL, Creatinine 1.1 mg/dl, GRF 94 mL/min, A/G ratio 1.4, Glu 128 mg/dl, K 4.2 mmoL/L, Na 145 MMOL/L Cl 108 mmoL/L Urine analysis, spec grav 1018, 3-5 RBC/hpf, no WBC or bacteria on hpf, no casts, urine culture negative x 2. A KUB (Flat plate of abdomen) showed no opaque calculi nor other abnormalities. Cystoscopy and blue light cystoscopy revealed no abnormalities.

An enhanced 4 phase MDCT was performed The pre-enhancement phase was entirely unremarkable; no parenchymal lesions were detected. Following administration of 100 ml non-ionic contrast medium at a flow rate of 5 mL/sec, the 12 second delayed arterial phase Ct demonstrated a relatively poorly enhancing 1.6 cm mass at the cortico-medullary junction (Figure-1), the lesion is much better shown on reversal image. Both the parenchymal phase CT(50 second delay) and the excretory phase CT (4 minutes delay Figure-2) demonstrate a non-enhancing 16 mm mass at the cortico-medullary junction (Figure-3).

In the light of a clinical history of diabetes and microscopic hematuria, the non-enhancing hypovascular mass seen on parenchymal and excretory phase CTs in the medulla might have been written off as Medullary Necrosis (With characteristic CT findings of a negative pre-enhancement phase CT, but a non-enhancing lesion shown on parenchymal and excretory phase; an early avascular necrosis) (1). However, the reversal image of the arterial phase CT clearly shows an enhancing lesion, though somewhat hypovascular for a RCC. The hypo-density on parenchymal and excretory phase CT reflects the characteristic "wash-out" phenomenon of RCCs in these phases. The tumor having no tubules is less dense then adjacent normal parenchyma The correct diagnosis was made, and a laparoscopic resection carried out.

Figure 1 *- Massive gas in the bladder, dissecting in the submucosal layer and extending into the space of Retzius.*

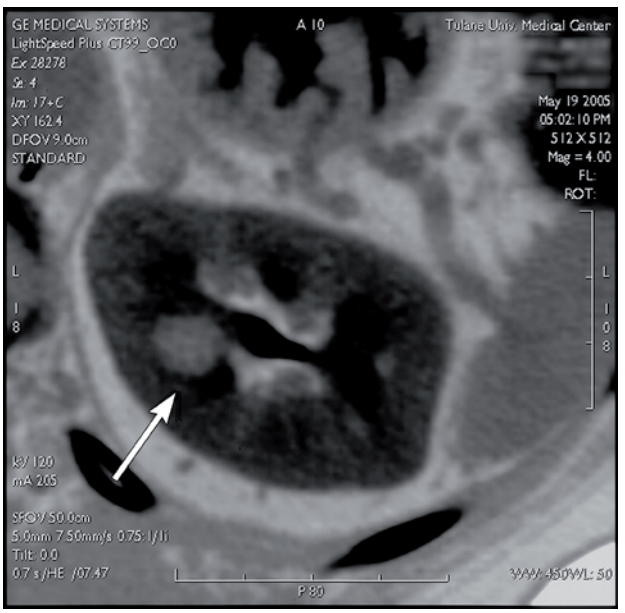

Figure 2 *- lateral extension of the gas-dissection in the pre-vesical space.*

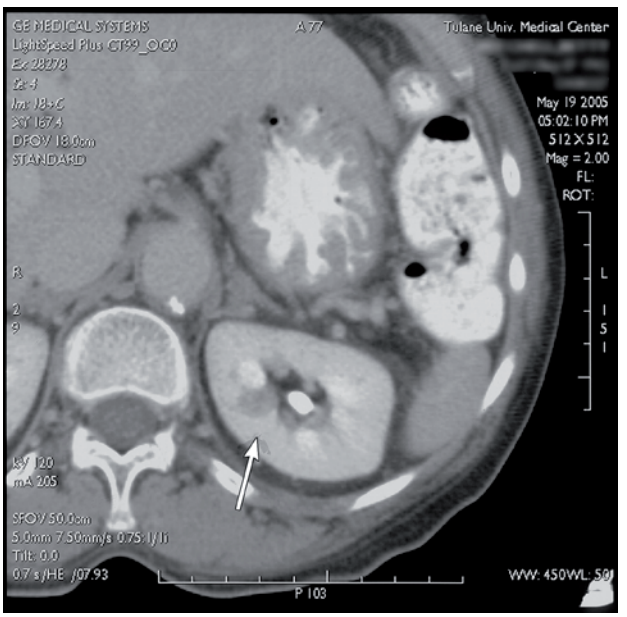

Figure 3 *- gas dissecting into the ureter.*

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International Braz J Urol
Vol. 37 (3): 397-418, May-June, 2011

UROLOGICAL SURVEY

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STONE DISEASE

The digital flexible ureteroscope: in vitro assessment of optical characteristics

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J Endourol. 2011;25:519-22

Introduction: Recent advances in endoscope design have placed the charged coupled device chip on the tip of the endoscope. The image is instantly digitalized and converted into an electrical signal for transmission. Digital technology was first introduced into flexible cystoscopes/nephroscopes and subsequently into rigid and flexible ureteroscopes. Herein, we assess the image characteristics and advantages of a new generation of digital flexible ureteroscopes.
Methods: The Olympus URF-V flexible digital ureteroscope and the Olympus URF-P3 fiberoptic ureteroscope were assessed in vitro for image resolution, distortion, color representation, grayscale imaging, field of view, and depth of field.
Results: The digital ureteroscope had a higher resolution at 3, 5, 10, and 20 mm (25.2 lines/mm vs. 8.0, 14.1 vs. 5.0, 6.3 vs. 2.8, and 3.2 vs. 1.3), respectively. Distortion with the digital flexible ureteroscope was lower, though not statistically significant. Color representation was better with the digital ureteroscope, whereas contrast evaluation was comparable between both scopes. The digital flexlible ureteroscope produced a 5.3 times larger image size compared with the standard fiberoptic flexible uretersocpe with a narrower field of view. The depth of field was limited by light and not the optic or the camera for both ureteroscopes.
Conclusions: The development of digital flexible ureteroscopes represents a significant technological advance in urology. These devices offer significantly improved resolution and color reproduction as compared with traditional fiberoptic flexible ureteroscopes. Future clinical trials are warranted to ultimately determine the advantages of these innovative endoscopes.

Editorial Comment

The authors conducted a comprehensive evaluation of a new digital flexible ureteroscope, however unfortunately they compared it to an old-generation fiberoptic scope - the URF-P3; it would have been preferable to evaluate the latest generation fiberoptic scope, the URF-P5. Despite this limitation, they noted some significant differences, and some significant similarities between the two scopes. Both modalities provided good image contrast and minimal distortion, as well as good color representation and depth of field. While image quality (resolution, image size) was superior with the digital scopes, certain characteristics that may impact ease of manuevering and navigating (small scope size, larger field of view) was superior for the fiberoptic scope. The relative value of improved resolution and larger image (digital scopes) compared to the relative value of a larger field of view and smaller scope size (fiberoptic scopes) warrants a clinical trial. 8.5F at the tip.

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A comparison of treatment modalities for renal calculi between 100 and 300 mm2: are shockwave lithotripsy, ureteroscopy, and percutaneous nephrolithotomy equivalent?

