
UROLOGICAL SURVEY

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STONE DISEASE

Jejunioleal bypass reversal: effect on renal function, metabolic parameters and stone formation

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Purpose: While the effect of jejunioleal bypass (JIB) reversal has been well studied regarding hepatic function, there is little information regarding the effect of reversal on renal function and even less data regarding the metabolic urinary stone environment. We evaluated the results of JIB reversal on renal function, the urinary stone milieu and the clinical development of recurrent calculi in affected patients.

Materials and Methods: From 1995 to 2003, 4 female patients with a mean age of 48.2 years underwent JIB reversal primarily for refractory stone disease. The clinical and metabolic courses prior to and following bypass reversal were reviewed specifically to evaluate renal function, serum and urinary metabolic stone profiles, and clinical stone formation.

Results: At initial presentation following JIB all 4 patients had significantly increased 24-hour urinary oxalate (range 80 to 160 mg, mean 112.5, normal less than 50) and significantly low 24-hour urinary citrate (range 5 to 62 mg, mean 21.5, normal greater than 320). Following reversal 24-hour urinary oxalate normalized to between 31 and 36 mg (mean 33.75). However, 24-hour urinary citrate continued to be low (range 215 to 248 mg, mean 226.5). After JIB reversal all 4 patients continued to have new stones until the commencement of urinary alkalization, following which only 1 had 1 calculus, which occurred 47 months after reversal. After JIB mean serum creatinine was 1.48 mg/dl (range 0.8 to 1.9) and mean urinary creatinine excretion was 0.91 mg per hour (range 0.69 to 1.15). After JIB reversal mean serum creatinine was 1.28 mg/dl (range 0.6 to 2.0) and mean urinary creatinine excretion was 1.0 mg per hour (range 0.85 to 1.10).

Conclusions: JIB reversal normalizes 24-hour urinary oxalate. While urinary citrate improves, it continues to be low and such patients are at high risk for recurrent stone formation. However, in this setting appropriate replacement therapy has a significant and positive impact on that propensity.

Editorial Comment

Bone loss, liver disease and renal calculi are only a few of the metabolic consequences of jejunioleal bypass. Stones form as a consequence of hyperoxaluria, low urine volume and pH and hypocitraturia that occur because of metabolic acidosis and malabsorption. Stone disease in some patients has been severe enough to prompt JI bypass reversal. Dhar and colleagues seized a unique opportunity to study 4 such patients before and after JI bypass reversal. They documented a significant reduction in stone formation rate, from 3.2 to 0.19 stones/patient/year after bypass reversal. Of note, however, reversal of the JI bypass failed to completely reverse the marked hypocitraturia associated with bypass surgery that is due to severe metabolic acidosis. Initiation of alkalization with potassium citrate, however, led to complete cessation of stone formation in all but 1 of the 4 patients, who produced a single stone. These findings are particularly relevant as laparoscopic intestinal bypass surgery has become increasingly popular. We should heed the lessons learned from JI bypass surgery and take a proactive approach to avert the metabolic consequences of intestinal surgery, and further, to continue to follow patients after bypass reversal since their risks may not completely reverse without pharmacologic intervention.

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Medical-expulsive therapy for distal ureterolithiasis: randomized prospective study on role of corticosteroids used in combination with tamsulosin-simplified treatment regimen and health-related quality of life

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Urology. 2005; 66: 712-5

Objectives: To assess the clinical efficacy of the addition of a corticosteroid drug to tamsulosin in the medical-expulsive therapy of distal ureterolithiasis.

Methods: Sixty consecutive patients with a symptomatic distal ureteral stone were included in our study and randomized to one of two home treatment groups. Group 1 patients (n = 30) received tamsulosin (0.4 mg daily), and group 2 patients (n = 30) were treated with a corticosteroid drug (deflazacort, 30 mg daily) plus tamsulosin. The treatment duration was until stone expulsion or 28 days, whichever came first. The primary endpoint of the study was the stone expulsion rate. The secondary endpoints were the expulsion time; use of analgesics; number of emergency room admissions, hospitalizations, and workdays lost; drug side effects; and quality of life of the patients (EuroQol questionnaire, EQ-5D) during treatment.

Results: The two groups had a similar expulsion rate (90% for group 1 and 96.7% for group 2; P = 0.612), but the expulsion time was significantly reduced in group 2 patients (P = 0.036). During the treatment period, we did not observe significant differences between the two groups in the number of emergency room visits or hospitalizations, analgesic use, number of workdays lost, or incidence of drug side effects. The quality of life of the patients during therapy, as determined using the EQ-5D, was similar in both groups.

Conclusions: The use of a corticosteroid drug in association with tamsulosin seemed to induce more rapid stone expulsion. In addition, tamsulosin alone as medical-expulsive therapy for distal ureteral calculi had excellent expulsive effectiveness.

Editorial Comment

One of the most significant advances in stone management that has come about in the last few years is the use of pharmacotherapy to facilitate spontaneous passage of ureteral calculi. A number of well-designed, prospective, randomized trials demonstrated the efficacy of calcium channel blockers and tamsulosin, in conjunction with corticosteroids, in promoting stone passage and reducing the pain associated with it. With comparable efficacy demonstrated for nifedipine and tamsulosin, the reduced side-effect profile of tamsulosin has made it the drug of choice in treating patients with ureteral calculi. However, prior trials included corticosteroids along with tamsulosin or nifedipine, although many practitioners simply skipped this component of the pharmacologic regimen for fear of steroid-related complications such as ulcer disease. Dellabella and colleagues performed a head-to-head comparison of tamsulosin with or without corticosteroids for the management of patients with > 4 mm distal ureteral calculi. Although spontaneous passage rates (90% versus 97%, respectively), ER/admission rates, and pain medication requirements were comparable between the 2 groups, the group receiving corticosteroids passed their stones an average of 2 days sooner. Consequently, the addition of corticosteroids results in quicker stone passage, but the benefit of improved stone passage rates and reduced need for pain medication are still obtained with tamsulosin alone. Thus, for patients without a contraindication to corticosteroids, the use of both tamsulosin and prednisone provides optimal therapy. However, tamsulosin alone is effective and even in patients in whom corticosteroids are best avoided.

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ENDOUROLOGY & LAPAROSCOPY

Laparoscopic radical cystoprostatectomy with bilateral nephroureterectomy: initial report

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Objectives: To present our experience with laparoscopic radical cystoprostatectomy and bilateral nephroureterectomy for organ-confined, muscle-invasive transitional cell carcinoma (TCC) of the bladder in two patients with dialysis-dependent end-stage renal disease (ESRD).

Patients and Methods: Two men aged 77 and 65 years with organ-confined, muscle-invasive TCC of the urinary bladder and pre-existing dialysis-dependent ESRD underwent laparoscopic bilateral pelvic lymphadenectomy, radical cystoprostatectomy and bilateral nephroureterectomy. Urine spillage was avoided and en bloc urothelial integrity between the bladder and the two renal specimens was maintained throughout the procedure. The intact, entrapped specimens were removed en bloc via a Pfannenstiel incision at the end of the procedure.

Results: The total operative duration was 573 and 660 min, respectively, including repositioning and re-draping between each major step. Blood loss was 350 and 1000 mL, respectively. Both patients tolerated the procedure well and there were no intraoperative complications. The first patient resumed oral intake 3 days after surgery and was discharged home after 5 days. The second patient's course after surgery was complicated by a prolonged adynamic ileus and infection of the catheter placed for continuous ambulatory peritoneal dialysis. He was discharged 28 days after surgery and died from unknown causes at 30 days.

Conclusions: To our knowledge, this is the first report of radical urotheliectomy, consisting of bilateral pelvic lymph node dissection, radical cystoprostatectomy, and bilateral nephroureterectomy, using entirely intracorporeal laparoscopic techniques.

Editorial Comment

This paper demonstrates a new era of laparoscopic procedures, which are extremely complicated. The oncological steps were respected and blood loss diminished for complex combined procedures. Although the number of patients was small, I believe the authors should be congratulated for the pioneer work in the area of minimally invasive surgery.

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Haemostatic partial nephrectomy using bipolar radiofrequency ablation

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BJU Int. 2005; 96: 1101-4

Objective: To determine whether an electrode array with a bipolar radiofrequency ablation (RFA) energy source can be used to perform a haemostatic partial nephrectomy by simultaneously ablating and coagulating renal tissue.

