Brazilian Journal of Urology
Official Journal of the Brazilian Society of Urology
Vol. 28 (1): 64-79, January - February, 2002

UROLOGICAL SURVEY

ENDOUROLOGY AND LITHIASIS

Post-ESWL, clinically insignificant residual stones: reality or myth?

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Objectives: To assess the significance of asymptomatic residual stone fragments of less than 4 mm (clinically insignificant residual fragments [CIRFs]) after extracorporeal shock wave lithotripsy (ESWL).

Methods: Eighty-one patients were followed up for 6 to 60 months (mean 15) after ESWL to determine the fate of the CIRFs.

Results: Of the 81 patients, 6 were lost to follow-up, leaving 75 patients. During follow-up, fragments passed spontaneously in 18 patients, remained stable in 13 patients, and became clinically significant in 44 patients who developed one or more complications. For the latter patients, repeated ESWL was done in 16, percutaneous nephrolithotomy in 3, and ureteroscopic stone removal in 4 patients. The remaining 21 patients were treated conservatively with analgesics. We found that 53% of the CIRFs located in the pelvis passed spontaneously, and most of the CIRFs in caliceal location became clinically significant. Also, as the stone burden and number of stone fragments increased, the risk of CIRFs becoming clinically significant increased. The outcome was the same whether a metabolic abnormality was present or not, provided the patient received appropriate treatment. The clearance rate was highest in the first 6 months. Finally, as the duration of follow-up increased, the rate of complications increased.

Conclusions: Patients with residual stones after ESWL require close follow-up and timely adjuvant therapy. As the number and size of residual fragments increased, the risk of complications increased. A pelvic location was a favorable factor for spontaneous passage. Metabolic defects, if treated adequately, did not increase the regrowth rate. Although the complete clearance rate of CIRFs with repeated ESWL was lower than for the operative interventions, most patients improved with this modality.

Editorial Comment

The controversy of clinical significance of asymptomatic residual stone fragments (less than 4 mm) after ESWL still persists among urologists (1). Streem et al. (1996) first drew our attention to this subject following 160 patients with such residual fragments. They found that by one year, 23.8% of patients became stone free and this probability increased to 36% at 5 years, nevertheless, fragments increased in size in 18.1% of patients. Also, 43.1% of patients had a symptomatic episode or required intervention 1.6 to 85.4 months (mean 26 months) after ESWL, with a probability estimated at 0.71 at 5 years. In a subsequent paper, Chen & Streem (1996) treated 206 patients for isolated lower pole calculi with ESWL. They reported that of those patients with residual fragments, 12.6% demonstrated stone growth, became symptomatic or required a secondary intervention at a mean follow-up of 33 months.

The recent article by Khaitan et al. demonstrated that 53% of stone fragments located in the pelvis passed spontaneously, while most of residual fragments in caliceal location became clinically significant. Also, this work showed that as the stone burden and number of stone fragments increased, the risk of becoming clinically significant increased. According to the proposal of Streem et al. (1996) 6 years ago, the term clinically insignificant fragments is not appropriate, because the patients with residuals after ESWL require continued monitoring as they have potential for recurrent symptomatic episodes and need for additional treatment.

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Francisco J.B. Sampaio

Randomized study of transurethral resection of the prostate and combined transurethral resection and vaporization of the prostate as a therapeutic alternative in men with benign prostatic hyperplasia

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Background and Purpose: In recent years, various minimally invasive alternatives to transurethral resection have become available for treatment of benign prostatic hyperplasia (BPH). Transurethral electrovaporization has become popular, with reported improvements in subjective and objectives measures, but a high rate of postoperative irritative symptoms and lack of tissue for histologic examination are the two most commonly reported disadvantages of this procedure. To decrease the postoperative irritative symptoms while minimizing intraoperative and postoperative bleeding and also to obtain tissue samples, we have combined the techniques of vaporization, which was termed "vapor-cut." The aim of this randomized study was to compare the efficacy and safety of vapor-cut with those of the gold standard, transurethral resection.

Patients and Methods**:** A series of 100 consecutive men (mean age 63.5 ± 3.4 years) with moderate to severe symptoms of prostatism were randomized to receive transurethral resection of the prostate (TURP) or vapor-cut since November 1997. Adverse events during the procedure, including serial changes in both serum hematocrit and sodium and postoperative irritative symptoms, were recorded after removal of the urethral catheter. Preoperative and postoperative symptom scores and maximum flow rates (Qmax) were obtained from all patients. The volume of the prostate was measured preoperatively and postoperatively using transrectal ultrasonography. The mean follow-up of the patients was 6.7 months (range 6-10 months).