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J Endourol. 2011;25:481-5

Background and Purpose: Shockwave lithotripsy (SWL) is considered a standard treatment for patients with upper-tract stones that are less than 10 mm in diameter, whereas stones that are larger than 20 mm are best managed by percutaneous nephrolithotomy (PCNL). The management of stones between these sizes remains controversial. Our purpose was to review our contemporary series of SWL, ureteroscopy (URS), and PCNL outcomes for intermediate-sized upper tract calculi (100-300 mm(2)).
Patients and Methods: Analysis was restricted to those patients who were treated for a renal calculus that measured between 100 and 300 mm(2) during a 4-year span. Demographic, stone, patient, treatment, and follow-up data were collected from a prospectively maintained database.
Results: A total of 137 patients were referred with nonstaghorn calculi with an area between 100 and 300 mm(2). Fifty-three (38.7%) patients were treated with SWL, while 41 (29.9%) and 43 (31.4%) underwent ureteroscopy and PCNL, respectively. Mean stone area was higher in the PCNL group ($P < 0.001$), whereas stone density was higher for patients undergoing SWL ($P = 0.002$). Single treatment success rates were better for PCNL at 95.3%,vs 87.8% for ureteroscopy and 60.4% for SWL, $P < 0.001$. When allowing for two SWL treatments, the success rate improved to 79.2%, thus equalizing the success of the three treatment modalities ($P = 0.66$). Auxiliary treatments were more common after SWL (42.3%; $P < 0.01$).
Conclusions: For intermediate-sized upper-tract stones, when allowing for up to two SWL treatments, there was no significant difference between treatment modalities. Thus, SWL is a reasonably successful treatment alternative for patients who are not fit for a general anesthetic or who prefer SWL over competing treatments, provided they accept a potentially higher number of treatments.

Editorial Comment

This study has significant limitations. Selection bias may impact choice of treatment. The authors state that stone characteristics impacted selection of treatment modality, yet they do not elaborate on what characteristics were considered or how they impacted the decision tree. Stone density was higher in the SWL group, while stone size was larger in the PCNL group. Post-operative imaging modality was not standardized. Different definitions for success were used between the three groups; with a more stringent definition for PCNL, and liberal definition for URS and SWL. The authors correctly note that the higher retreatment rates with SWL may be counter-balanced by the lower hospitalization rate, length of stay and need for ureteral stents. They appropriately conclude that the final choice of treatment depends on the patient preference, clinical scenario, and available equipment and expertise.

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ENDOUROLOGY & LAPAROSCOPY

Complications and conversions of upper tract urological laparoendoscopic single-site surgery (less): multicentre experience: results from the NOTES Working Group

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BJU Int. 2010: 14. doi: 10.1111/j.1464-410X.2010.09663.x [Epub ahead of print]

Study Type - Therapy (case series) Level of Evidence 4

Objective: To present complications and rates of conversion from LESS to conventional laparoscopy (CL) at the time of upper tract LESS urologic procedures.

Patients and Methods: Patients undergoing LESS upper tract procedures between September, 2007 and November, 2008 (n = 125) were identified at six high-volume academic centers pioneering urologic LESS procedures. All LESS procedures were performed transperitoneally via a single umbilical incision using either adjacent conventional trocars or a dedicated single-site access device. Reconstructive procedures incorporating a single planned 2mm accessory needle port were included as LESS procedures and were not considered conversions. Patients, undergoing LESS procedures requiring conversion to CL with the placement of additional ports were identified. Conversion was defined as the placement of additional 5 or 10/12mm ports beyond the primary incision. In each case the operative reports were reviewed, the reason for conversion was determined, and the number and types of additional ports and complications were noted.

Results: Upper tract LESS procedures were performed in 125 patients comprising 13.3% of the total 937 laparoscopic procedures performed at the participating institutions during this time period. Conversion to CL was necessary in 7 patients (5.6%) undergoing LESS requiring the addition of 2-5 ports. Reasons for conversion included: facilitate dissection in 3 (43%), facilitate reconstruction in 3 (43%), and control of bleeding in 1 (14%). All attempted LESS cases were completed laparoscopically without need for open conversion. Complications occurred in 15.2% of patients undergoing LESS surgery. Three of the 7 patients that required conversion to CL developed postoperative complications (Clavien grade II in two and IIIa in one). Limitations of this study included the inability to standardize LESS patient selection criteria, instrumentation and surgical technique as well as the lack of available complete data from a CL control group for comparison.

Conclusion: LESS surgery is technically feasible for a variety of upper urinary tract reconstructive and ablative procedures, although it appears to be associated with higher rates of complications than in mature CL series. Conversion to CL occurs infrequently and may be a reflection of stringent patient selection.

Editorial Comment

The authors present a multi-center study on patients undergoing LESS upper tract procedures between September, 2007 and November, 2008 (n = 125). A total of 6 high-volume academic centers pioneering urologic LESS procedures were identified and participated in the study. Since the first laparoscopic procedure was performed the objective of ultimate less tissue damage and faster recovery of patients with optimal cosmetic results have been the “holy grail” of minimally invasive surgery. From a total of 937 Laparoscopic 77 (8.2%) had upper tract urological procedures, 125 underwent LESS, 7.8%, 48 (5.1%) Extirpative/Ablative LESS

Procedures with Complication rates of had reconstructive LESS Procedures with complication rates of 27.1%. The authors completed LESS Extirpative/Ablative Procedures in 74 patients with complication 6.7%. Three (0.3%) were converted to conventional laparoscopy with rates of complication rates of 33%. In the reconstructive LESS Procedures 44 patients had completion of surgery while conversion to conventional laparoscopic surgery rate was 0.4%. It is important to note that these are highly skill surgeons from high volume centers. Overall, the LESS procedures seem to be the next step to create new platforms and instrumentations to better serve our patients with less invasive techniques.

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Living donor kidney transplantation with multiple renal arteries in the laparoscopic era

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Urology. 2011; 77: 1116-21

Objectives: To compare the postoperative complications and survival metrics after multiple renal arteries (MRA) and single renal artery (SRA) laparoscopically procured living donor kidney transplantation (LLDKT). MRA are the most frequently encountered anatomic variation during kidney transplantation. The long-term outcomes of LLDKT with MRA are not well characterized.
Methods: A retrospective review of our institution's LLDKT database was performed. All surgeries were performed at a single tertiary care academic center between June 1999 and September 2008. Patients were divided into 2 cohorts (MRA vs. SRA), and analysis was limited to patients with at least 1-year follow-up.
Results: Of 584 LLDKTs, 510 had at least 1-year follow-up (median: 36 months). A total of 393 grafts had an SRA, whereas 117 (23%) had MRA. When complications were stratified by the Clavien classification system, no differences were noted between groups (P = .5). Furthermore, rates of vascular (P = .2) and urological (P = .9) complications were similar between groups. There was, however, a higher incidence of slow graft function in the MRA group (P = .01), despite similar rates of delayed graft function (P = .9) and acute rejection (P = .4). Furthermore, allograft survival was similar between both groups with 76% of MRA and 81% of SRA grafts functioning at 5 years (P = .49). Patient overall survival was likewise similar between groups with 88% of MRA and 86% of SRA recipients surviving at 5 years (P = .76).
Conclusions: Despite a higher incidence slow graft function, MRA in LLDKT does not adversely affect long-term allograft and patient overall survival.

