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UROLOGICAL SURVEY

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STONE DISEASE

Cost-effectiveness of medical expulsive therapy using alpha-blockers for the treatment of distal ureteral stones

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Objective: Medical expulsive therapy (MET) has recently emerged as an efficacious and safe option for the initial management of ureteral stones. The objective of this study was to assess the cost-effectiveness of MET compared with conservative therapy for the treatment of ureteral stones using international cost data from the United States and four European countries.
Material and Methods: A decision analysis model was built with the use of TreeAge Pro 2004 software with linear success rate assumptions. The likelihood of spontaneous passage of ureteral stones according to their size and location was estimated with the use of data derived from a published meta-analysis. The estimated cost of ureteroscopy (URS) in the United States ($4973) was based on the mean cost of 121 consecutive cases performed at a large metropolitan hospital. URS costs for other countries were obtained from a published international survey. The cost of tamsulosin ($2.08 per day), currently the most commonly used medical expulsive agent, was estimated as a mean of the costs obtained from two national pharmacy chains. MET and conservative therapies were compared with the use of one-way and two-way sensitivity analyses.
Results: In the United States, MET using tamsulosin resulted in a $1132 cost advantage over observation. MET maintained its cost advantage even in countries where the cost of URS is much lower than in the United States. Two-way sensitivity analysis showed that MET remained cost-effective even with very low rates of spontaneous passage, minimal benefit of MET, or low cost of URS.
Conclusion: MET is a cost-effective strategy for the management of distal ureteral stones-even those with a low rate of spontaneous passage-providing another incentive for initial "facilitated observation" before embarking on surgical intervention.

Editorial Comment

Medical expulsive therapy has gained acceptance as a safe and efficacious option for the management of ureteral calculi, and is now incorporated into the new American Urological Association practice guidelines for ureteral stones. The authors present an elaborate evaluation of the cost-effectiveness of medical expulsive therapy (MET) compared to conservative therapy for ureteral stones from a global perspective.

One might argue that the acute management of renal colic and the postoperative course following ureteroscopy is not uniformly conducted in the outpatient setting, as assumed in the decision model. Though based on a historical metaanalysis, the spontaneous stone passage rates utilized in this decision making tree (< 4 mm 38%, > 6 mm 1%) is lower than more recent studies would suggest for distal ureteral stones. Indeed, in our practice we would counsel patients with a 3 mm distal stone that they have a 70% chance of spontaneous stone passage and a patient with a 6 mm distal stone would have a 30% chance (1). This aspect of the study design would accentuate the cost-advantages of MET predicted by the decision making model. The authors assumed that the cost of follow-up would be the same in each group; however, one would anticipate that the need for follow-up imaging, unanticipated emergency room visits and lost wages would be lower in the MET group. This aspect of the study design would diminish the potential cost-benefit for the MET approach.

As such, the study serves the important function of quantifying the expected - that improving stone passage will save money in addition to saving patient morbidity. It highlights the large discrepancy in global health care costs – a topic for another day.

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Practical use of investigations in patients with hematuria

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Objective: The majority of patients with microscopic hematuria undergo a complete evaluation resulting in negative findings. The outcome of patients with hematuria was analyzed in an effort to optimize the use of investigations.
Patients and Methods: The records for 404 patients who presented with hematuria were reviewed. Data were collected on demographics, type of hematuria, investigations, and final diagnosis.
Results: The hematuria was microscopic in 140 patients (35%) and gross in 264 patients (65%). In gross hematuria patients, 10% had urinary tract tumors and 12% had calculi. All patients with genitourinary tumors and 87% of patients with calculi had gross hematuria and/or 5 RBCs/HPF (red blood cells per highpower microscopic field) on urinalysis. The sensitivity and specificity were 94% and 6% for the dipstick urine test, 37% and 71% for urine cytology, 92% and 93% for computed tomography (CT), 50% and 95% for ultrasound scans, and 38% and 90% for intravenous pyelography, respectively. Logistic regression analysis showed that age and number of RBCs/HPF in the urinalyses were the only significant factors predicting genitourinary cancer. In patients 40 years old, there was one patient with malignancy and seven patients with stones. In older patients, there were 31 patients with malignancy and 32 patients with stones.
Conclusions: Patients with 5 RBCs/HPF on three urinalyses are unlikely to have significant pathology and could possibly be followed up conservatively. Patients 40 years of age should have a noncontrast CT or ultrasound study if they present with microscopic hematuria, and a cystoscopy should be added if gross hematuria exists. In older patients, a pre- and postcontrast CT and a cystoscopy should be performed.