Results: The mean operative times for the vapor-cut group and the TURP group were 48.2 minutes and 42.7 minutes, respectively ($P > 0.05$). In the TURP group and the vapor-cut group, the International Prostate Symptom Score (I-PSS) decreased from 21.6 to 5.0 ($P < 0.01$) and from 19.4 to 4.0 ($P < 0.01$), respectively, at 6 months. The Qmax increased from 9.2 ± 2.6 mL/sec to 24.6 ± 3.4 mL/sec ($P < 0.01$) in the TURP group and from 7.9 ± 2.1 mL/sec to 26.7 ± 3.7 mL/sec ($P < 0.01$) in the vapor-cut group. The mean reductions in the weight of the prostate were 49.8% in the TURP group ($P < 0.05$) and 53.6% in the vapor-cut group ($P < 0.05$). Both catheterization time and hospital stay were significantly shorter for the vapor-cut group ($P < 0.05$). The decreases in the mean serum sodium concentration were statistically insignificant in both groups. However, the decrease in the mean hematocrit was statistically significant in the TURP group but not in the vapor-cut group. No patient in either group had the transurethral resection syndrome or required blood transfusion. After removal of the urethral catheter, irritative voiding symptoms, usually associated with frequency, were greater in

those patients treated with TURP than in those having vapor-cut. None of the patients demonstrated sphincteric incontinence, bladder neck contracture, or urethral stricture.

Conclusion: From our preliminary experience, vapor-cut seems to give results comparable to those of TURP. Because there is almost no bleeding during vapor-cut, the procedure is performed under excellent visibility, which permits more rapid and effective resection.

Editorial Comment

Transurethral electrovaporization of the prostate, as performed with classic electrodes, has proved to be an excellent method to treat prostates between 40 to 60 g, as evidenced by the International Prostate Score of Symptoms and flow study. Main advantages are the low blood loss, and easy to perform. A high rate of postoperative irritative symptoms and lack of tissue for histologic examination are the two most commonly reported disadvantages of this procedure. The combination of transurethral resection followed by vapor-cut of the prostate performed with thicker and wider loop permit tissue resection and vaporization concomitant. Thus, resection of bigger prostates is possible without extend the operative time, low blood loss, and extraction of samples to pathological examination. This technique may be kept in mind and performed due to its advantages.

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Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria

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Background: A low-calcium diet is recommended to prevent recurrent stones in patients with idiopathic hypercalciuria, yet long-term data on the efficacy of a low-calcium diet are lacking. Recently, the efficacy of a low-calcium diet has been questioned, and greater emphasis has been placed on reducing the intake of animal protein and salt, but again, long-term data are unavailable.

Methods: We conducted a five-year randomized trial comparing the effect of two diets in 120 men with current calcium oxalate stones and hypercalciuria. Sixty men were assigned to a diet containing a normal amount of calcium (30 mmol per day) but reduced amounts of animal protein (52 g per day) and salt (50 mmol of sodium chloride per day); the other 60 men were assigned to the traditional low-calcium diet, which contained 10 mmol of calcium per day.

Results: At five years, 12 of the 60 men on the normal-calcium, low-animal-protein, low-salt diet and 23 of the 60 men on the low-calcium diet had had relapses. The unadjusted relative risk of a recurrence for the group on the first diet, as compared with the group on the second diet, was 0.49 (95 percent confidence interval, 0.24 to 0.98; P=0.04). During follow-up, urinary calcium levels dropped significantly in both groups by approximately 170 mg per day (4.2 mmol per day). However, urinary oxalate excretion increased in the men on the low-calcium diet (by an average of 5.4 mg per day [60 µmol per day]) but decreased in those on the normal-calcium, low-animal-protein, low-salt diet (by an average of 7.2 mg per day [80 µmol per day]).

Conclusions In men with recurrent calcium oxalate stones and hypercalciuria, restricted intake of animal protein and salt, combined with a normal calcium intake, provides greater protection than the traditional low-calcium diet.

Editorial Comment

Nearly 10% of persons in the United States will have at least one stone in the course of their lives. Once lithiasis is formed, there is a probability of 50% that a second lithiasis will be formed in a period of 5 to 7 years without treatment. Thirty to 50% of patients with renal lithiasis have idiopathic hypercalciuria (1). Thus, the intensity of the problem described by these authors becomes evident.

There are several management options to avoid lithiasis recurrence in patients with idiopathic hypercalciuria, but the dietary intervention has always been the most logical and attractive idea. Anyway, thought of dietary calcium restraint and consequent decreased urinary calcium excretion to avoid lithiasis recurrences in patients with hypercalciuria has not shown clinical efficacy. Furthermore, it seems to increase the incidence of lithiasis recurrence (2), due to the increase of the urinary oxalate excretion.

This randomized clinical trial, with 5-year follow-up, evaluated the effect of two diets on urinary lithiasis recurrence in men who suffer from idiopathic hypercalciuria. The relative risk of recurrence was lower in the group submitted to a normal calcium, and low animal protein and salt diet than the group submitted to a low calcium diet. Probably, this effect was caused by a lower animal protein intake that reduced metabolic acids production, and finally resulted in a lower urinary calcium excretion induced by acids, as well increased citrate excretion which forms a soluble complex with calcium. Since diet sodium, and consequently urinary sodium, correlate directly with urinary calcium excretion, a decrease in sodium intake should decrease urinary calcium excretion.