Editorial Comment

The authors compared the postoperative complications and survival metrics after multiple renal arteries (MRA) and single renal artery (SRA) laparoscopically procured living donor kidney transplantation (LLDKT). The advances of minimally invasive surgery after the pioneer work of Kavoussi et al. transcends biases limitations that we never imagine would be possible to transpose.

The challenges of procuring a kidney with multiple renal arteries is a difficult task even to open surgeons, while laparoscopically it became a reality and this report reveals a higher incidence of slow graft function in recipients of allografts with multiple renal arteries but the multiplicity of renal arteries in laparoscopically procured living donor kidney transplantation does not adversely affect 5-year allograft and patient overall survival.

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IMAGING

Comparison of CT Urography and Excretory Urography in the Detection and Localization of Urothelial Carcinoma of the Upper Urinary Tract

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AJR Am J Roentgenol. 2011;196:1102-9

Objective: The purpose of this study was to compare the accuracy of CT urography and excretory urography for the detection and localization of upper urinary tract urothelial carcinoma.
Materials and Methods: Of 128 patients at high risk for upper tract urothelial carcinoma who were examined with both CT urography and excretory urography between 2002 and 2007, 24 were undiagnosed and excluded. CT urography and excretory urography results of the remaining 104 patients and 552 urinary tract segments were compared with histopathologic examination or follow-up imaging at 1 year. Two readers independently scored the confidence levels for the presence or absence of upper urinary tract urothelial carcinoma in each of six upper urinary tract segments on both CT urography and excretory urography; differences were resolved by consensus.
Results: Upper urinary tract urothelial carcinoma was diagnosed in 77 (14%) segments of 46 (44%) patients. Per-patient sensitivity, specificity, overall accuracy, and area under the receiver operating characteristic curves for detecting carcinomas with CT urography (93.5% [43/46], 94.8% [55/58], 94.2% [98/104], and 0.963, respectively) were significantly greater than those for excretory urography (80.4% [37/46], 81.0% [47/58], 80.8% [84/104], and 0.831, respectively) ($p = 0.041$, $p = 0.027$, $p = 0.001$, and $p < 0.001$, respectively). Per-segment sensitivity and overall accuracy for the localization of upper urinary tract urothelial carcinoma were significantly greater with CT urography (87.0% [67/77] and 97.8% [540/552]) than with excretory urography (41.6% [32/77] and 91.5% [505/552]) ($p < 0.0001$).
Conclusion: CT urography was more accurate than excretory urography in the detection and localization of upper urinary tract urothelial carcinoma and should be considered as the initial examination for the evaluation of patients at high risk for upper urinary tract urothelial carcinoma.

Editorial Comment

This is a retrospective study looking at the accuracy of CT urography compared to excretory urography (EU) for the detection and localization of urothelial carcinoma of the upper urinary tract. The authors enrolled 104 patients in the study all of whom at risk for pelvocalyceal cancer. Their results show that the accuracy of CT urography for both the detection and localization of upper urinary tract urothelial carcinoma was significantly better than that of excretory urography. CT urography was superior particularly to detect small (< 15 mm) masses, usually hidden by contrast material or obscured by gas on EU. CT urography was able to detect tumor in obstructed and unopacified kidney. The main limitations of CT urography, were the incapacity of distinguish between inflammatory and cancerous pelvocalyceal wall thickening; incapacity to detect CIS or localize superficial extension of the tumor and to localize multiple papillary tumors smaller than 10 mm within unopacified collapsed segments.

In our experience differentiation between inflammatory and cancerous focal thickening of the pelvocalyceal system wall can be very difficult. Presence of endothelial irregularities, invasion of local tissue, obliteration of local fat plane and contrast enhancing are features characteristic of tumor. In the absence of these findings however, endoscopy with biopsy is mandatory for the differential diagnosis.

Evidence is growing that in near future, an optimized CT-urography protocol, will replace EU for the evaluation of hematuria and follow-up of patients at risk for urothelial cancer.

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Areas suspicious for prostate cancer: MR-guided biopsy in patients with at least one transrectal US-guided biopsy with a negative finding-multiparametric MR imaging for detection and biopsy planning

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Purpose: To prospectively investigate the incremental value of multiparametric magnetic resonance (MR) imaging compared with standard T2-weighted imaging for biopsy planning.
Materials and Methods: The study was approved by the institutional review board; informed consent was obtained. Consecutive patients underwent T2-weighted imaging supplemented with multiparametric 1.5-T MR imaging, consisting of hydrogen 1 ((1)H) MR spectroscopy, diffusion-weighted (DW) imaging, and contrast material-enhanced MR imaging. Quantitative parameters were calculated: (choline plus creatine)-to-citrate ratio, apparent diffusion coefficient, and volume transfer constant and exchange rate constant. The prostate was divided into 20 standardized areas. Each area was classified as benign, inconclusive, or suspicious at T2-weighted imaging, followed by quantitative evaluation of all inconclusive and suspicious areas with multiparametric MR imaging. MR-guided biopsy was performed in lesions classified as suspicious for cancer with at least one of the techniques after transfer to three-dimensional T2-weighted images. Diagnostic parameters were calculated on a per-lesion and per-patient basis for all combinations of T2-weighted imaging with multiparametric MR imaging.

Results: Fifty-four patients had a median of two prior transrectal ultrasonographic biopsies with negative findings. Each patient had a median of three suspicious lesions. Prostate cancer was demonstrated in 21 of 54 patients. Biopsy was performed in 178 lesions; 53 were positive for prostate cancer. Detection rates and test negative results, respectively, were as follows: T2-weighted imaging, 70% and 50%; T2-weighted imaging and (1)H MR spectroscopy, 81% and 32%; T2-weighted imaging and contrast-enhanced MR imaging, 83% and 29%; T2-weighted imaging and DW imaging, 85% and 30%; T2-weighted imaging, (1)H MR spectroscopy, and contrast-enhanced MR imaging, 91% and 13%; T2-weighted imaging, (1)H MR spectroscopy, and DW imaging, 94% and 15%; T2-weighted imaging, DW imaging, and contrast-enhanced MR imaging, 94% and 13%; T2-weighted imaging, (1)H MR spectroscopy, DW imaging, and contrast-enhanced MR imaging, 100% and 0%.
Conclusion: Only the combination of T2-weighted imaging with all three multiparametric techniques depicts all identifiable prostate cancers; a double combination with DW imaging and (1)H MR spectroscopy or contrast-enhanced MR imaging misses 6%, while reasonably reducing the number of areas needing biopsy.

Editorial Comment

This is a prospective study looking at the incremental value of multiparametric MR imaging representing the integration of spectroscopy (MRSI), diffusion-weighted imaging (DWI) and dynamic-contrast enhanced MR imaging (DCE) in comparison with conventional T2-weighted imaging for the detection of prostate cancer. The authors enrolled 54 patients with at least one negative transrectal US-guided prostate biopsy and elevated or rising PSA. Their results show that in this selected group of patients MRI-guided biopsy oriented by findings obtained with the combinations of T2-weighted imaging, DWI, and DCE and T2-weighted imaging, MRSI and DWI depicted cancer in 21 out 54 patients (39%) representing 94% of all prostate cancer areas (19% higher than if biopsy were oriented by the results of anyone isolated technique).