Materials and Methods: Lower-pole partial nephrectomy was performed in 12 porcine kidneys using a bipolar RFA system. Intraoperative ultrasonography was used to identify and avoid the collecting system. Tissues were positioned between opposing electrodes and tissue impedance monitored using a proprietary feedback and control algorithm. Ablation time and power, lesion width and length, and tissue thickness were recorded. The kidneys were assessed in vivo to show haemostasis of the remaining renal unit. Collecting system integrity was assessed with methylene blue injection, and the resected tissue analysed histologically.

Results: Partial nephrectomies were successful in all 12 porcine kidneys; the mean nephrectomy specimen was 3.2 x 2.6 cm. The total ablation time (sem) per lesion was 211 (15) s and the mean power was 23 W. Methylene blue injection showed an intact collecting system in 11 of the 12 kidneys, and haematoxylin and eosin staining showed a mean zone of necrosis of 9 mm at the resection margin. Ultrasonography revealed flow to the remaining kidneys after RFA and the in vivo assessment of haemostasis revealed no abnormal bleeding or haemorrhage from the kidneys.

Conclusions: Applying bipolar RF energy to an electrode array can enable transmural excision of renal parenchyma in vivo in a bloodless fashion without collecting system injury.

Editorial Comment

Laparoscopic partial nephrectomy remains a complex and difficult procedure to be performed, particularly due to the challenges to achieve optimal hemostasis after renal mass excision. The authors demonstrated a new application of RFA energy facilitating the hemostatic control during partial nephrectomy. The remaining renal parenchyma preserved the flow measured by ultrasonography. Perhaps this new technology and application maybe used for a laparoscopic nephron-sparing surgery.

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Kidney displacement simulator for retroperitoneal laparoscopic nephrectomy

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J Urol. 2005; 174: 2111-4

Purpose: We evaluated the efficacy of a renal displacement simulator originally developed at our department for retroperitoneal laparoscopic nephrectomy.

Materials and Methods: A total of 12 patients with a malignant localized renal (7) or ureteral (5) neoplasm underwent multidetector row computerized tomography. Imaging data were sent to a dedicated work station to create volume rendering and virtual laparoscopic images of the kidney, which was displaced ventral using a retroperitoneal balloon. These findings were compared with video images obtained during laparoscopy surgery.

Results: The kidney displacement simulator depicted all renal arteries (100% sensitivity) and 13 of 14 renal veins (93% sensitivity). Hilar anatomy, including the tumor, as well as major vessels and their relationships were visualized by the simulator in the laparoscopic views. The major vessel portions completely corresponded to those seen during surgery, and the left adrenal and gonadal veins were also synchronized quite well.

Conclusions: Our kidney displacement simulator was able to visualize the major vessel portions and branched small vessels, such as the adrenal and gonadal veins, prior to surgery. It is considered useful for providing guidance to surgeons and decreasing operative risks and possible complications.

Editorial Comment

Due to new regulations and complexity of surgical procedures, new training tools are demanded for better understanding of surgical steps and schooling of dexterity for development of surgical skills. This study combines pre-operative imaging technique with the laparoscopic procedure allowing identifying several anatomical landmarks, particularly the vascular structures allowing surgeons to carefully plan the surgical steps minimizing possible complications. It is possible that in the future a software will allow pre-planned surgeries to be performed prior to the actual procedure, as well as for training purpose.

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IMAGING

MRI of prostate cancer at 1.5 and 3.0 T: comparison of image quality in tumor detection and staging

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AJR Am J Roentgenol. 2005; 185: 1214-20

Objective: This prospective study was performed to compare the image quality, tumor delineation, and depiction of staging criteria on MRI of prostate cancer at 1.5 and 3.0 T.

Subjects and Methods: Twenty-four patients with prostate cancer underwent MRI at 1.5 T using the combined endorectal-body phased-array coil and at 3.0 T using the torso phased-array coil, among them 22 before undergoing radical prostatectomy. The prostate was imaged with T2-weighted sequences in axial and coronal orientations at both field strengths and, in addition, with an axial T1-weighted sequence at 1.5 T. Preoperative analysis of all MR images taken together was compared with the histologic findings to determine the accuracy of MRI for the local staging of prostate cancer. In a retroanalysis, the image quality, tumor delineation, and conspicuity of staging criteria were determined separately for both field strengths and compared. Statistical analysis was performed using Wilcoxon's and the McNemar tests.

Results: In the preoperative analysis, MRI (at both 1.5 and 3.0 T) had an accuracy of 73% for the local staging of prostate cancer. The retroanalysis yielded significantly better results for 1.5-T MRI with the endorectal-body phased-array coil in terms of image quality ($p < 0.001$) and tumor delineation ($p = 0.012$) than for 3.0-T MRI with the torso phased-array coil. Analysis of the individual staging criteria for extracapsular disease did not reveal a superiority of either of the two field strengths in the depiction of any of the criteria.

Conclusion: Intraindividual comparison shows that image quality and delineation of prostate cancer at 1.5 T with the use of an endorectal coil in a pelvic phased-array is superior to the higher field strength of 3.0 T with a torso phased-array coil alone. As long as no endorectal coil is available for 3-T imaging, imaging at 1.5 T using the combined endorectal-body phased-array coil will continue to be the gold standard for prostate imaging.

Editorial Comment

The best results for local staging of prostate cancer with MR imaging is obtained using 1.5 T MR scanner and an integrated endorectal pelvic-phased array coil. Using this combination of coils and following strict and definite criteria for extraprostatic disease, a high degree of specificity can be obtained (97%). As 3T MR units are becoming more available, and offering higher signal-to-noise ratios and increased temporal and spatial resolution it would be useful to have a study comparing both techniques.

The authors present a very interesting paper where they did a prospective analysis comparing the results of both equipments in a group of 22 patients who underwent prostatectomy. Since endorectal coils are not yet approved for clinical use at 3.0 T, they performed a direct comparison between 1.5 T MR scanner and an integrated endorectal pelvic-phased array coil with a 3.0 T MR scanner and the torso phased-array coil alone. Among these patients 15 had stage T2 tumor, and 7 had stage T3 tumor. The accuracy of staging using the MR images obtained at both field strengths was 73%. The author's conclusion was that at this moment, 1.5-T MRI of the prostate with the endorectal coil will continue to be the gold standard for MRI of the prostate because of its superior overall image quality compared with MRI at 3.0 T using only the torso phased-array coil.

It has been shown that in experimental studies, the initial results of endorectal 3T MR imaging in prostate cancer is potentially useful (1). This should be expected since with this new endorectal coil, we would obtain an increase in spatial and temporal resolution and also an increase in spectral resolution (better MR spectroscopic imaging). Endorectal 1.5 T MR imaging combined with spectroscopic imaging has already demonstrated a potential for improved diagnosis and staging of prostate cancer. Thus it is all right to predict that the 3.0 T MR scanner with adequate endorectal coil will very soon offer a significant improvement in conventional MR images and also in spectroscopic analysis causing a significant impact in the evaluation of patients with prostate cancer.

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How to decrease pain during transrectal ultrasound guided prostate biopsy: a look at the literature

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J Urol. 2005; 174: 2091-7

Purpose: There is growing interest among urologists on the need for decreasing pain during transrectal ultrasound (TRUS) guided prostate biopsy.

Materials and Methods: We performed a systematic MEDLINE search of clinical trials of any kind of anesthesia, analgesia or sedation during TRUS guided prostate biopsy published since 2000. We critically analyzed the impact of pain and discomfort associated with the procedure, the described methods for evaluating it and the different techniques that have been described.

Results: There is strong evidence in the current literature that patient tolerance and comfort during TRUS guided prostate biopsy can be improved by anesthesia/analgesia. What remains is the need to urge all urologists to introduce it in clinical practice as a routine part of the procedure, whatever the biopsy scheme.

Conclusions: Of the various options periprostatic anesthetic infiltration has been shown to be safe, easy to perform and highly effective. It should be considered the gold standard at the moment, even if the optimal technique remains to be established. Further studies addressing this issue are warranted.