Low calcium diets to prevent recurrence of calcium oxalate urinary lithiasis in men with idiopathic hypercalciuria can not be recommended anymore by physicians due to the results of this careful clinical trial and another literature evidence. However, the results of this clinical trial can be questioned if one extrapolate their findings to women, which suffer from idiopathic hypercalciuria, because this study was conduced exclusively in men.

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E. Alexsandro da Silva

UROLOGICAL ONCOLOGY

Contemporary update of prostate cancer staging nomograms (Partin tables) for the new millennium

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Objectives: We previously presented nomograms combining preoperative serum prostate-specific antigen (PSA), clinical (TNM) stage, and biopsy Gleason score to provide the likelihood of various final pathologic stages at radical retropubic prostatectomy. The data for the original nomograms were collected from men treated between 1982 and 1996. During the past 10 years, the stage at presentation has shifted, with more men presenting with Stage T1c, Gleason score 5 to 6, and serum PSA levels less than 10.0 ng/mL. In this work, we update the "Partin Tables" with a more contemporary cohort of men treated since 1994 and with revised PSA and Gleason categories.

Methods: Multinomial log-linear regression analysis was used to estimate the likelihood of organ-confined disease, extraprostatic extension, seminal vesicle or lymph nodal status from the preoperative PSA stratified as 0 to 2.5, 2.6 to 4.0, 4.1 to 6.0, 6.1 to 10.0, and greater than 10 ng/mL, clinical (AJCC-TNM, 1992) stage (T1c, T2a, T2b, or T2c), and biopsy Gleason score stratified as 2 to 4, 5 to 6, 3 + 4 = 7, 4 + 3 = 7, or 8 to 10 among 5079 men treated with prostatectomy (without neoadjuvant therapy) between 1994 and 2000 at Johns Hopkins Hospital. The average age was 58 years.

Results: In this cohort, more than 60% had T1c, more than 75% had Gleason score of 6, more than 70% had PSA greater than 2.5 and less than 10.0 ng/mL, and more than 60% had organ-confined disease. Nomograms of the robust estimated likelihoods and 95% confidence intervals were developed from 1000 bootstrap analyses. The probability of organ-confined disease improved across the groups, and further stratification of the Gleason score and PSA level allowed better differentiation of individual patients.

Conclusions: These updated "Partin Tables" were generated to reflect the trends in presentation and pathologic stage for men newly diagnosed with clinically localized prostate cancer at our institution. Clinicians can use these nomograms to counsel individual patients and help them make important decisions regarding their disease.

Editorial Comment

This paper was published as a rapid communication, and it is recommended to all physicians who deals with patients with prostate cancer, familiarized or not with "Partin Tables" (1). The main purpose of this paper was to update prognostic values because the profile of new diagnosed prostate cancer patients has been changed. Localized disease is more often diagnosed than in last decades. The authors followed the same anteriorly well-succeeded rule: an easy monogram, and easy variables (serum PSA value, Gleason score on biopsy and clinical staging) obtained from the clinical practice. With the use of only 3 prognostic variables, among other possible for prostate cancer, this nomogram lacks sensitivity as we compare, for example, with the probabilities that can be calculated using an *Artificial Neural Network.*

Although clinical results obtained from cohort study must be carefully considered, this nomogram has an eminent practical value. The anterior series (1) was organized with patients submitted to surgery between 1982 and 1996. On this cohort, 5079 patients treated with retropubic radical prostatectomy between 1994 and 2000 and without neoadjuvant treatment were included. Thus, it is a recent series that presents a significant number of patients. The main limitation of this cohort is that only 6% of Afro-American patients were included, and these results can be questionable for this specific group.

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E. Alexsandro da Silva

Comprehensive comparison of health-related quality of life after contemporary therapies for localized prostate cancer

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J Clin Oncol, 20: 557-566, 2002

Purpose: Health-related quality-of-life (HRQOL) concerns are pivotal in choosing prostate cancer therapy. However, concurrent HRQOL comparison between brachytherapy, external radiation, radical prostatectomy, and controls is hitherto lacking. HRQOL effects of hormonal adjuvants and of cancer control after therapy also lack prior characterization.

Patients and Methods: A cross-sectional survey was administered to patients who underwent brachytherapy, external-beam radiation, or radical prostatectomy during 4 years at an academic medical center and to age-matched controls. HRQOL among controls was compared with therapy groups. Comparison between therapy groups was performed using regression models to control covariates. HRQOL effects of cancer progression were evaluated.