Recently several methods have been used to orient the rebiopsy of prostate based on suspicious areas of cancer found in multiparametric MR imaging. In our institution, suspicious areas detected on multiparametric MRI have been sampled by transrectal US-guided biopsy. Since 2004 we have been using a visual method of overlaying suspicious multiparametric MRI findings onto axial US scans (1). Internal and external prostatic and periprostatic anatomic landmarks are used to project suspicious MRI findings on US scans .Our method has limitations since demands high level of expertise in prostate imaging. Recently however electronic real-time fusion of endorectal MR images with endorectal US images and the use of specially designed MRI-guided biopsy device, have been implemented and this task has been be facilitated as shown by the authors of this manuscript. However in any of these circumstances, a close relationship between radiologist and urologist is mandatory.

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PATHOLOGY

The Contemporary Concept of Significant Versus Insignificant Prostate Cancer

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Eur Urol. 2011 May 17. [Epub ahead of print]

Context: The notion of insignificant prostate cancer (Ins-PCa) has progressively emerged in the past two decades. The clinical relevance of such a definition was based on the fact that low-grade, small-volume, and organ-confined prostate cancer (PCa) may be indolent and unlikely to progress to biologic significance in the absence of treatment.
Objective: To review the definition of Ins-PCa, its incidence, and the clinical impact of Ins-PCa on the contemporary management of PCa.
Evidence Acquisition: A review of the literature was performed using the Medline, Scopus, and Web of Science databases with no restriction on language up to September 2010. The literature search used the following terms: insignificant, indolent, minute, microfocal, minimal, low volume, low risk, and prostate cancer.
Evidence Synthesis: The most commonly used criteria to define Ins-PCa are based on the pathologic assessment of the radical prostatectomy specimen: (1) Gleason score ≤ 6 without Gleason pattern 4 or 5, (2) organ-confined disease, and (3) tumour volume < 0.5cm(3). Several preoperative criteria and prognostication tools for predicting Ins-PCa have been suggested. Nomograms are best placed to estimate the risk of progression on an individualised basis, but a substantial proportion of men with a high probability of harbouring Ins-PCa are at risk for pathologic understaging and/or undergrading. Thus, there is an ongoing need for identifying novel and more accurate predictors of Ins-PCa to improve the distinction between insignificant versus significant disease and thus to promote the adequate management of PCa patients at low risk for progression.
Conclusions: The exciting challenge of obtaining the pretreatment diagnostic tools that can really distinguish insignificant from significant PCa should be one of the main objectives of urologists in the following years to decrease the risk of overtreatment of Ins-PCa.

Editorial Comment

With screening for prostate carcinoma, an increasing number of small tumors have been diagnosed. These small tumors may be indolent and unlikely to progress to biologic significance in the absence of treatment. In the past two decades criteria based on needle biopsies have emerged to identify tumors that may behave as indolent (insignificant). The criteria are based on pathologic findings of the radical prostatectomy specimen.

The most used criteria to define insignificant cancer on needle biopsy were proposed by Epstein: 1. no more than 2 cores with carcinoma; 2. no more than 50% of extent on any core; 3. no Gleason pattern 4 or 5; 4. PSA density < 0.15; and, 5. clinical stage T1c. A contemporary analysis found that 84% of patients satisfying these criteria, showed organ-confined disease and Gleason score < 6 without Gleason pattern 4 or 5 on the surgical specimen (1).

Other studies, however, found a less predictive value for insignificant cancer on radical prostatectomies using Epstein's criteria: 76%, 69% and 54% from Europe (Germany), Asia (South Korea), and Middle East (Epypt), respectively (2-4). Obviously, racial, enviromental, alimentary and methodological

factors may be involved in these discrepancies.

Due to the relevance of identifying patients harboring indolent tumors, the authors emphasize the need for identifying novel and more accurate predictors of insignificant cancer to improve the distinction between insignificant versus significant disease and thus to promote the adequate management of prostate cancer patients at low risk for progression.

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Treatment decision-making for localized prostate cancer: What younger men choose and why

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Prostate. 2011 Apr 25. doi: 10.1002/pros.21406. [Epub ahead of print]

Background and Objective: The literature lacks knowledge about information preferences and decision-making in young prostate cancer patients. This study provides insight into information sources consulted and factors dictating treatment decision-making in young prostate cancer patients.
Methods: Subjects were identified from pathology consult service of a National Center of Excellence. Questionnaires were mailed to 986 men, under 50 years of age, diagnosed with Gleason score 6 prostate cancer between 2001 and 2005.
Results: Four hundred ninety-three men responded. The most common primary therapies were surgery 397 (81.4%), radiation 52 (10.7%), and active surveillance (AS) 26 (5.3%). Participants with at least some college education ($P = 0.003$) or annual income > $100,000 ($P = 0.003$) were more likely to consult three or more doctors. Amongst all treatments, "doctor's recommendation" was the most influential information source, although relatively less important in the AS group. Internet was the second most frequent information source. Participants with higher education ($P = 0.0003$) and higher income ($P = 0.002$) considered sexual function more important while making a treatment choice. Only 2% of the men preferred a passive role in the decision-making. Informed decision-making was preferred more by patients who chose radiation and AS while shared decision-making was preferred more by surgery patients ($P < 0.05$). The majority (89%) of the respondents did not regret their decision. No difference in satisfaction levels was found between different treatment modalities.

Conclusions: This study provides insight into information sources consulted, such as the greater internet use, and various factors dictating treatment decision-making in young prostate cancer patients. There was an overall very high satisfaction rate regardless of the therapy chosen.

Editorial Comment

This is an interesting survey from the Johns Hopkins. Four hundred ninety-three men under 50 years diagnosed with Gleason score 6 prostate cancer answered a questionaire related to type of therapy. The most common primary therapy was surgery 397 (81.4%), followed by radiation 52 (10.7%), and active surveillance 26 (5.3%) patients.

Interesting findings include: 1. Participants with some college education or higher annual income were more likely to consult 3 or more doctors; 2. Amongst all types of treatment "doctor's recommendation" was the most influential information source; 3. Internet was the second most frequent information source; 4. Participants with higher education and higher income considered sexual function more important while making a treatment choice; 5. Only 2% of the men preferred a passive role in the decision-making; and, 6. Informed decision-making was preferred more by patients who chose radiation and active survaillance while shared decision-making was preferred more by surgery patients.

The study provided insight into information sources consulted, such as the greater internet use, and various factors dictating treatment decision-making in young prostate cancer patients.