Editorial Comment

The authors performed a systematic MEDLINE search of clinical trials of any kind of anesthesia, analgesia or sedation during TRUS guided prostate biopsy published since 2000. They retrieved and critically analyzed more than 40 articles dealing with different methods of decreasing pain during this procedure. As we know there is no rule to adequately predict if a patient will or will not feel too much pain or discomfort during TRUS biopsy. However, as mentioned by the authors, some risk factors associated with painful biopsy are younger age, anxiety, number of cores taken and repeat biopsy (due to the inclusion of the transition zone). This report nicely discusses the several methods and different approaches for local anesthesia during TRUS biopsy. The discussion includes the different amounts and different periprostatic sites for injection of lidocaine, the importance of using or not using intrarectal anesthetic gel instillation and its association or not with nonsteroidal anti-inflammatory. They also discuss about the possibility of using general anesthesia, entonox (50% nitrous oxide and oxygen) induced analgesia or anesthesia with intravenous injection of propofol. All the pros and cons of each procedure are well presented and discussed.

At our institution we have been using some type of local analgesia/anesthesia since 2000. We start with oral administration of 500 mg of paracetamol (acetaminophen; nonopiate, nonsalicylate analgesic), 30 minutes before the procedure (for better analgesia). Intrarectal injection of 10 ml of 2% lidocaine gel is done 10 minutes before the biopsy (to decrease pain during probe insertion), with the patient already in the left lateral decubitus. Then, periprostatic nerve block is obtained (to decrease pain during biopsy), by infiltrating, on sagittal plane, 2.5 ml of 2% lidocaine into the left and the right nerve plexus located at the junction of the seminal vesicle and prostate. After that, and on axial plane, 2.5 ml of 2% lidocaine is injected in each side of prostate apex. We have found that with this protocol, TRUS biopsy is well tolerated by the patients even when they are submitted to an extended or saturation biopsy scheme (16 - 22 cores) or rebiopsy. Only sporadically we use intravenous injection of propofol, and when it used the anesthesiologist always performs the procedure.

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UROGENITAL TRAUMA

The literature increasingly supports expectant (conservative) management of renal trauma -- a systematic review

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J Trauma. 2005; 59: 493-503

Background: The perfect degree of operative intervention in renal trauma is unknown. However, expectant management for most blunt renal trauma is the standard of care, and nonoperative management is increasingly accepted for stab wounds. The best treatment of gunshot wounds and vascular injuries is still unclear; however, recent data indicates that a trial of nonoperative therapy may be warranted in those not exsanguinating from the kidney. Conservative management has many benefits, the greatest of which is decreasing the rate of iatrogenic nephrectomy. We have reviewed the world's literature to determine the level of support for expectant management of renal injury.

Methods: The English language literature concerning renal trauma was identified with the assistance of Medline, and additional cited works not picked up in the initial search were obtained. One hundred and ten citations were ultimately reviewed dating back to 1947.

Results: Most modern citations support at least a trial of expectant management for renal trauma patients not exsanguinating from the kidney, and without ureteral or renal pelvis injuries. The treatment of renovascular injuries has less consensus, but it appears that 'conservative' management by the application of nephrectomy is often the best approach, although renovascular repair may be attempted in rare cases.

Conclusion: Dozens of papers going back as far as 50 years seem to support the wider use of nonoperative therapy of renal injuries, although for unclear reasons, this approach is not yet universally accepted.

Editorial Comment

The take home message is that contemporary blunt renal trauma management is nearly always conservative (expectant). Absolute criteria for renal trauma exploration are life threatening renovascular injuries. A pulsatile, expanding or uncontained retroperitoneal hematoma suggests a major vascular injury and thus demands exploration. Also, the location of the hematoma, zone 1 (medial, over the great vessels) usually demands exploration. All other renal injuries are relative indications for exploration, which include segmental renal infraction, urinary extravasations, or concomitant pancreatic or colonic injuries. For blunt renal AAST Grade IV injuries (parenchymal laceration with urinary extravasation), only 20% plus that are managed expectantly will require ureteral stent placement, percutaneous urinoma drain placement or selective embolization. UPJ avulsion injuries typically require surgical repair. Penetrating injuries theoretically should be able to be managed stage for stage, the same as blunt renal injuries. The difference with penetrating injuries, particularly, gunshot wounds, are that due to blast injury there is delayed parenchymal and vascular injury - which can later upstage the injury and thus increase delayed renal bleeding and urinary leak. Delayed bleeds and leaks can still mostly be managed endoscopically or percutaneously. The last take home message, is that in inexperienced or non-urologist hands, renal exploration typically ends with a high nephrectomy rate. Thus, when it comes to renal injuries, expectant management is usually best, unless there is a major renovascular injury (1,2).

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Predictors of death in patients with life-threatening pelvic hemorrhage after successful transcatheter arterial embolization

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J Trauma. 2003; 55: 696-703

Objective: The purpose of this study was to determine predictors of death in patients with pelvic fracture whose pelvic arterial hemorrhage is controlled successfully by transcatheter arterial embolization (TAE).

Methods: From January 1996 to December 2000, 61 patients with a pelvic fracture who had pelvic arterial hemorrhage were treated at our Level I trauma center according to a protocol that assigns a high priority to diagnostic and therapeutic angiography within the algorithm. Angiography is performed before laparotomy in patients with hemoperitoneum, who can be stabilized by fluid resuscitation, and otherwise afterward. External fixation was performed immediately after TAE in the angiography suite. Predictors of outcome were determined retrospectively by univariate and multivariate analysis using anatomic and physiologic parameters.

Results: Forty-eight patients survived and 13 died. TAE successfully controlled pelvic arterial hemorrhage in all patients. Predictors of death included posterior pelvic arterial injury and an elevated Acute Physiology and Chronic Health Evaluation II score (odds ratio, 15.6 and 23.9, respectively). Need for fluid requirements to achieve hemodynamic stability were higher in nonsurvivors than in survivors. Outcome did not correlate with the type of fracture or the Injury Severity Score.

Conclusion: Application of angiography as a therapeutic intervention in patients with pelvic arterial bleeding may reduce the need for surgery, thereby avoiding or minimizing this additional trauma.

Editorial Comment

This article from Tokyo, nicely illustrates the controversy over the timing and optimal order of external fixation (ex-fix) and transarterial embolization (TAE). One camp utilizes external fixation as first-line treatment and reserves TAE for ongoing instability after pelvic stabilization. Others aggressively advocate TAE early in the treatment and place an ex-fix after TAE. Bleeding sources from pelvic fracture are cancellous bone at fracture sites, pelvic venous plexuses and pelvic arteries. The methods to control venous bleeding are pelvic ring stabilization, re-approximation of bleeding bone edges, and closure of the pelvic ring to reduce the true pelvic volume. To control pelvic arterial bleeding usually needs TAE of injured pelvic arteries. Making the distinction of predominant arterial versus venous bleeding is often difficult in the multi-injured trauma patient. In our experience, patients with hypotension and pelvic fracture that respond poorly or transiently to resuscitation typically have arterial bleeding, while good responses to resuscitation typically excludes arterial pelvic bleeding. The other main point illustrated is the concept of "damage control". Clearly, patients who have the fatal triad of cold, coagulopathy, and acidosis have a high mortality. Rapid resuscitation, control of bleeding, and deferring definitive repair to a later date, are the keys to the injured patient's survival (1).

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PATHOLOGY

Urothelial neoplasms in patients 20 years or younger: a clinicopathological analysis using the World Health Organization 2004 bladder consensus classification

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J Urol. 2005; 174: 1976-80

Purpose: Urothelial neoplasms in patients younger than 20 years are rare, with conflicting data regarding clinical outcomes.

Materials and Methods: We identified 23 patients 4 to 20 years old with urothelial neoplasms, reclassified the microscopic diagnoses using the 2004 WHO/International Society of Urologic Pathology grading classification and collected data on presentation, risk factors and outcomes.

Results: Pathological grading revealed 2 urothelial papillomas, 10 papillary urothelial neoplasms of low malignant potential (PUNLMPs), and 8 low grade and 3 high grade papillary urothelial cancers, all without invasion. Mean patient age was 13.2 years (range 4 to 20), 19 patients were male and 19 presented with gross hematuria. All lesions were solitary and measured 0.1 to 6 cm. One patient had a history of smoking and 1 had parents who smoked. Three patients (13%) had recurrences classified as either urothelial papilloma (1) or PUNLMP (2). All patients were alive with no evidence of disease after a mean followup of 4.5 years (range 6 months to 13 years).