Results: One thousand fourteen subjects participated. Compared with controls, each therapy group reported bothersome sexual dysfunction; radical prostatectomy was associated with adverse urinary HRQOL; external-beam radiation was associated with adverse bowel HRQOL; and brachytherapy was associated with adverse urinary, bowel, and sexual HRQOL ($P = .0002$ for each). Hormonal adjuvant symptoms were associated with significant impairment ($P < .002$). More than 1 year after therapy, several HRQOL outcomes were less favorable among subjects after brachytherapy than after external radiation or radical prostatectomy. Progression-free subjects reported better sexual and hormonal HRQOL than subjects with increasing prostate-specific antigen ($P < .0001$).

Conclusion: Long-term HRQOL after prostate brachytherapy showed no benefit relative to radical prostatectomy or external-beam radiation and may be less favorable in some domains. Hormonal adjuvants can be associated with significant impairment. Progression-free survival is associated with HRQOL benefits. These findings facilitate patient counseling regarding HRQOL expectations and highlight the need for prospective studies sensitive to urinary irritative and hormonal concerns in addition to incontinence, sexual, and bowel HRQOL domains.

Editorial Comment

Prostate cancer can be managed with several kinds of treatments, from watchful waiting to radical surgery. Even in the surgery group, several surgical approaches can be used. Medical literature provides defenses to each group of treatment. However, once a prostate cancer is diagnosed, the patient would like to know which is the most efficient and less life intervening treatment, and he does not know that disagreement among physicians who manage prostate cancer exist. This article shows clinical helpful results that provide advice to patient's quality of life on which therapeutic will be used.

The authors performed a comparative study among contemporary treatments of prostate cancer, using a validated questionnaire to evaluate quality of life, directly oriented to health-related quality-of-life. The most conspicuous point of this article is that the results on long-term symptoms related to urinary and intestinal tracts, as well as sexual function showed that prostate brachytherapy do not result in lower morbidity when compared to radical prostatectomy. The surgical treatment of prostate cancer has now one more favorable argument.

E. Alexsandro da Silva

PEDIATRIC UROLOGY

Congenital micropenis: long-term medical, surgical and psychosexual follow-up of individuals raised male or female

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Horm Res 56: 3-11, 2001

Objectives: To document long-term medical, surgical and physchosexual outcome of individuals with congenital micropenis (13 males, 5 females).

Methods: Physical measurements from childhood were collected retrospectively from medical records and at adulthood by physical examination. An adult psychosexual assessment was conducted with a written questionnaire and oral discussion.

Results: Adult penile length was below the normal mean in all men. Three women had vaginoplasty resulting in normal length. All men reported good or fair erections but 50% were dissatisfied with their genitalia. Dissatisfaction with body image resulted from having a small penis (66%), inadequate body hair (50%), gynecomastia (33%) and youthful appearance (33%). Ten men were heterosexual, 1 homosexual and 2 bisexual. Among women, 4 (80%) were dissatisfied with their genitalia. Three women reported average libido with orgasm and were also heterosexual. Two women had no sexual interest or experience. Finally, males were masculine and females feminine in their gender-role identity, and both groups were satisfied with their sex of rearing.

Conclusions: Regarding choice of gender, male sex of rearing can result in satisfactory genital-sexual function. Female gender can also result in success, however it requires extensive feminizing surgery.

Editorial Comment

Because the congenital micropenis can result in inadequate male sexual function later in life, some parents have chosen to raise their child female with the hope that genital reconstruction is more likely to result in a strong sexual identity, positive body image and pleasurable sex life. This is a carefully point, and the right answer is unclear. Thus, just studies like this, that the long-term follow-up was evaluated, can rise helpful information.

The authors evaluated 18 adult patients with the age ranging from 21 and 54 years. Of the 12 men who responded, 10 reported a male heterosexual orientation, six were married, and 11 said they were satisfied with their sex of rearing. Among the women, 3 reported a female heterosexual orientation, none was married, and all were satisfied with the sex of their rearing, although men were more often satisfied with the appearance of their genitalia.

The present study shows that patients reared male considered themselves to be masculine and those raised females considered themselves to be feminine. However, the recommendation that babies be raised males is based not on problems with gender identity but on the difficulties associated with the surgical construction of a vagina and subsequent hormone treatment.

E. Alexsandro da Silva

Gubernacular development in Mullerian inhibiting substance receptor-deficient mice

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Objective: To determine, in mice with disrupted Mullerian inhibiting substance (MIS) receptor genes, whether MIS affects gubernacular development; MIS causes Mullerian duct regression and is proposed to be involved in the first stage of testicular descent, because gubernacular development is abnormal in humans with persistent Mullerian duct syndrome.

Material and Methods: Ten wild-type, 11 heterozygotic and 12 homozygotic mice for MIS receptor mutations were killed at 17.5 or 18.5 days after conception or at birth, to provide serial sagittal sections of the pelvis. The amount of cremaster muscle, mitotic bodies in the gubernacular bulb, and gubernacular size were quantified by computer analysis (four mice/group).