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RECONSTRUCTIVE UROLOGY

Management of Adult Anterior Urethral Stricture Disease: Nationwide Survey Among Urologists in The Netherlands

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Eur Urol. 2011;21. [Epub ahead of print]

Background: Adult anterior urethral stricture disease is most often treated with dilatation or direct vision internal urethrotomy (DVIU). Although evidence suggests that anastomotic urethroplasty for short bulbar strictures is more efficient and cost effective in the long term, no consensus exists. It is unclear by whom and how often urethroplasties are performed in The Netherlands and how results are being evaluated.
Objective: To determine national practice patterns on management of anterior urethral strictures among Dutch urologists. This information will help to define the nationwide need for training in urethral surgery.
Design, Setting, and Participants: We conducted a 16-question survey among all 323 Dutch urologists.
Results and Limitations: The response rate was 74%. DVIU was practised by 97% of urologists. Urethroplasty was performed at least once yearly by 23%, with 6% performing more than five urethroplasties annually. In the group of urologists younger than 50 yr of age, 13% performed urethroplasty, with 3% of those performing more than five annually. In the case of a 3.5-cm-long bulbar stricture, DVIU was preferred by 49% of responders. Even after two recurrences, 20% continued to manage a 1-cm-long bulbar stricture endoscopically. Of responders, 79% believed that urethroplasty should be proposed only after a failed endoscopic

attempt. Diagnostic workup and evaluation of success varied greatly.
Conclusions: Most Dutch urologists believe that urethroplasty is an option only after failed DVIU. Endoscopic procedures are widely used, even when the risk of recurrence is virtually 100%. The definition of success is hampered by nonstandardised methods of follow-up. Only a small group of mainly older urologists frequently performs urethroplasties. Training programmes seem necessary to guarantee a high standard of care for stricture disease in The Netherlands. A pan-European practice survey might be interesting to clarify the need for centralised fellowship programmes.

Editorial Comment

The authors describe the results of a survey distributed to Dutch urologists about their management of urethral stricture disease. Interestingly, these results are highly similar to a survey done of urologists in the United States a couple of years ago (1). Indeed, in both countries, the common perception is that internal urethrotomy or dilation is appropriate management of strictures that, based on currently available evidence, would be better treated with urethroplasty. Several series demonstrate that the success rate with urethral dilation or urethrotomy for strictures over 2cm or recurrent strictures in unacceptably low (2,3). Yet, rather than a misunderstanding about treatment effectiveness, these practice patterns may merely represent the reality that properly trained reconstructive urologists are not available in many parts of the world, even in highly industrialized countries like the Netherlands and U.S. Only 3% of urologists surveyed performed more than 5 urethroplasties a year. The argument in favor of training additional surgeons in these techniques is quite appropriate.

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The Cleveland Clinic experience with adult hypospadias patients undergoing repair: their presentation and a new classification system

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BJU Int. 2011; 107: 1142-6
Objective: To characterize and categorize adults with hypospadias who presented to our clinic with urethral stricture and fistula to better clarify the presentation, history and intraoperative findings in this heterogeneous group and to better describe the natural history of this anomaly in adulthood.
Patient and Methods: A retrospective chart review was performed on adults with hypospadias who underwent urethroplasty for urethral stricture, urethrocutaneous fistula, and/or hypospadias repair at Cleveland

Clinic between 1993 and 2009. All procedures were performed by a single staff surgeon (K.W.A.). The charts were reviewed for site of hypospadias, presenting complaint, overall symptoms, history of repair and type of surgery performed.
Results: Fifty-five adult patients were identified. Median age was 37 years (range: 18-72). About half of the patients had distal (glanular/subcoronal or pendulous) hypospadias (56.4%) and the others had more proximal (bulbar) hypospadias (43.6%). Voiding symptoms (such as dysuria, weak stream, spraying, urgency, frequency) were the most common presenting complaint (50.9%) and overall symptom (81.8%). About half of patients underwent a two-stage urethroplasty (52.7%). Based on their history of repair, patients were divided into three categories: I, patients who have undergone continuous multiple surgeries for repair with significant scarring and tissue loss; II, delayed complications after an initially successful childhood repair; and III, no previous repair. Most patients were category I (58.2%); however, seven patients (12.7%) were category III. Balanitis xerotica obliterans (BXO) was more common in this subgroup compared with other categories (42.9% vs 8.3%, respectively, P = 0.037). In two of the three patients in category III with BXO, the stricture length was longer than 7 cm.
Conclusions: Adults with hypospadias represent a heterogeneous group. More than half of adults with complications related to hypospadias have had multiple operations (category I) representing one of the most difficult challenges to the reconstructive urologist. Roughly 30% of patients undergo an initially successful repair in childhood with recurrent problems in adulthood (category II), suggesting that the outcomes of repair may not be as durable as estimated by studies with shorter-term follow-up. Finally, BXO is over-represented in men with hypospadias who have not previously undergone repair, which contradicts the previous suggestion that the risk of BXO is related to the use of skin grafts/flaps from previous repairs and suggests that there may be an increased risk of severe stricture disease in patients who have never undergone corrective surgery for this anomaly.

Editorial Comment

The take home messages from this article are that (1) repair of previously operated-upon adult hypospadias is extremely difficult and (2) failure of childhood hypospadias repair may be more frequent than we understand it to be based on pediatric surgical series in which the follow-up stops at or before adolescence. An additional insight covered briefly in the article is the psychological challenges faced by adult men with hypospadias complications. Some are bothered by a sense that their penis is different in appearance from their peers are seek additional surgery in pursuit of a “normal” penis. Here, the words of Voltaire are often appropriate counsel: “Le mieux est l’ennemi du bien”, or “The best is the enemy of the good”. It is ill-advised to pursue additional surgeries to correct a urethra that is free of stricture but has a mild sacculation that causes post-void dribbling. Similarly, whereas an orthotopic mid-glans meatus is the goal in pediatric hypospadias repair, a sub-coronal meatus is preferable in adult hypospadias reconstruction because the glansplasty is fraught with complications. Another psychological consideration is that some men with restenosis after childhood hypospadias repair approach any additional surgery with great anxiety and fear. Repeat surgery can bring up memories of suffering through repeat interventions as a child. Truly, these represent challenging patients, pre-operatively, intra-operatively and post-operatively. They require skilled attention and careful counseling.

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UROLOGICAL ONCOLOGY

Cancer control and functional outcomes after radical prostatectomy as markers of surgical quality: analysis of heterogeneity between surgeons at a single cancer center

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Background: Previous studies have shown that complications and biochemical recurrence rates after radical prostatectomy (RP) vary between different surgeons to a greater extent than might be expected by chance. Data on urinary and erectile outcomes, however, are lacking.
Objective: In this study, we examined whether between-surgeon variation, known as heterogeneity, exists for urinary and erectile outcomes after RP.
Design, Setting, and Participants: Our study consisted of 1910 RP patients who were treated by 1 of 11 surgeons between January 1999 and July 2007.
Intervention: All patients underwent RP at Memorial Sloan-Kettering Cancer Center.
Measurements: Patients were evaluated for functional outcome 1 yr after surgery. Multivariable random effects models were used to evaluate the heterogeneity in erectile or urinary outcome between surgeons, after adjustment for case mix (age, prostate-specific antigen, pathologic stage and grade, comorbidities) and year of surgery.
Results and Limitations: We found significant heterogeneity in functional outcomes after RP ($p < 0.001$ for both urinary and erectile function). Four surgeons had adjusted rates of full continence < 75%, whereas three had rates > 85%. For erectile function, two surgeons in our series had adjusted rates < 20%; another two had rates > 45%. We found some evidence suggesting that surgeons' erectile and urinary outcomes were correlated. Contrary to the hypothesis that surgeons "trade off" functional outcomes and cancer control, better rates of functional preservation were associated with lower biochemical recurrence rates.
Conclusions: A patient's likelihood of recovering erectile and urinary function may differ depending on which of two surgeons performs his RP. Functional preservation does not appear to come at the expense of cancer control; rather, both are related to surgical quality.