Conclusions: Urothelial neoplasms in individuals younger than 20 years more commonly occur in males and are predominantly low grade with a favorable clinical outcome. Before the current classification system the 10 patients with a diagnosis of PUNLMP would have been classified as having papillary carcinoma. Thus, the diagnostic category of PUNLMP allowed 43.5% of patients in this series to avoid being labeled with “cancer” at a young age.

Editorial Comment

In 1998, the International Society of Urologic Pathology (ISUP) proposed a new classification for urothelial neoplasms (1). The new classification included the so-called superficial papillary urothelial neoplasms of low malignant potential (PUNLMP). These tumors correspond to papillary urothelial carcinomas, grade 1, pTa in the traditional classification. One of the reasons for this new nomenclature is shown in the present article. Ten patients younger than 20 years had the diagnosis of PUNLMP. Two of these patients had recurrence but all were alive with no evidence of disease after a mean follow-up of 4.5 years (range 6 months to 13 years). Thus, the diagnostic category of PUNLMP allowed 43.5% of patients in the series to avoid being labeled with “cancer” at a young age. This is also valid for patients older than 20 years of age due to the low recurrence rate of these tumors.

Considering that many urologists are unaware (or do not agree with this new classification), I have recommended to the pathologists to use both nomenclatures. PUNLMP is a papillary urothelial lesion with an orderly arrangement of cells within papillae with minimal architectural abnormalities and minimal nuclear atypia irrespective of cell thickness. In general, the major distinction from papilloma (a rare lesion), is that in papillary urothelial neoplasm of low malignant potential the urothelium is much thicker and/or nuclei are significantly enlarged. The urothelial papilloma, in contrast, has no architectural or cytologic atypia.

Because urologists should not minimize the significance of this diagnosis, pathologists are encouraged to include the following note in cases diagnosed as papillary urothelial neoplasm of low malignant potential (PUNLMP): “Patients with these tumors are at risk of developing new bladder tumors (“recurrence”), usually

of a similar histology. However, occasionally, these subsequent lesions manifest as urothelial carcinoma, such that follow-up of the patients is warranted.”

As for the flat lesions, the ISUP recommends a new nomenclature: intraurothelial neoplasia instead of the term dysplasia/flat carcinoma in situ of the traditional classification. Grade 2 dysplasia corresponds to low-grade intraurothelial neoplasia and grade 3/flat carcinoma in situ (pTis) to high-grade intraurothelial neoplasia. ISUP recommends not to include in the pathology report dysplasia grade 1.

For grading of urothelial papillary carcinomas, ISUP recommends call low-grade to carcinomas grade 1, and high-grade to carcinomas grade 2 or 3.

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Patient and urologist driven second opinion of prostate needle biopsies

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Purpose: We reviewed second opinion prostate needle biopsies that were patient and urologist driven to determine how often an expert opinion resulted in a different diagnosis.

Materials and Methods: Of 3,155 prostate needle biopsy consultations received during a 6-month interval 684 were sent at the request of the patient or urologist. A significant change in outside diagnosis was one that could potentially result in a change in therapy or prognosis.

Results: The second opinion was requested by patients (21.6%), urologist (63.9%) and patients plus urologists (14.5%). The distribution of the 684 outside diagnoses was benign in 6.1%, HGPIN in 7.6%, atypical (ATYP) in 29.8% and cancer in 56.5%. In 241 cases (35.2%), a change in diagnosis was rendered upon expert review. We agreed with the majority of outside cancer, benign and HGPIN diagnoses, in contrast to only 36.8% of outside ATYP cases ($p < 0.0001$). Uncommonly did a cancer diagnosis become a benign one or vice versa. Of changes affecting outside cancer diagnoses 73.5% were due to changes in Gleason score. The diagnosis was more likely to be changed when the consultation was requested by the urologist rather than by the patient (41.4% vs 25%, $p < 0.0001$).

Conclusions: Cases diagnosed as ATYP have the highest likelihood of being changed upon expert review. Urologists should consider sending such cases for consultation to attempt to resolve the diagnosis as definitively benign or malignant before subjecting the patient to repeat biopsy.

Editorial Comment

It is a common practice in the United States a second opinion related to pathology reports. In Brazil, is not a common practice but definitely increasing in relation to prostatic needle biopsies. It is worth noting that

the diagnosis was more likely to be changed when consultation was requested by the urologist rather than by the patient (41.4% vs 25%, $p < 0.0001$). Many patients, due to lack of symptoms or for other reasons, ask a second opinion because do not accept or doubt the diagnosis but uncommonly a cancer diagnosis become a benign one after a review.

A special issue is related to Gleason score. Urologists should be careful with low Gleason scores. A Gleason score of $2 + 2 = 4$ in a needle biopsy, frequently corresponds to a Gleason score of $4 + 4 = 8$. The reason is that well circumscribed tumors not always correspond to low-grade carcinoma. The pathologist must be aware if there is either invasion of the stroma or fused glands in the middle of the lesion.

In a consensus conference on Gleason grading of prostatic carcinoma, the International Society of Urological Pathology (ISUP) recommended that the diagnosis of Gleason score 4 on needle biopsy should be made “rarely, if ever” (1). The consensus conference cautioned that, although the potential exists for rendering a diagnosis of Gleason score 4 on needle biopsy, it is a diagnosis that general pathologists should almost never make without consultation. Even when that exceedingly rare Gleason score 4 cancer is diagnosed on needle biopsy by an expert, a note should be added that almost always a higher grade cancer would be seen in the corresponding prostate (if examined at radical prostatectomy).

There was only a 36.8% of agreement when the consultation referred to atypical lesions. This lesion is also known as ASAP (atypical small acinar proliferation). It is important for the urologist to know that ASAP is not a diagnostic entity and is not synonymous with high-grade prostatic intraepithelial neoplasia (HGPIN). It represents descriptive diagnostic terminology in which there is architectural and/or cytologic atypia that does not reach an individual pathologist’s threshold required for the diagnosis of cancer. In a consensus conference sponsored by the World Health Organization, the committee members recommended designating atypical biopsies as either “suspicious” or “highly suspicious for cancer” (2). The reasons for this, include the equation by some urologists of the term ASAP with HGPIN and because all of the atypical foci are not always “small” acinar but may include glands with larger diameter (such as pseudohyperplastic pattern of cancer or adenocarcinoma with ductal features).

The conclusion of the paper surveyed is that atypical lesions (“suspicious for cancer”) have the highest likelihood of being changed upon expert review and that urologists should consider sending such cases for consultation to attempt to resolve the diagnosis as definitively benign or malignant before subjecting the patient to repeat biopsy.

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INVESTIGATIVE UROLOGY

Liposomal recombinant human superoxide dismutase for the treatment of Peyronie's disease: a randomized placebo-controlled double-blind prospective clinical study

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Eur Urol. 2005; 48: 656-6

Objective: To demonstrate the efficacy and safety of a topical gel containing liposomally encapsulated recombinant human Superoxide Dismutase (LrhSOD) in the treatment of painful Peyronie's Disease. The theoretical background is that LrhSOD, by scavenging of free oxygen radicals, might interrupt inflammatory cascades and thereby limit further disease progression.

Methods: In a placebo-controlled randomized clinical trial, 39 patients with Peyronie's Disease and significant pain symptoms were treated with LrhSOD or placebo for a 4 week period. At this time, statistical evaluation of pain resolution was performed as primary study endpoint. Patients then were continued in a cross-over study design to ensure a total of 8 weeks of LrhSOD therapy for all study participants. Pain, plaque and curvature assessment was performed at study entry and every 4 weeks until week 12.

Results: LrhSOD treatment resulted in a statistically significant reduction of pain ($p=0.017$) compared to placebo already after 4 weeks. At week 12 pain was significantly reduced in 89% of patients who all had received 8 weeks of LrhSOD therapy at that time. Response to other disease parameters was assessed at week 12: plaque size was reduced in 47% of patients, as was plaque consistence in 38%. Penile curvature was improved at 5-30 degrees in 23% of patients. The expected spontaneous disease progression rate of up to 40%, as reported by several investigators, was significantly reduced to <10% under LrhSOD therapy, and patients satisfaction was high, also consequent to the lack of therapy-related side effects observed in the present study.