Results: Mullerian ducts were present in the homozygous mutants, partially present in the heterozygotes and absent in the wild-type controls. All mice had descended testes. The cremaster muscle was significantly less developed in homozygous mutants than in wild-type controls ($P<0.001$) and heterozygotes ($P<0.001$) at birth. The mitotic index between the gubernacula of all groups was indistinguishable. There was no statistical difference in gubernacular area amongst the groups. Poor cremaster muscle development in homozygous mutants gave the muscle a loose mesenchymal appearance.

Conclusions: Although there was an observable effect on cremaster muscle development in these mutant mice, gubernacular development and testicular descent were otherwise normal, and thus there must be other reasons for the observed differences in humans with persistent Mullerian duct syndrome.

Editorial Comment

Gubernaculum is the main anatomical structure in the testicular descent. Placental gonadotrophins and testicular androgens surely affect gubernacular development and the testicular descent. However, the role of the Mullerian inhibiting substance (MIS) in the testicular descent, and in the gubernacular development is unclear. MIS is a glycoprotein, produced by Sertoli cells of the fetal testes, which produces regression of the Muller ducts during the embryonic development. Because the persistent Mullerian duct syndrome can be associated to cryptorchidism, the role of MIS in the testicular descent may be attractive.

The present article describes an interesting experimental study in transgenic mices, evaluating the MIS influence on the first stage of the testicular descent. This is a very elegant study with a nicely histological examination of the gubernaculum and cremaster muscle. The authors' results showed that MIS have not a key role in the gubernacular development of mices, although a significant development of the cremaster muscle in individuals treated with MIS has been occurred.

This is a relevant article that brings new information about a controversial point, that is the hormonal influence on testicular descent. However, all data obtained from this study may have a carefully consideration in extrapolating this results to humans. Mices are not an ideal experimental model to study testicular descent of human fetus.

Luciano Alves Favorito

Increased incidence in post-transplant diabetes mellitus in children: a case-control analysis

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There is limited information regarding the incidence and features of post-transplant diabetes mellitus (PTDM) in pediatric renal transplant recipients. We noted a recent increased frequency of PTDM and reviewed charts of children who underwent renal transplantation from 1 September 1986 to 31 August 1999 to characterize the risk factors and natural history of PTDM. Sixteen children were identified with PTDM, and were each matched with two transplanted controls who did not develop PTDM. Clinical presentation varied from asymptomatic hyperglycemia to hyperosmolar dehydration or diabetic ketoacidosis. The mean time from transplantation to PTDM presentation was 1.2 years (range 1 day to 6.2 years). Significant risk factors for PTDM included: first degree family history of type 2 DM [odds ratio (OR) 23.9]; second degree family history of type 2 DM (OR 5.8); tacrolimus use (OR 9.1 versus cyclosporin); and hyperglycemia in the 2 weeks immediately after transplantation (OR 4.7). Seven of eight children with persistent PTDM continue to receive insulin. Patients with persistent PTDM had later onset disease (mean 1.9 years) compared to those with transient PTDM (0.3 years), suggesting different pathophysiologic processes. We suggest that all children undergoing renal transplantation be screened routinely for PTDM after transplantation, and that such patients may benefit from the avoidance of tacrolimus, as it may cause permanent beta-cell injury.

Editorial Comment

Hyperglycemia and diabetes mellitus (DM) are well known post-transplant complications. Diabetes mellitus can cause long-term complications and, moreover, a worst prognosis (increased rejection and mortality rates) is observed in renal transplanted patients who develop DM.

The prevalence mentioned by the authors (16 cases) in this retrospective trial may be underestimated, so as the problem may be higher than described. Eight patients (50%) have persistent DM and continued to receive insulin and/or hypoglycemic agents. A sudden increase in the incidence of post-transplant DM in the last four years is reported by the authors. The most recent patients in this series presented an incidence of DM of 20%, and only 4% of children developed pos-transplantation DM in the first 9 years of study. The introduction of the tacrolimus (FK506) as an immunity suppressor agent in 1995 is a possible reason, as suggested by the authors. However, family history of type II DM especially in a first-degree relative must be remembered as the most important risk factor (OR 23.9).

Luciano Alves Favorito

RECONSTRUCTIVE UROLOGY

Urethroplasty for refractory anterior urethral stricture

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J Urol, 167: 127-129, 2002

Purpose: We present our results managing anterior urethral strictures previously treated with urethroplasty and/or urethrotomy.

Materials and Methods: During a 32-month period 69 males 10 to 76 years old (mean age 36) underwent treatment for anterior urethral stricture, including 32 (46%) and 26 (38%) previously treated with urethroplasty and urethrotomy, respectively. In 11 patients (16%) no previous procedures had been done. Anastomotic and dorsal patch urethroplasty was performed for bulbar stricture in 13 and 14 cases, respectively, while in 4 a penile skin flap was placed for penile stricture and in 38 a 2-stage procedure was done with urethral substitution using buccal mucosa or post-auricular skin grafts. Patients were followed with ascending urethrography at 3 weeks, and 12 and 18 months as well as with uroflowmetry. Symptoms were assessed for 6 months to 4 years.