Editorial Comment

Surgical volume or institutional volume is regarded as markers of quality and outcome in cancer surgery. Here, the authors show that within a single, high-volume institute large differences in cancer control and functional results exist between the 11 surgeons involved. Furthermore, in contrast to other available data which report incredible results of specialized centers the data presented here can be regarded as very honest. Overall, the mean adjusted proportion of patients with good erectile function at 1 year for all surgeons was 30% and the mean adjusted proportion of patients who were continent at 1 year for all surgeons was 80%. The adjusted rates of good erectile functions ranged from 8% to 49% and rates of continence ranged from 64% to 97%, showing large differences between surgeons. Interestingly, surgeons with better functional outcomes also had higher rates of cancer control.
In short, the surgeon matters, and not so much the institution.

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Adverse renal outcomes in subjects undergoing nephrectomy for renal tumors: a population-based analysis

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Eur Urol. 2011; 59: 333-9

Background: There has been increasing interest in determining renal outcomes after nephrectomy for renal tumors. Previous studies have not assessed all relevant risk factors, including proteinuria.
Objective: We sought to determine the risk and predictors for the development of adverse renal outcomes in a population-based cohort of subjects undergoing partial or complete nephrectomy.
Design, Setting, and Participants: A large population-based data set was used to identify all subjects undergoing nephrectomy in Alberta, Canada, from 2002 to 2007 using administrative codes. Comorbid conditions were determined using validated algorithms, and baseline estimated glomerular filtration rate (eGFR) and proteinuria status were determined.
Measurements: Postsurgical outcomes of end-stage renal disease, acute dialysis, chronic kidney disease (CKD) (eGFR < 30 mL/min per 1.73 m(2)), and rapidly progressive CKD (eGFR < 60 mL/min per 1.73 m(2) and eGFR loss ≥ 4 mL/min per 1.73 m(2) per year) were assessed. The risk and risk factors for developing the composite renal outcome were determined using a multivariable Cox proportional hazards model.
Results and Limitations: Of 1151 subjects, 10.5% developed an adverse renal outcome over a mean of 32 mo. Complete (vs. partial) nephrectomy was associated with a hazard ratio (HR) of 1.75 (95% confidence interval [CI], 1.02-2.99) for the primary outcome, as was lower baseline eGFR. Subjects with proteinuria were more likely to experience the primary outcome (42% vs. 9%), conferring an adjusted HR of 2.40 (95% CI, 1.47-3.88).
Conclusions: Clinically important adverse renal outcomes are common in patients undergoing nephrectomy for renal tumors. In addition to baseline eGFR and the extent of the renal mass removed, proteinuria is a strong independent risk factor. Assessment of proteinuria, in addition to other risk factors, should be performed to inform prognosis and the optimal treatment strategy.

Editorial Comment

The authors analyzed 1151 patient who underwent complete or partial nephrectomy. Surprisingly, they found that a significant proportion of subjects (10.5%) developed clinically relevant adverse renal outcomes within 2.7 years after nephrectomy. The most relevant information within this report is that in addition to the expected association of decreased baseline renal function, proteinuria at baseline was a strong independent risk factor, conferring more than a two-fold risk.
A good and simple clinical advise therefore is to check for proteinuria before the operation and if proven, to regard this as a significant prognostic factor for adverse renal outcome. Partial nephrectomy or nephron-sparing surgery should be strongly considered in these cases.

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NEUROLOGY & FEMALE UROLOGY

Tape Fixation: An Important Surgical Step to Improve Success Rate of Anti-Incontinence Surgery

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Purpose: Mid urethral slings are effective surgical treatment for stress urinary incontinence. However, 5% to 20% of patients still experience surgical failure with clinically significant recurrent or persistent stress urinary incontinence. Since a subset of these failures may be caused by improper tape position, we elucidated whether additional paraurethral fixation of a tape to prevent displacement during tensioning could improve the transobturator sling outcome.
Materials and Methods: The study was done in 463 patients with stress urinary incontinence who were randomly allocated to treatment with a standard transobturator intravaginal monofilament sling procedure (232) or to an intravaginal transobturator monofilament sling with additional 2-point tape fixation (231). Another 2 absorbable sutures parallel to the urethra were added to fix the tape and prevent displacement during tape tensioning. Outcome was assessed by a cough test and a 1-hour pad test at 12 months.
Results: Clinical efficacy of the procedure with fixation was significantly higher with 195 women (95.12%) cured or improved compared to the 199 (88.73%) cured or improved with the standard sling (chi-square 5.71, p = 0.0169). There was no increase in intraoperative or postoperative complications. Also, among patients with intrinsic sphincter deficiency we noted a significantly better outcome in the fixation group than in the control group, that is 39 of 41 patients (95.1%) cured or improved vs. 31 of 42 (73.8%) (chi-square 10.65, p = 0.0011).
Conclusions: Tape fixation significantly increases the clinical efficacy of the transobturator sling, especially in patients with intrinsic sphincter deficiency.

Editorial Comment

In this well designed work by Rechberger and cols. mid urethral slings are compared regarding their efficacy when coupled with a simple addition in the surgical technique: a pair of Vycril stitches alongside the urethra to assure better tape fixation and prevent displacement. Not only this simple technique improved results objectively and subjectively, but it also provided better clinical outcome in patients with ISD, which are known to be harder to treat. Some urogynecologists already perform this maneuver intuitively but this paper adds strong evidence that this is a valid intraoperative detail that may reflect in treatment results improvement.

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Bladder augmentation and urinary diversion in patients with neurogenic bladder: Non-surgical considerations

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J Pediatr Urol. 2011 Apr 12. [Epub ahead of print]

Segments from almost all parts of the bowel have been used for urinary diversion. As a result, the available absorptive surface area of the bowel is reduced, and the incorporation of bowel segments into the urinary tract may have metabolic consequences. This is an area somewhat neglected in the literature. Metabolic complications are rare, but sub-clinical metabolic disturbances are quite common. Several studies have demonstrated that some of the absorbent and secreting properties of the bowel tissue are preserved after incorporation into the urinary tract. Hyperchloraemic metabolic acidosis can occur if ileal and/or colon segments are used, as well as malabsorption of vitamin B(12) and bile acid after the use of ileal segments. These metabolic effects are not as severe as may be suspected and can be prevented by prophylactic substitution. Secondary malignancies can develop as a long-term consequence of bladder augmentation. Using colonic segments, tumours are most likely to occur at the ureteral implantation site. To prevent metabolic complications, careful patient selection and meticulous and lifelong follow-up, as well as prophylactic treatment, are mandatory. Endoscopy for early detection has been recommended, starting 10 years postoperatively for patients who underwent surgery for a benign condition.

Editorial Comment

This a nice review on the topic of non surgical complications implicated in bladder augmentation and urinary diversion in pediatric neurogenic bladder patients. Although the article does not bring any outrageously new fact out it does remind us of the severe implications that may take place following this type of surgery, notably in children. There should be a concern regarding this specific population as less invasive treatments lack efficacy and must be repeated continuously and regularly for a lifelong period.

Although the use of intestinal segments have been widely used for many years it seems clear that it is far from being the ideal solution. Research in tissue engineering may bring a more suitable alternative in the future.