Conclusion: LrhSOD is an easily administrable, safe and effective local therapeutic for the painful phase of Peyronie's Disease.

Editorial Comment

Around 4 years ago, the authors in an uncontrolled phase-2 study, treated 20 Peyronie's disease patients with a gel containing LrhSOD (1.5 mg/g). The study included patients with penile deviation greater than 45 degrees or plaque calcifications of greater than 5 mm. The authors found 100% pain relief and plaque size reduction in 56% of patients after a maximum of 6 weeks of LrhSOD therapy.

In the present placebo controlled study, the authors confirmed a statistical significant reduction of pain symptoms when compared to placebo, resulting in an overall efficacy of more than 80% after 8 weeks of therapy.

As the authors state, conservative therapies for Peyronie's disease are symptom-directed (analgesic and preventive against disease progression), while correction of deviation is surgical. The liposomally encapsulated recombinant human SOD is a good alternative because shows good efficacy when administered in patients with painful Peyronie's disease lesions. Also, the expected rate of spontaneous disease progression would be reduced, as well as morbidity and the need for future surgery. Probably, the association of clinical and minimally invasive therapy (such as ESWL) would be the future first line treatment for Peyronie's disease.

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The precise location and nature of the nerves to the male human urethra: histological and immunohistochemical studies with three-dimensional reconstruction

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Eur Urol. 2005; 48: 858-64

Objectives: The precise location, origin and nature of nerve fibers innervating the male urethral sphincter have not been clearly established. Classical anatomical studies based on cadaver dissections have provided conflicting results concerning the location of somatic and autonomic nerve fibers. This study was designed to identify nerve fibers innervating the male urethral sphincter and to provide a three-dimensional representation of their tissue relations in the human male fetus.

Materials and Methods: Histology and immunohistochemistry (Hematein-Eosin-Safran, Luxol Fast Blue, Protein S 100 immunolabeling and smooth fibers actin immunolabeling) were performed in male external urethral sphincter of ten male fetuses (114-342 mm crown-rump length). Three-dimensional reconstruction of the urethral structure and innervation were obtained from serial sections using Surf Driver 3.5.3 software.

Results: The three-dimensional reconstruction of the same section levels with different strains allowed to identify the precise structure of the muscular layers and the nature of nervous elements (myelinated and unmyelinated), their distributions and their relations with the urethral wall, the prostate and the seminal vesicles.

Conclusion: Histological and immunohistochemical three-dimensional reconstruction of the nervous elements of the urethral sphincter gives a very didactical understanding of the three dimensional arrangement of the urethral nerves and their relationships with the urethral layers. It allows a better understanding of the origin, the course and the nature of the nervous elements participating in the urinary continence.

Editorial Comment

This is one more interesting applied anatomical study from Saint Peres, Paris, under the leadership of Vincent Delmas. The authors analyzed the innervation of the male urethral sphincter in 10 male fetuses of different CR lengths. After elegant and precise 3D reconstruction, the authors give an understanding of the origin and course of the nerves. They also confirmed the previous findings of Yucel and Baskin (1), that the majority of unmyelinated nerve fibers penetrates the male urethral smooth muscle layers at 5 o'clock and at 7 o'clock, where the majority of myelinated nerve fibers penetrates the striated muscles of the prostatic capsule and of the urethral sphincter at 9 o'clock and at 3 o'clock. This very intimate relations of somatic and autonomic nerve fibers place them at risk during any pelvic cancer surgery or urethral trauma. I strongly recommend all surgeons involved in pelvic surgery to read carefully this anatomical article.

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RECONSTRUCTIVE UROLOGY

Donor-site morbidity in buccal mucosa urethroplasty: lower lip or inner cheek?

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BJU Int. 2005; 96: 619-23

Objective: To evaluate donor-site complications of buccal mucosa urethroplasty and whether there is a difference in morbidity between harvesting the mucosa graft from the inner cheek or the lower lip.

Patients and Methods: Twenty-four consecutive patients with recurrent urethral strictures were treated with buccal mucosa urethroplasty in our department between September 2002 and April 2004. In 12 patients the graft was harvested from the lower lip or cheek and lower lip (group 1), and in 12 patients from the cheek (group 2). The mean (range) age of patients was 51 (26-66) years in group 1 and 53 (32-75) years in group 2. The mean (range) graft length was 6.2 (2-16) cm in group 1 and 5.7 (2-13) cm in group 2. All patients were followed up using a mailed questionnaire that asked about pain, numbness, difficulties in mouth opening or ingestion, and satisfaction, monthly for the first 3 months and then every 6 months. The mean (range) follow-up was 12.5 (6-23) months.

Results: There were no bleeding complications or disturbances in wound healing. All of the patients reported numbness in the area of the mental and buccal nerves, and graft-site tenderness after surgery. In group 1, the pain lasted for a mean (range) of 5.9 (0.5-22) months, compared to 1 (0.1-7) months in group 2 ($P = 0.022$). Perioral numbness lasted for a mean (range) of 10.3 (0.5-23) months in group 1 and 0.85 (0.1-3) months ($P = 0.0027$) in group 2. There were no statistically significant differences in problems with mouth opening or food intake between the two groups, but the patients in group 1 seemed to be less satisfied (6/12 patients satisfied) than those in group 2 (11/12 patients satisfied).

Conclusions: Buccal mucosa graft harvesting from the lower lip and the inner cheek are both feasible, but harvesting from the lower lip resulted in a significantly greater long-term morbidity, which resulted in a lower proportion of satisfied patients. This seems to be due to a long-lasting neuropathy of the mental nerve. We therefore have changed our technique entirely from lower lip to inner cheek graft harvesting, whenever possible.

Editorial Comment

During the last 25 years, the buccal mucosa graft became the first choice in the field of urethral reconstructive surgery after being unused or even forgotten for over half a century prior. The buccal mucosa is probably the endothel closest to the urothelium and has been demonstrated to be the best graft for urethral reconstruction with the lowest tendency of tissue contraction.

The presented paper investigated the morbidity on the donor side of the buccal mucosa. Two harvesting locations were compared: the inner lip vs. the inner cheek with a follow-up of up to 23 months (mean 12.5). Kamp et al. demonstrated that pain and numbness are important factors for the donor location, whereas, infection has no influence because of the disinfectant qualities of the saliva enzymes.

In the donor location, the lower lip pain lasts 5 times longer vs. harvests from the inner cheek; the numbness lasts 10 months vs. one month for the inner cheek. In our experience, we close the wound of the inner cheek, whereas the lower lip is left open to prevent cosmetic poor results. The harvest tissue is dissected in a hexagon pattern to make a cosmetic closure of the wound possible. In addition the hexagon shaped tissue fits immediately into the recipient location without any further trimming. For the wound closure of the inner cheek, the edges are brought together to decrease possible numbness to the smallest area possible. By using inverted

interrupted sutures, the patient does not feel the wound 2 weeks after surgery. The closing of the wound of the inner cheek might even pronounce the difference of lasting numbness compared to the open procedure of the lower lip.

The harvested buccal mucosa of the inner cheek is a durable transplant for the reconstructive area. With the data presented, it is noted that the location of the inner cheek should be favored because of its significantly lower morbidity for pain and numbness. The lower lip is still available but should only be used in those cases with a long stricture. Finally, it is preferred to treat urethral stricture sufficiently early when the stricture itself is still shorter in order to have the best surgical outcome in the harvest location and the reconstructed urethra.

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Bulbar urethroplasty using buccal mucosa grafts placed on the ventral, dorsal or lateral surface of the urethra: are results affected by the surgical technique?

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J Urol. 2005; 174: 955-7; discussion 957-8

Purpose: The use of buccal mucosa graft onlay urethroplasty represents the most widespread method of bulbar urethral stricture repair. The graft may be placed on the ventral or dorsal urethral surface according to surgeon experience and preference. We investigated whether the results are affected by the surgical technique by comparing the outcome of 3 types of bulbar urethroplasty using buccal mucosa graft.