Results: Only 1 stricture recurred in patients treated with anastomotic or patch urethroplasty, or a skin flap. Of the patients scheduled for a 2-stage procedure stage 1 revision was required due to graft scarring or stenosis at the urethrostomy site in 21% and stage 2 revision was required in 23%. Other complications in this series included fistula in 3% of cases, wound infection in 3% and post-void dribbling in 12%.

Conclusions: Overall early results are good in our urethroplasty series in patients with a previously instrumented urethra. Patients should be advised of the possible need for multiple revisions of planned staged procedures. The increased rate of revision in these staged procedures compared with the excellent outcome of 1-stage procedures appears to be inherent in this operation in patients with multiple previous procedures rather than due to surgeon experience.

Editorial Comment

Despite advances in the reconstructive surgery, the urethral stricture treatment remains no completely solved. The development of innumerous surgical techniques to treat the urethral stricture disease can not blind us to the fact that a little is known about its pathogenesis.

The authors present their management of previously manipulated strictures of the anterior urethra. The worst outcomes were in the previously two-staged procedures. This is not necessarily means that this technique is inadequate, and that it can be condemned. Probably, cases that the authors' choice was a two-stage procedure were much more complex than, for example, a post urethrotomy restenosis. Although two-staged procedures are condemned to extinction, mainly due to the hopefully results in the tissue engineering field, reconstructive surgeons who perform urethroplasties may always keep in mind these procedures.

On the origin of urethral grafts, the authors used buccal mucosa, penile skin and the retroauricular graft (Wolfe graft). The use of extragenital skin for urethral surgery is not widely accepted. A key point to be considered is that the best tissue to substitute the urethra is the urethra itself. Actually, there is not an ideal substitute to the urethral tissue. Thus, a statement to the urethral reconstructive surgery can be constructed: since possible, an anastomotic urethroplasty may be performed, even in selected cases of restenosis.

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URONEUROLOGY AND URODYNAMICS

The risk of lower urinary tract symptoms five years after the first delivery

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Neurourol Urodynam, 21:2-29, 2002

Aim of the study: To estimate the prevalence and 5-year incidence of lower urinary tract symptoms (LUTS) after the first delivery and to evaluate the impact of pregnancy per se and delivery per se on long-lasting symptoms.

Materials and methods: A longitudinal cohort study of 305 primiparae questioned a few days, 3 months, and 5 years after their delivery. The questionnaire used was tested and validated, and the questions were formulated according to the definitions of the International Continence Society (ICS). Maternal, obstetric, and neonatal data concerning every delivery and objective data concerning surgeries during the observation period were obtained from the records. From the sample of 278 women (91%) who responded 5 years after their first delivery, three subpopulations were defined: 1) women without initial LUTS before or during the first pregnancy or during the puerperal period, 2) women with onset of LUTS during the first pregnancy, and 3) women with onset of LUTS during the first puerperium. The risk of LUTS 5 years after the first delivery was examined using bivariate analyses. The obstetric variables in the bivariate tests with a significant association with long-lasting urinary incontinence were entered into a multivariate logistic regression.

Results: The prevalence of stress and urge incontinence 5 years after first delivery was 30% and 15%, respectively, whereas the 5-year incidence was 19% and 11%, respectively. The prevalence of urgency, diurnal frequency, and nocturia 5 years after the first delivery was 18%, 24%, and 2%, respectively, whereas the 5-year incidence was 15%, 20%, and 0.5%, respectively. The prevalence of all LUTS except nocturia increased significantly during the 5 years of observation. The risk of long lasting stress and urge incontinence was related to the onset and duration of the symptom after the first pregnancy and delivery in a dose-response - like manner. Vacuum extraction at the first delivery was used significantly more often in the group of women with onset of stress incontinence during the first puerperium, whereas an episiotomy at the first delivery was performed significantly more often in the group of women with onset of stress incontinence in the 5 years of observation. The prevalence of urgency and diurnal frequency 5 years after the first delivery was not increased in women with symptom onset during the first pregnancy or puerperium compared with those without such symptoms. The frequency of nocturia 5 years after the first delivery was too low for statistical analysis.

Conclusion: The first pregnancy and delivery may result in stress and urge incontinence 5 years later. Women with stress and urge incontinence 3 months after the first delivery have a very high risk of long-lasting symptoms. An episiotomy or a vacuum extraction at the first delivery seems to increase the risk. Subsequent childbearing or surgery seems without significant contribution. Long-lasting urgency, diurnal frequency, or nocturia cannot be predicted from onset during the first pregnancy or puerperium.