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GERIATRIC UROLOGY

The importance of pelvic lymph node dissection in the elderly population: implications for interpreting the 2010 national comprehensive cancer network practice guidelines for bladder cancer treatment

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Purpose: National Comprehensive Cancer Network practice guidelines indicate that pelvic lymph node dissection can be omitted at radical cystectomy in elderly patients. We examined the pelvic lymph node dissection rate in patients 80 years old or older and the impact of pelvic lymph node dissection on cancer specific and overall mortality in these patients.
Materials and Methods: We examined the records of 11,183 patients treated with radical cystectomy in 17 Surveillance, Epidemiology and End Results registries. We performed univariate and multivariate Cox regression analysis to test the effect of pelvic lymph node dissection on cancer specific and overall mortality.
Results: Overall pelvic lymph node dissection was omitted in 25% of patients, including 24.2% younger than 80 years and 30.8% 80 years old or older ($p < 0.001$). The 5-year rate of freedom from cancer specific mortality for pelvic lymph node dissection vs no pelvic lymph node dissection was 62.5% vs 59.9% in patients younger than 80 years, and 50.0% vs 46.1% in those 80 years old or older ($p = 0.01$ and 0.005, respectively). The 5-year rate of freedom from overall mortality for the same categories was 48.8% vs 43.9% and 28.3% vs 24.7% ($p < 0.001$ and 0.01, respectively). On multivariate analysis omitting pelvic lymph node dissection was associated with a 1.3-fold higher cancer specific rate at ages less than 80 and 80 years or greater (each $p < 0.001$). Omitting pelvic lymph node dissection was also associated with a 1.3-fold higher overall mortality rate, including 1.3 at ages less than 80 years and 1.2-fold at ages 80 years or greater (each $p \leq 0.005$).
Conclusions: Results indicate that pelvic lymph node dissection was more often omitted in patients 80 years old or older than in those younger than 80 years. However, the protective effect of pelvic lymph node dissection on cancer specific and overall mortality was virtually the same in the 2 age categories. Thus, advanced age should not be a limiting factor for performing pelvic lymph node dissection at radical cystectomy.

Editorial Comment

Unfortunately, evidence-based practice guidelines regarding the oncological management of elderly patients are sparse. In this scenario, authors are commended for highlighting that elderly patients might be denied the opportunity to receive the most effective treatment for their disease on the basis of chronological age alone.

Based on Surveillance, Epidemiology and End Results (SEER) database, pelvic lymph node dissection (PLND) was more often omitted in elderly patients (> 80 years) and when performed, tended to be less extensive (< 10 lymph nodes). However, metastasis rate was similar in patients younger than 80 and 80 years old or older (26.1% vs 25.1%) and patients with a lymph node count of 10 or greater had significantly more favorable cancer specific and overall mortality rates than their counterparts with < 10 lymph nodes. These results remained constant when patients were stratified by age less than 80 vs 80 years or greater.

Interestingly, PLND omission was less common in more contemporary study years, that is 38.6% between 1988 and 1992 vs 17.5% between 2003 and 2006 ($p < 0.001$).

Although virtually all patients treated with radical cystectomy are judged to be fit candidates for such a major surgical procedure, future studies should consider comorbidities and the perspective of quality-of-life adjusted relative to survival benefits in a prospective design to confirm presented results, to provide better understanding of the effect of age on tumor biology and patient survival and to improve cancer care in the elderly.

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The illusion of prostate-specific antigen decline in patients with metabolic syndrome and insulin resistance

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BJU Int. 2011; 20. doi: 10.1111/j.1464-410X.2011.10225.x. [Epub ahead of print]

Study Type - Symptom prevalence (prospective cohort) Level of Evidence 1b What's known on the subject? and What does the study add? Studies have shown that PSA is negatively associated with obesity as a result of hemodilution or metabolic effect. Hemodilution could be the main reason for low PSA levels in obese men. However, the intrinsic metabolic effects such as insulin resistance (IR) or metabolic syndrome (MS) on PSA level have not been clearly evaluated although obesity is closely tied to MS and IR. We regarded MS and IR as the pathophysiological cornerstone of metabolic disorder in obesity and analyzed the relationships among MS, IR, and PSA levels, and plasma volume by using the concept of PSA mass, the total circulating PSA protein. PSA mass did not change depending on the severity of the obesity, MS or IR. Even the group with both MS and IR, which could be the most metabolically disturbed in this study, did not have different PSA mass, comparing with the group without any MS or IR. Thus, the decline in PSA level in men with MS or IR can be also explained by increased plasma volume other than any intrinsic metabolic effects.
Objective: To investigate the detailed mechanism of prostate-specific antigen (PSA) decline in metabolic syndrome (MS) and insulin resistance (IR), which lowers the predictive value of the PSA test, we examined the effect of haemodilution and the possibility of an intrinsic metabolic effect.
Patients and Methods: We analysed 28.315 men who underwent routine check-ups. We compared the age-adjusted mean PSA levels in subjects with and without MS before and after adjusting or stratifying the plasma volume. We analysed changes in PSA level, plasma volume and PSA mass according to obesity grade, number of MS components, IR severity and diagnosis of MS, IR or both using an analysis of covariance.
Results: The PSA levels were lower in the group with MS than in the group without MS ($P = 0.001$), but this difference disappeared after adjusting or stratifying the plasma volume ($P > 0.05$ for all). The PSA levels decreased, plasma volume increased, and PSA mass did not change as the number of MS components increased ($P = 0.002$, $P < 0.001$, $P = 0.55$, respectively) or the IR severity increased ($P = 0.001$, $P < 0.001$, $P = 0.34$, respectively). Similarly, PSA levels were lower, plasma volumes were higher and PSA masses were the same in subjects with MS ($P = 0.002$, $P < 0.001$, $P = 0.10$, respectively), IR ($P = 0.018$, $P < 0.001$, $P = 0.94$, respectively), or both ($P = 0.003$, $P < 0.001$, $P = 0.86$, respectively) than in subjects without those conditions.
Conclusion: The PSA decline in MS and IR may result simply from a haemodilution effect and be unrelated to intrinsic metabolic disturbances. For this reason, PSA levels could be underestimated in patients with MS or IR because of haemodilution.

Editorial Comment

Prostate-specific antigen (PSA) is the most widely used marker for prostate cancer screening. However, the presence of other benign processes and a myriad of situations may confound the interpretation of PSA levels.

Authors present an elegant cross-sectional study regarding conditions that could affect the validity of PSA tests in prostate cancer screening and showed no difference in PSA levels between subjects with and without metabolic syndrome after adjusting for the plasma volume.

The decrease in PSA levels observed in patients with metabolic syndrome (MS) or insulin resistance (IR) could simply be the result of a haemodilution effect and not related to intrinsic metabolic disturbances.

Thus, when interpreting PSA levels in men with MS or IR, we should consider that the PSA level could be underestimated because of haemodilution.

Although the utilization of the concept of PSA mass is a virtue, most of study limitations were recognized by authors and further analyses considering direct measurement of plasma volume using an isotope, prostate volume and visceral adipose tissue together are necessary to define the relationships and the use of such calculations for PSA evaluation must also be validated.

On top of that, these patients are commonly exposed to drugs such as nonsteroidal anti-inflammatory (NSAID; P = 0.03), statin (P = 0.01), and thiazide diuretic (P = 0.025) that intake was recently inversely related to PSA levels (1). In this setting, adjusting for potential confounders including demographics, clinical characteristics, physical examination, laboratory studies, and duration of medication use are warranted once five years of NSAID, statin, and thiazide diuretic use was associated with PSA levels lower by 6%, 13%, and 26%, respectively. The combination of statins and thiazide diuretics showed the greatest reduction in PSA levels: 36% after 5 years. On the other hand, concurrent calcium channel blocker use minimizes or negates the inverse relationship of statin use and PSA level.