Material and Methods: We repaired 50 bulbar urethral strictures with buccal mucosa grafts from 1997 to 2002. Mean patient age was 42 years. The etiology of stricture was ischemia in 12 cases, trauma in 6, instrumentation in 4 and unknown in 28. Patients with lichen sclerosus, failed hypospadias or urethroplasty and stricture extending into the penile urethra were not included. A total of 47 patients (94%) had undergone previous urethrotomy or dilation. The buccal mucosa graft was always harvested from the cheek using a 2 team approach. Mean graft length was 4.2 cm. The graft was placed on the ventral, dorsal and lateral bulbar urethral surface in 17, 27 and 6 cases, respectively. Clinical outcome was considered a success or failure at the time that any postoperative procedure was needed, including dilation. Mean followup was 42 months (range 12 to 76).

Results: Of 50 cases 42 (84%) were successful and 8 (16%) failed. The 17 ventral grafts provided success in 14 cases (83%) and failure in 3 (17%). The 27 dorsal grafts provided success in 23 cases (85%) and failure in 4 (15%). The 6 lateral grafts provided success in 5 cases (83%) and failure in 1 (17%). No surgical complications were observed. Failures involved the anastomotic site (distal in 2 and proximal in 3) and the whole grafted area in 3 cases. They were treated with urethrotomy in 5 cases and 2-stage urethroplasty in 3.

Conclusions: In our experience the placement of buccal mucosa grafts into the ventral, dorsal or lateral surface of the bulbar urethra showed the same success rates (83% to 85%) and the outcome was not affected by the surgical technique. Moreover, stricture recurrence was uniformly distributed in all patients.

Editorial Comment

The outcome of using a buccal mucosa onlay graft improved during recent years to over 85% in the long-term follow-up. Strictures in the area of the anastomoses still occur. It might be possible to reduce those

strictures with the increased knowledge of pathology in the areas of anastomoses, which are not functional or even macroscopically visual at the time of the surgery.

With increased knowledge of urethral anatomy, the best approach to urethral strictures makes it possible to perform reconstruction with the best outcome. It not only allows reconstruction of the lumen of the urethra, it keeps the urethra functional. Its importance of function was not understood for a long time.

The presented data of urethral repair with a buccal mucosa onlay flap were performed in three different locations of the stricture: ventral, dorsal and lateral. The documented success rate of Barbagli et al. describes a trend for the 3 approaches but cannot be used to attribute preference to one approach or another. Despite the fact that most sacculations occurred in patients with a ventral graft, which is the most performed method, that indeed requires further explanation.

There is an attempt to explain the urethral sacculation or post voiding dribbling with the results of the Yucel & Baskin investigations (1). The approach with innervation of the bulbospongiosus muscles might lead to the correct direction; however, other factors probably influence the sacculation as well. The buccal mucosa graft is one of the best tissues for the urethral reconstruction, but it has never been investigated as to how the urine flows through the “tube” with its physiological curbs to bring pressure towards the graft. This patch becomes a part of the “tube”-wall and the pressure that appears might weaken the graft; whereas, in a different location, it might not be influenced as strongly. This might be an explanation of the late occurrence of sacculation in the follow-up after 2 years.

Other factors, including the 2 discussed, might influence the functional outcome. The understanding of the physiology and the physics are important in addition to prospective studies in order to perform urethral reconstruction with the highest success rate and the best functional outcome in the long term.

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Bladder growth and development after complete primary repair of bladder exstrophy in the newborn with comparison to staged approach

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Purpose: We assessed bladder growth and dynamics following complete primary repair of bladder exstrophy (CPRE) compared to the staged approach.

Materials and Methods: We reviewed the records of 16 boys and 7 girls who underwent CPRE within 3 days of life from 1996 to 2004 and compared them to the records of 8 boys and 6 girls treated with a staged repair from 1979 to 1996. Screening methods included voiding cystourethrogram, radionuclide cystogram and urodynamic study. We estimated growth curves for bladder capacity following repair in each group, and compared

percent predicted bladder capacity (PPBC), compliance and detrusor overactivity between the CPRE and staged repair groups following bladder neck reconstruction.

Results: Bladder capacity in the staged repair group was 69.8 ml (95% CI 46.7-104.4) immediately after bladder neck reconstruction and increased by 15.0% per year thereafter (95% CI 6.2-24.5, $p = 0.002$). In the CPRE group bladder capacity was 29.0 ml (95% CI 21.3-39.5) initially and increased by 28.9% per year thereafter (95% CI 17.4-41.5, $p < 0.001$). PPBC started at 45.6% (95% CI 35.7-55.5) and increased 1.2% per year (95% CI -1.1-3.5, $p = 0.29$) following repair for all genders and surgery groups. Compliance was 124.4% (95% CI 22.6-310.7, $p = 0.01$) greater in the CPRE group at all times following repair. Detrusor overactivity was present in 0 of 19 patients in the CPRE group and 6 of 13 (46%) in the staged group (exact $p = 0.002$).

Conclusions: Within the CPRE group bladder stability was universal, and sphincter electromyography was normal suggesting no neuromuscular compromise of the pelvic floor. At early followup, our results suggest that PPBC is equivalent irrespective of gender or management. Further objective evaluation is needed in both groups.

Magnetic resonance imaging of pelvic musculoskeletal and genitourinary anatomy in patients before and after complete primary repair of bladder exstrophy

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J Urol. 2005; 174 (4 Pt 2): 1559-66; discussion 1566

Purpose: We characterize pelvic soft tissue and bony anatomy of patients before and after complete primary repair of exstrophy (CPRE).

Materials and Methods: We evaluated 15 measurements on pelvic magnetic resonance imaging (MRI) in patients who underwent CPRE without osteotomy at our institution from 1996 to 2004. MRI protocols included axial, sagittal and coronal fast spin echo proton density sequences. Measurements were compared before and after CPRE using a paired t test, and between patients after CPRE, and age and gender matched controls using linear regression adjusting for the matched case-control groups. Patients older than 3 years with continent intervals longer than 3 hours after CPRE were compared to age and gender matched controls using linear regression.

Results: A total of 29 MRIs in 18 patients with exstrophy were available for analysis. Median patient age at postoperative MRI was 25 months (range 4 to 36). The configuration of the post-CPRE pelvis was significantly different from that of controls in all parameters measured including wider symphyseal diastasis (34.5 mm vs less than 1 mm) and more obtuse iliac wing (121 degrees vs 98 degrees), puborectalis (94 degrees vs 49 degrees) and ileococcygeus angles (111 degrees vs 98 degrees). The anatomy of continent patients after CPRE was not significantly different from that of controls in most parameters measured.

Conclusions: Comparison of the pelvic anatomy in patients before and after CPRE suggests that after CPRE patients have parameters that more closely approximate, but are still significantly different, from those of control patients. Patients with greater than 3-hour continent intervals after CPRE have anatomic parameters most similar to those of age matched controls.

Editorial Comment

The authors compared their data regarding lower urinary tract function as well as renal function in 16 boys and 7 girls treated with a complete primary repair of bladder exstrophy. Early primary repair is defined as

repair within the first 3 days of life; these patients were compared to a group of 8 boys and 6 girls treated with a staged repair in bladder exstrophy. Furthermore the same authors studied MRI findings in 18 of these patients at various intervals after complete primary repair (and in some patients also prior to surgery).

Bladder capacity, compliance and detrusor overactivity were surrogates for detrusor function in both primary and staged repair groups. The “percent predicted bladder capacity” per individual patient was not different between neither surgical groups nor gender. The conclusion was therefore that bladder capacity is more dependent on intrinsic factors than surgical technique. 72% of female and 86% of male patients did require a bladder neck reconstruction in the long-term follow up after complete primary repair in order to achieve continence. It is therefore speculated that the better results after early primary repair regarding overactivity (none of the patients in the primary repair group did show detrusor overactivity versus 46% in the staged group) may be the result of a decreased bladder outlet resistance.

The results concerning compliance were also better in the primary repair group, which can be partially explained by decreased outlet resistance. It is a fact that in both groups male patients showed a decline in compliance, which supports the speculation about the role of resistance and bladder function in the long term.

Apart from bladder function, complete voiding and continence are additional important long-term outcome parameters and it is only partially resolved. Among the anatomical landmarks seen upon endoscopy in adolescence and adults, location of the verumontanum and length and width of the urethral sphincteric segment are important. Even for the most experienced surgeons it is extremely difficult to adequately reconstruct the sphincteric structures within the first few days of life. Good functionality of the earliest possible reconstruction is here hampered by what the surgeon can do with only partially developed and in times invisible structures.