Editorial Comment

The etiology of lower urinary tract symptoms (LUTS) during pregnancy and after delivery is complex, multifactorial, and not completely understood. Probable risk factors are related to the mother (obesity, diabetes, tabagism), foetus (fetal weight), and pelvic floor instrumentation. Studies focusing on the impact of the sensitive nerves injury of the urinary tract and adjacent tissues are rare, as well those evaluating a possible common pathophysiology to the stress, urgency or mix incontinence. Furthermore, the actual knowledge is based on animal models or retrospective human studies that present contradictory results.

The present article is a control-case study with a long-term follow-up, including 305 primiparae between 17 and 41 year-old (median 26). The risk of long-lasting stress incontinence 5 years after the first delivery was significantly higher in the onset during first pregnancy group (OR, 3.0; 95% CI, 1.7-5.4) and in the onset during first puerperium (OR, 4.6; 95% CI, 1.8-11.8) compared with the onset before first pregnancy group.

LUTS and urinary incontinence in particular are not inevitable results of vaginal delivery, although pregnancy and delivery may provoke long-lasting urinary incontinence. Many women may have multiple vaginal deliveries without pelvic floor damage, but certain women may have a vulnerable pelvic floor that places them at high risk. This group of women needs to be identified.

Francisco J.B. Sampaio

IMAGING

Ultrasonography and abdominal radiography versus intravenous urography in investigation of urinary tract infection in men: prospective incident cohort study

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BMJ, 324: 1-6, 2002

Objectives: To compare ultrasonography and abdominal radiography with intravenous urography in the investigation of urinary tract infection in men.

Design: Prospective study in two hospital departments. Radiological procedures and urological assessments performed on different days by different clinicians

Setting: District general hospital.

Participants: Consecutive series of men (n=114) referred to the Department of Urology for investigation of proved urinary tract infection.

Interventions: Ultrasonography and intravenous urography of renal tract and assessment of urinary flow rate. Clinical assessment, cystoscopy, urodynamic studies, and transrectal ultrasonography with biopsy.

Main outcome measures: Sensitivity and specificity of ultrasonography and abdominal radiography compared with intravenous urography.

Results: The combination of plain radiographs of kidneys, ureter, and bladder and ultrasonography detected more abnormalities than intravenous urography alone. No important abnormality was missed by this combination (sensitivity 100% and specificity 93%).

Conclusions: Ultrasonography with abdominal radiography is as accurate as intravenous urography in detecting important urological abnormalities in men presenting with urinary tract infection. This combination is safer than intravenous urography and should be the initial investigation for such patients. Additional determination of urinary flow rate is useful for the assessment of an incompletely emptying bladder.

Editorial Comment

It is well known that ultrasonography is the method of choice for urinary tract infection screening in children, and this fact allowed a more liberal imaging evaluation of these infants, reducing the incidence of missed reflux and renal scarring. Also, this method is comparable to intravenous urography in the evaluation of

women with urinary infections. Nevertheless, controversy still exists concerning the evaluation of urinary tract infections in men.

This prospective study was performed for evaluating the capacity of abdominal radiography together with ultrasonography in detecting urogenital abnormalities in men with urinary tract infections and compares these findings with those of intravenous urography. Important abnormalities were seen in 53 of 100 fully evaluated patients, the most common being a poorly emptying bladder (34). In men aged over 50 an incompletely emptying bladder is the most common abnormality, and in such patients flow rate determination is especially useful. Interestingly, plain radiography (KUB) with ultrasonography was able to detect more abnormalities than intravenous urography. The authors concluded that abdominal radiography with ultrasonography, and determination of flow rate should be the initial investigations of choice in men with urinary infections.

Francisco J.B. Sampaio

INVESTIGATIVE UROLOGY

Type I collagen-mediated proliferation of PC3 prostate carcinoma cell line: implications for enhanced growth in the bone microenvironment

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Matrix Biol, 20: 429-437, 2001

Prostate cancer is the second leading cause of male cancer-related deaths in the United States. Interestingly, prostate cancer preferentially metastasizes to bone. Once in the bone microenvironment, advanced prostate cancer becomes highly resistant to therapeutic modalities. Several factors, such as, extracellular matrix components, have been implicated in the spread and propagation of prostatic carcinoma. The prostate cell line, PC3, adhere and spread on collagen I to a greater degree than on fibronectin (FN) or poly-L-lysine (PLL). Flow cytometry analysis reveals the presence of the alpha(1), alpha(2) and alpha(3) collagen binding integrin subunits. Antibody function blocking studies reveal that PC3 cells can utilize alpha(2)beta(1) and alpha(3)beta(1) integrins to adhere to collagen I. Cells plated on collagen I exhibit increased rates of proliferation over cells plated on FN or tissue culture plastic. Additionally, cells plated on collagen I show increased expression of cyclin D1, a molecule associated with progression through G1 phase of the cell cycle. Inhibitor studies point to a role for phosphatidylinositol 3-kinase (PI3K), map kinase (MAPK) and p70 S6 kinase in collagen I-mediated PC3 cell proliferation and cyclin D1 expression. Type I collagen may facilitate the colonization and growth of metastatic prostate tumor cells in the bone microenvironment.