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PEDIATRIC UROLOGY

Instituting a conservative management protocol for pediatric blunt renal trauma: evaluation of a prospectively maintained patient registry

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Purpose: Retrospective studies show that even high grade pediatric renal trauma can be safely managed conservatively. We evaluated a prospective patient registry at our level 1 pediatric trauma center, where patients with renal trauma were treated with an institutional review board approved conservative blunt renal trauma protocol. Standardized treatment included a trial of expectant management for all stable cases.
Materials and Methods: We identified 39 children with blunt renal trauma treated between 2003 and 2008. A strict conservative approach was used, ie nonoperative management in cases that were hemodynamically stable or had a favorable response with up to 2 units of blood transfused and no operative renal lesion on imaging. Adult imaging protocols were followed and exploratory laparotomy for nonrenal causes did not alter course of expectant renal management. Outcomes evaluated were injury grade, hematuria, operative management, length of stay and associated injuries.
Results: Based on the American Association for the Surgery of Trauma organ injury severity scale, 13 patients were considered to have grade I disease, 8 grade II, 11 grade III, 6 grade IV and 1 grade V. Conserva-

tive management resulted in a 97% nonoperative rate and a single renorrhaphy.
Conclusions: Using a prospective patient registry, this study demonstrates that conservative treatment of blunt pediatric renal trauma is safe and effective. Also, serious renal injuries are not missed by applying adult diagnostic imaging protocols in children.

Editorial Comment

These authors instituted a conservative management protocol for blunt renal trauma in pediatric patients that mirrored their adult protocol. This study reports on their five-year experience using the new protocol at their institution. They also used adult imaging guidelines to diagnose and categorize renal injuries. They had 39 patients with confirmed blunt renal trauma during this time frame and all but one was able to be managed conservatively. As expected, most of the injuries were lower grade injuries but they did have six Grade IV injuries and one Grade V injury. Endoscopic management or percutaneous drainage was still categorized as being conservative. When this new prospective data is combined with their prior retrospective experience, nearly 80% of pediatric patients with high-grade blunt renal trauma were able to be managed expectantly. This study helps provide further evidence that the adult approach of non-operative management for high-grade blunt renal trauma can be applied safely in hemodynamically stable children; however, long-term functional outcome data is still needed.

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Tonsillectomy does not improve bedwetting: results of a prospective controlled trial

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J Urol. 2010; 184: 2527-31

Purpose: Sleep disordered breathing caused by tonsillar hypertrophy has been implicated as a cause of primary and secondary nocturnal enuresis in children. We prospectively studied the preoperative and postoperative rates of nocturnal and daytime incontinence in a group of children with tonsillar hypertrophy undergoing tonsillectomy compared to a matched control group undergoing surgery unrelated to the airway or urinary tract.
Materials and Methods: A total of 326 toilet trained children 3 to 15 years old were included, with 257 in the tonsillectomy group and 69 in the control group. Severity of tonsillar hypertrophy was graded preoperatively on a scale of 1 to 4. A voiding questionnaire regarding number of bedwetting and daytime incontinence episodes per week, voids per day, bowel movements per week, secondary or primary enuresis and family history was completed by parents preoperatively, and at 3 and 6 months postoperatively.
Results: Preoperatively the respective rates of nocturnal enuresis and daytime incontinence were 33% and 17% in the tonsillectomy group ($p = 0.89$), and 35% and 14% in the control group ($p = 0.3$). The respective cure rates for bedwetting at 3 and 6 months postoperatively were 40% and 50% in the tonsillectomy group ($p = 0.60$), and 35% and 48% in the control group ($p = 0.61$). Similarly no difference was seen in improvement or cure of daytime incontinence at 3 and 6 months postoperatively.
Conclusions: We found no association between tonsillar hypertrophy and urinary incontinence before or after tonsillectomy.

Editorial Comment

There have been a number of reports in the literature suggesting that tonsillectomy may be beneficial for the treatment of nocturnal enuresis. Because the current literature contains largely retrospective reviews and case reports, the authors sought to design a prospective controlled trial to determine whether tonsillectomy would improve daytime or nighttime incontinence postoperatively. They had 257 patients in the tonsillectomy group that all had evidence of tonsillar hypertrophy and 69 patients in the control group who were scheduled to undergo minor outpatient surgery for unrelated problems. They found similar rates of daytime and nighttime incontinence in both groups. They performed follow-up visits at three and six months and found improvement in both the study and control groups. There was no statistically significant difference between the two groups in terms of resolution or improvement of their incontinence either during the daytime or at night.

This was a nice prospective controlled study that should give one pause before suggesting to patients or parents that bedwetting is an indication for tonsillectomy. While there still remains an association between disordered breathing during sleep, upper airway obstruction, and enuresis, it is not clear yet how to tease out which patients would benefit from removal of their tonsils and/or adenoids versus the more proven methods of medical and behavioral management.

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International Braz J Urol
Vol. 37 (3): 419-420, May-June, 2011

A Novel "no-touch" Robot-assisted Laparoscopic Technique Facilitates Ureteral Reconstructive Surgery

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ABSTRACT

Objectives: One of the current limitations of robotic surgery is the lack of haptic feedback. In order to overcome this drawback we developed a "No-Touch" (NT) technique utilizing the distal portion of a feeding tube to intubate and manipulate both the ureter and the renal pelvis during anastomosis.
Materials and Methods: Ureteral spatulation and pelvic reduction were performed as necessary. An 8 centimeter distal end segment of a 3 to 5 French feeding tube was used to intubate and manipulate the lumen of the proximal ureter and renal pelvis or recipient ureter during anastamosis. Manipulation of the discarded segment of the pelvis served as a handle to control and limit tissue handling. The NT technique allows for precise suture placement and prevented inadvertent backwall suture placement, thus ensuring luminal patency. No nephrostomy tubes or ureteral stents were utilized during these procedures. Patients were followed every three months for the first year with renal ultrasonography. Review of operative videos and surgical results was performed.
Results: Ten robotic pyeloplasties, one robotic pyeloureterostomy, and one robotic distal ureteroureterostomy were performed using the NT technique. No backwall suture placements, tissue crush or crimping injuries or occurred in any case. There were no intraoperative or post-operative complications. Resolution of hydronephrosis and symptoms was demonstrated in all patients after post-operative examination and ultrasonography.
Conclusions: A "No-Touch" robotic technique utilizing the distal blunt end of a feeding tube is a safe, effective, and inexpensive adjunct tool that minimizes tissue handling in robot-assisted laparoscopic surgery.

Int Braz J Urol. 2011; 37 (Video #4): 419-420
Available at: www.brazjurol.com.br/videos/may_june_2011/Swords_419_420video.htm

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EDITORIAL COMMENT

Authors nicely illustrate the No Touch (NT) technique to perform anastomosis, namely robotic pyeloplasty. The use of a feeding tube facilitates manipulation of the ureter during the anastomosis. This allows for minimal tissue handling which hypothetically may lead to less tissue injury and edema. Authors claim that this in turn will result in higher probability of ureteral patency. While this hypothesis is plausible, it remains to be proven. Cost efficacy and safety is premature to be determined at the present time.

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