In an attempt to predict continence in patients with complete primary repair with the same group studied an array of measurements in pelvic MRI using various bone and soft tissue landmarks and angles. It is not surprising that the measurements performed were significantly different from age for most parameters. However, the closer the landmarks and angles of the treated exstrophy patients were compared to normal age- and gender matched controls, the better were the results with regards to continence and bladder capacity. Whether all these measurements can be reduced for practicality e.g. symphyseal diastases and the puborectalis sling angle will have to be proven in larger studies with more patients.

These 2 papers nicely demonstrate that early reconstruction seems to improve the physiological function of the exstrophy bladder smooth muscle cell. However, some of the sphincteric structures are not sufficiently developed to allow a satisfactory reconstruction in most patients. Furthermore we need to include the reconstruction of the entire bony and muscular pelvis to achieve success with storage, emptying and continence. The liberal and sophisticated use of new imaging techniques can be helpful as in many other parts of reconstructive surgery.

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UROLOGICAL ONCOLOGY

Low serum testosterone levels are associated with positive surgical margins in radical retropubic prostatectomy: hypogonadism represents bad prognosis in prostate cancer

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J Urol. 2005; 174: 2178-80

Purpose: It has been reported that more aggressive prostate cancer (PC) can be associated with low serum testosterone levels. The relationship between serum androgens and PC is still not completely understood. In this study we examined the association of prognostic factors in men who underwent radical retropubic (RRP) prostatectomy with low or normal total testosterone.

Materials and Methods: We retrospectively evaluated 64 consecutive patients with localized PC treated with RRP between July 2002 and November 2003. PC was diagnosed by transrectal ultrasonography guided biopsy performed for either a suspicious digital rectal examination or serum prostate specific antigen greater than 4.0 ng/mL. Gleason score was determined in prostatic biopsies. Pathological TNM staging (1997), capsular perforation, seminal vesicle involvement and surgical margin status were determined in all surgical specimens. The threshold for serum total testosterone was 270 ng/dL. In all analyses $p < 0.05$ was considered statistically significant.

Results: There were no statistically significant differences among prostate specific antigen, Gleason score (biopsy or specimen), pathological stage, capsular perforation and seminal vesicle involvement. However, patients with low total testosterone had increased positive surgical margins ($p = 0.026$).

Conclusions: Patients with low total testosterone more frequently present with positive surgical margins in RRP specimens. The true association between low testosterone and poor clinical outcome in the long term needs validation in large prospective studies.

Editorial Comment

Prostate cancer is hormone dependent. Suppression of androgen levels inhibits cancer growth, at least for a while. Does this statement justify the inverse assumption that high androgen levels support growth of prostate cancer in males? The authors from Brazil address this important topic in correlating the histological parameters of prostatectomy specimen with androgen levels in the respective patients. No correlation was found except that patients with low testosterone had more positive margins. Interestingly, testosterone levels were significantly increased after the operation.

Thus, upon first view, testosterone seems to be inversely correlated to cancer growth in males. Other researches on the cellular testosterone receptor also support this notion.

Certainly, more data from much larger patient cohorts are needed to clarify this important issue.

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Treatment delay and prognosis in invasive bladder cancer

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J Urol. 2005; 174: 1777-81; discussion 1781

Purpose: We studied treatment delay, and the impact on disease specific survival and stage progression in a series of patients who had undergone cystectomy.

Materials and Methods: All 141 patients underwent radical cystectomy between 1990 and 1997 due to locally advanced bladder cancer. Treatment delay was defined as time from pathological confirmation of invasive disease to performance of cystectomy, and was registered retrospectively from the patient charts. Two patients received neoadjuvant chemotherapy and were excluded from further analyses. Followup continued until April 2003 with death due to bladder cancer as the end point. Causes of death were retrieved from the Swedish Cause of Death Registry.

Results: The median treatment delay was 49 days, but was significantly longer for the 71 cases who were referred from other hospitals (63 vs 41 days, $p < 0.001$). Treatment delay did not influence cumulative incidence of death from bladder cancer. Considering all cases, there was no significant correlation between treatment delay and stage progression. For clinical stage T2 tumors, median treatment delay was 76 days among patients with stage progression compared to 41 and 48 days for those with stage regression and stage equivalence, respectively ($p = 0.20$).

Conclusions: Treatment delay was not found to influence disease specific survival in the present study. Furthermore, treatment delay was not significantly longer in cases that progressed compared to those with equal or lower pathological stage in the cystectomy specimen.

Editorial Comment

Does delay of radical cystectomy confer an increased risk of progressive bladder cancer? Several authors have addressed this issue with contradictory results. These authors from Sweden did not find an influence if radical treatment was given before or after 60 days post diagnosis. Median time to surgery (treatment delay) was only 48 days among those alive at the end of follow-up and 4 days longer (52 days) among those who died of bladder cancer.

Why did the authors chose 60 days threshold? It seems that in a relatively well-organised health care system as in Sweden a relevant delay (> 90 days or 3 months) is a rare event. It is noteworthy to read the editorial comment from M. Cookson who states that the window for curability is not open for all time and may begin to close from 90 days.

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FEMALE UROLOGY

The effect of fluid intake on urinary symptoms in women

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J Urol. 2005; 174: 187-9

Purpose: We determined the effect of caffeine restriction and fluid manipulation in the treatment of patients with urodynamic stress incontinence and detrusor overactivity.

Materials and Methods: This was a 4-week randomized, prospective, observational crossover study in 110 women with urodynamic stress incontinence (USI) or idiopathic detrusor overactivity (IDO) to determine the effect of caffeine restriction, and of increasing and decreasing fluid intake on urinary symptoms. Data were recorded in a urinary diary for the entire study period on urgency episodes, frequency, pad weight increase, wetting episodes and quality of life.

Results: A total of 69 women with a mean age of 54.8 years completed the study, including 39 with USI and 30 with IDO. In the IDO group decreasing fluid intake significantly decreased voiding frequency, urgency and wetting episodes with improved quality of life. In the USI group there was a significant decrease in wetting episodes when fluid intake was decreased. Changing from caffeine containing to decaffeinated drinks produced no improvement in symptoms.

Conclusions: Conservative and life-style interventions are first line treatments in the management of incontinence and storage lower urinary tract symptoms. This study shows that a decrease in fluid intake improves some of these symptoms in patients with USI and IDO and, therefore, it should be considered when treating such patients.

Editorial Comment

The authors reviewed the effect of restricting caffeine and manipulating fluid intake in patients who had been diagnosed urodynamically with stress incontinence or detrusor overactivity. The study cohort was a 69 woman. The participants were analyzed after a 4-week randomized prospective observational crossover study where they underwent caffeine restriction and either increase or diminution of fluid intake. Data was recorded in the urinary diary. Findings included that changing from caffeine to non-caffeine drinks did not improve symptoms. They also found that in patients suffering from detrusor overactivity, decreased fluids significantly diminished the urgency and frequency syndrome and improved the quality of life, which was also mirrored in the stress urinary incontinent patients.

An excellently written article that provides sound scientific analysis for the common advice given to patients for the conservative management of urinary incontinence. It is noteworthy that by not taking in caffeine there was no true improvement in the patients' urinary symptoms while diminishing fluid intake did significantly help diminish incontinent episodes whether the patient had overactive bladder or stress urinary incontinence. This lack of effect by diminishing caffeine has been noted by other researchers (1). The authors make a very salient point that in by asking patients to stop caffeine a serendipitous secondary effect may be that overall fluid intake is diminished as well thus causing the perception that less caffeine improves overall bladder control. It would be of interest to find that if patients who suffered from urinary urgency and frequency with the diagnosis of interstitial cystitis would also not have an improvement in their voiding symptoms when stopping caffeine in view that caffeine may be a mild urothelial irritant as well as a mild diuretic. Nevertheless, the authors should be complimented on analyzing a very common first line treatment and illuminating the readership to the value of this counsel.

Reference

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The completely dry rate: a critical re-evaluation of the outcomes of slings

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Objective: To critically evaluate sling outcomes and revisit the realistic goals of anti-incontinence surgery.

Materials and Methods: A review of an Institutional Review Board-approved prospective database revealed the outcomes of four different sling techniques that are utilized at our institution.