Editorial Comment

It is well established that, during metastasis, cells from certain tumors have greater affinity for specific tissue types. Notable examples are the adrenal and neural metastasis of bronchogenic carcinoma, and the bone metastasis of prostate carcinoma. This preference is determined largely by anatomic factors, which facilitate the access of metastatic cells to target organs, and, most importantly, by cellular and molecular factors. Published data on the latter factors refer essentially to the preferential interactions between receptors expressed at the cytoplasmic membrane of the circulating tumor cell and specific ligands on the endothelial surface of vessels in the target organ. However, the present paper shows clearly that a specific interaction between the tumor cell and type I collagen, an extracellular matrix molecule, may be involved with the high incidence of

bone metastasis in the prostate carcinoma. This interaction increases not only the tropism of prostate tumor cells toward bone, which has large amounts of type I collagen in its organic matrix, but also stimulates the proliferation of these cells. In addition to demonstrating the specificity of the interaction and the receptors involved, the authors also investigated the intracellular mechanisms responsible for the increase in cell proliferation. This information is particularly important as it allows the development and improvement of pharmacological therapies.

Luiz E. M. Cardoso

Effects of sodium hyaluronate on epithelial healing of the vesical mucosa and vesical fibrosis in rabbits with acetic acid induced cystitis

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J Urol, 166: 710-713, 2001

Purpose: To evaluate the effect of sodium hyaluronate on epithelial healing of the vesical mucosa and vesical fibrosis, and clarify the effect of the sodium hyaluronate solution concentration, we administered sodium hyaluronate in the bladder of rabbits with acetic acid induced cystitis.

Materials and Methods: Sodium hyaluronate at 3 concentrations (0.1%, 0.2% and 0.4%) was injected intravesically into rabbits with cystitis. Seven days after injection the effect of sodium hyaluronate was evaluated by bladder capacity measurement. Furthermore, the epithelial defective region of the mucosal membrane and bladder dry weight were determined and the condition of the epithelial membrane and extent of fibrosis were examined histologically.

Results: In all sodium hyaluronate treated groups a significant improvement in bladder capacity was observed compared to controls. In addition, a significant reduction was noted in the area of the epithelial defective region in the groups treated with 0.2% or 0.4% sodium hyaluronate and a significant decrease was noted in bladder dry weight in the group treated with 0.4% sodium hyaluronate. Histological examination revealed accelerated epithelial healing of the vesical mucosa and inhibited vesical fibrosis in the group treated with 0.4% sodium hyaluronate.

Conclusions: Our findings suggest that sodium hyaluronate is effective for promoting epithelial healing of the vesical mucosa and inhibiting vesical fibrosis.

Editorial Comment

The surface of the vesical mucosa is lined with a protective layer, which is rich in glycoproteins and complex carbohydrates. Since 1980 several experimental evidences (Parsons et al., 1980; Ruggieri et al., 1988, Hurst et al., 1996) have been showing that glycosaminoglycans (GAG), one of the complex carbohydrates of the urothelial surface, are particularly involved in this protective function. The data indicate that, due to their pronounced anionic nature, GAG are fundamental as an anti-adhesive factor against bacteria and also as regulators of urothelial permeability. Alterations in the synthesis and/or structure of GAG, with the consequent impairment of this latter function, seem to be implicated in the pathogenesis of interstitial cystitis. Indeed, the instillation in the bladder of GAG or other polymers with similar physicochemical properties, such as dextran sulfate or pentosan polysulfate, leads, at least temporarily, to a significant improvement of interstitial cystitis symptoms. The present article uses an experimental animal model of cystitis in which lesions are produced in vivo by means of an acetic acid treatment. Next, the bladders are instilled with hyaluronate (hyaluronic acid or

hyaluronan), a high molecular weight, non-sulfated GAG that is known to promote cellular proliferation and angiogenesis. The obtained results suggest that the GAG on the urothelial surface, besides their protective role, are also important for vesical epithelium repair. Thus, hyaluronan should be viewed as a potential pharmacological agent for the treatment of interstitial cystitis.

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BOOK REVIEW

The Dilated Kidney (El Riñón Dilatado)

R. Vela Navarrete

Editor Masson, 180 pp, Madrid, 2001

This book treats on a specific urological point, the hydronephrosis. However, it is a publication of general interest to the urologist and opportune in the present time. The book is monographic type and is divided into 7 chapters; it has an excellent presentation with figures and schemes of high quality. Historical notes that are intercalated in the text are pleasurable details. The author provides on this specific point a complete and broad approach. He easily discusses about anatomy, physiology, pharmacology, diagnostic and therapeutic procedures, showing his great experience, as evidenced by the numerous personal references in all chapters. Thus, this is a unique book that presents an original view of diagnosis and prognosis of the urinary tract obstruction.

Francisco J.B. Sampaio