Results: Four hundred ninety-eight patients had a mean follow-up varying from 9 to 24 months (range 6-50) after undergoing one of four different sling techniques utilized at our institution. The techniques had similar results with regard to completely dry rate, overall success rate, and rate of urgency regardless of the variation in follow-up time. Success was defined as completely dry or leakage = 1/week or = 70% improved by questionnaire in those patients who leaked 1/week. Success, by this definition, varied from 74.9% to 85.7%, but the completely dry rate varied from 36.1% to 45.2%. An additional 31.0% to 33.3% leaked = 1/week, and of the remaining patients, 24.5% to 44.4% considered themselves = 70% improved despite leakage > 1/week. Urge incontinence was reported by 24.4% to 33.3% of patients.

Conclusion: As surgeons, we must constantly reevaluate the outcomes and purposes of the procedures we perform on our patients.

Editorial Comment

The authors retrospectively reviewed the outcomes of 4 different sling techniques that they had performed in their practice. They were able to identify 498 patients with follow-up ranging from 6-15 months. Success in their patient population was well defined. The authors found a completely dry rate in the range of: 36.1 - 45.2%. Urge incontinence was reported at 24.4 - 33.3% of patients. Success in this patient population was noted to be 74.9 - 85.7%.

This is an important paper to read in view of the large patient population, which was retrospectively analyzed, and the forthrightness of the authors' report of their results. The authors noted that with this large population they were able to find that their completely dry rate was fewer than 50%. In addition, the urinary urge rate was also between almost one-fourth to one third of the patients studied. These < 90% completely dry rates combined with definite rates of urinary urge incontinence have been mirrored in the literature in the past by others (1). Despite the completely dry rate at < 50%, the success rate was still greater than three-fourths of patients treated. When reading this report the reader may well identify with the results noted by these surgeons as I did during my review.

Reference

1. Haab F, Trockman BA, Zimmern PE, Leach GE: Results of pubovaginal sling for the treatment of intrinsic sphincter deficiency determined by questionnaire analysis. *J Urol.* 1997; 158: 1738-41.

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PEDIATRIC UROLOGY

Does the less aggressive multimodal approach of treating bladder-prostate rhabdomyosarcoma preserve bladder function?

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Purpose: The treatment of bladder-prostate rhabdomyosarcoma has evolved into multimodal therapy, including chemotherapy, radiotherapy and organ sparing surgery with bladder preservation. We investigated bladder function in children who underwent multimodal therapy at our institution and retained the original bladder for at least 6 months after treatment ended.

Materials and Methods: We evaluated 8 children with bladder-prostate rhabdomyosarcoma treated at our institution between 1999 and 2003 according to inclusion criteria. All patients underwent history, physical examination and urodynamic study at least 6 months after completion of treatment (range 6 to 39 months).

Results: All patients were treated following the same chemotherapy and radiotherapy scheme. Three patients (37.5%) were asymptomatic and had normal urodynamic studies, and 1 had only dysuria (this patient later underwent continent urinary diversion with transverse colon). The 4 remaining patients had urological complaints, and the urodynamic findings were reduced bladder capacity in 4, overactivity plus sensory urgency in 2, sensory urgency only in 1 and suprapubic pain during filling in 1.

Conclusions: Among 8 patients 3 had normal urinary function and 4 had minor tolerable alterations. Cystectomy and urinary diversion were later necessary in only 1 patient due to disabling dysuria. The fact that the original functioning bladder was preserved in 7 of 8 patients suggests the feasibility of multimodal therapy. Long-term followup will still be necessary for definite conclusions, since we recognize that the deleterious effects, mainly of radiotherapy, may take longer to become evident.

Editorial Comment

The authors review their experience with an organ-sparing approach to treatment of pelvic rhabdomyosarcoma in your children. Eight patients were reported from those treated between 1999 and 2003. The results were very encouraging, with only one patient requiring cystectomy during follow-up for dysuria.

Although high cure rates are possible with aggressive therapy that includes surgical extirpation of the bladder, efforts in recent years have focused on obtaining the same cure rates while preserving the bladder. Data on whether this can be done successfully are somewhat limited. This report is an important follow-up that provides valuable data for the clinician facing a new patient with this problem.

Despite the positive message however, there are several caveats. First, two patients were excluded. One had an early recurrence (we do not know whether this patient survived) and another is reported as having a "head injury." Bladder preservation at the expense of survival may not be the best outcome. Second, perhaps even more important, only 3 of the 8 patients were asymptomatic at the time of follow-up, which is admittedly short. Will they stay asymptomatic? What about the 4 remaining with their bladders? Will they develop increasing symptoms over time? Will they ultimately require a cystectomy? Longer follow-up is needed. Despite these questions, the report provides promising and important information.

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Small intestinal submucosa bladder neck slings for incontinence associated with neuropathic bladder

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Purpose: We assess the results using small intestinal submucosa (SIS) for neuropathic urinary incontinence in a large single institutional experience. Ambulatory status was considered as a possible predictor of success.

Materials and Methods: We retrospectively reviewed the charts of patients treated with SIS bladder neck sling procedures for neuropathic urinary incontinence with a leak point pressure less than 25 cm H₂O and a minimum of 6 months followup. Continence was defined as wet (requiring pads or diapers) or dry (requiring no pads and dry underwear). Patients were classified as ambulatory (able to ambulate without assistance or using braces, crawling at home) or nonambulatory (confined to a wheelchair). Results were analyzed with regard to patient sex, ambulatory status and simultaneous bladder neck repair.

Results: A total of 21 females and 15 males 3 to 10 years old (mean age 9 years) were treated with SIS bladder neck slings (sling alone 27, bladder neck repair with SIS sling 9). Slings were performed along with reconstructive surgery in all cases (all had creation of urinary catheterizable channels and simultaneous or prior bladder augmentations). Minimum followup was 6 months (mean 15, range 6 to 42). Overall, 27 of the 36 patients (75%) are dry following bladder neck sling. In patients treated with the sling procedure alone 6 of 8 (75%) nonambulatory females and 8 of 10 (80%) ambulatory females were continent, and 3 of 4 (75%) nonambulatory males and 2 of 5 (40%) ambulatory males were dry.

Conclusions: SIS has equivalent rates of continence compared to series using rectus fascia in patients with neuropathic urinary incontinence. The ambulatory status of males should be considered when determining which treatment option is best for the patient with myelodysplasia and neuropathic sphincteric incontinence, as in our series ambulatory males undergoing sling placement alone had a poor outcome.

Editorial Comment

The authors report a series of 36 children with neurogenic bladder who underwent a bladder neck sling using small intestinal submucosal (SIS) as manufactured by Cook Urological. SIS has the advantage of being "off-the-shelf." In addition, in this neurogenic population, rectus muscle and fascia may not be normal and may be further weakened and scarred by harvesting it, making autologous rectus fascia a less favorable alternative. Overall, 75% of the authors' patients were dry afterwards.

In general, these results are good, but several important points need to be considered. For the reader, it is important to determine whether this success rate is due to the operative technique or the material being used. In reviewing the data, we do not know whether this is a consecutive series or whether these patients were selected for the SIS sling (and how they may have been selected). We do not know how many other types of slings were performed in the same or similar time period and we have no idea what the authors' success rates were with other materials or other techniques. Moreover, the 36 patients had widely varying characteristics, including gender, ambulatory status, history of/need for augmentation, and even the type of sling (with or without bladder neck surgery). The authors attempt some sub-group analyses and conclude that the operation works less well in ambulatory males. Though this may be true, it is difficult for the reader to determine this with any certainty in the large, varied group. Also, as in all studies of continence, how the continence is determined is of critical importance. In this case, it was reported by patients or their parents. However, it is not known how this was reported. For example, obtaining these data face-to-face with a provider has been shown to result in falsely elevated rates of continence, as the patient does not wish to disappoint the provider.

Moreover, perhaps the biggest concern is with durability. Mean follow-up was only 15 months. Presumably, SIS acts as a template for the in-growth of other tissues. What other tissues grow in? How strong are they? How durable are they? Many stress incontinence procedures have been shown to not stand the test of time. The patients in this series are young and, because of their neurogenic status, they will probably have their continence tested more due to straining than non-neurogenic patients. Although these results are encouraging, they should be considered preliminary. Much longer follow-up is needed.

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