Editorial Comment

The authors' findings suggest some significant differences in management approaches to those proposed in the American Urological Association practice guidelines. Most importantly, they suggest a cut-off of $\geq$ 5 RBC/hpf on microscopic evaluation as the threshold for which a hematuria work-up should be initiated. This contrasts to the $\geq$ 3 RBC/hpf threshold set by the AUA. As 17% of patients in their cohort had 3 or 4 RBC/hpf, a significant number of evaluations could have been avoided, resulting is savings of cost and patient discomfort. In addition, the authors draw a sharp distinction in the extent of work-up required for the younger patient with microhematuria – suggesting non-contrast imaging and no cystoscopy.

However, it is important to emphasize that this study does not represent a screening population with a urinalysis performed at a primary care point of care. Rather, it is a select cohort of patients referred for urologic

evaluation. Secondly, there was no standardization of imaging protocol or follow-up for delayed presentation of malignancy, to confirm the sensitivity of the ≥ 5 RBC/hpf approach.

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ENDOUROLOGY & LAPAROSCOPY

Laparoscopic radical cystectomy and extracorporeal urinary diversion: a single center experience of 48 cases with three years of follow-up

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Objectives: To report our experience with laparoscopic radical cystectomy and extracorporeal urinary diversion for high-grade muscle invasive bladder cancer in a consecutive series of 48 patients with 3 years of follow-up.
Methods: From June 1999 to April 2006, 48 patients (42 men and 6 women; mean age 59 years, range 24 to 80) with bladder cancer underwent laparoscopic radical cystectomy and bilateral pelvic lymph node dissection at our institution. Urinary diversion was done extracorporeally through the specimen extraction incision.
Results: The mean operating time was 310 minutes, and the mean blood loss was 456 mL. In 1 patient, conversion to open surgery was required because of severe hypercarbia. Three major complications were observed intraoperatively (rectal injury in 2 and external iliac vein injury in 1 patient). However, all these complications were managed laparoscopically, with completion of the procedure laparoscopically. The mean hospital stay was 10.2 days (range 7 to 25). One patient died in the postoperative period of severe lower respiratory tract infection and septicemia. Histologic examination showed organ-confined tumors (Stage pT1/pT2/pT3a) in 34 patients (71%) and extravesical disease (pT3b/pT4) in 14 (29%). Of the 48 patients, 12 (25%) had lymph node involvement. The mean number of nodes removed was 14 (range 4 to 24). At a mean follow-up period of 38 months (range 10 to 72), 35 patients were alive with no evidence of disease (disease-free survival rate 73%).
Conclusions: The results of our study have shown that laparoscopic radical cystectomy is a safe, feasible, and effective alternative to open radical cystectomy. Extracorporeal urinary diversion through a small incision decreases the operating time, while maintaining the benefits of laparoscopic surgery. The 3-year oncologic efficacy was comparable to that of open radical cystectomy.

Editorial Comment

The advantage of decreased blood loss provided by laparoscopy seems to be a major beneficial aspect of this approach compared to open surgery. This could be due to the insufflation, as well as, magnified vision that can provide better exposure of the anterior retropubic and posterior retrovesical dissection fields facilitating hemostasis.

Another major advantage of laparoscopy in radical cystectomy is the smaller skin incision to remove the bladder without prolonged overstretching of the tissues, possibly decreasing postoperative pain.

Controversy exists on whether urinary diversion should be performed intracorporeally or extracorporeally. Although the feasibility of total intracorporeal urinary diversion has been reported, it has been associated with prolonged operative times and prolonged anesthesia time may negate the benefits of laparoscopy. Moreover, prolonged operating time has also been associated with significant surgeon fatigue and increased cost of the procedure. In summary, this paper demonstrates the feasibility of the procedure but longer clinical follow-up is needed to validate the oncological outcomes of laparoscopic radical cystoprostatectmy in the treatment of localized invasive bladder cancer.

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Laparoscopic renal oncological surgery in the presence of abdominal aortic and vena caval pathology: 8-year experience

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Purpose: To our knowledge the outcomes of laparoscopic renal oncological surgery in patients with major aortic and/or inferior vena caval pathology are unknown. We present our experience spanning an 8-year period.
Materials and Methods: From March 1998 to October 2006, 1,826 laparoscopic renal procedures were performed for tumor. Of these patients 66 (3.6%) had major abdominal aortic or vena caval pathology concomitantly. Demographics, specific entities of the vascular disease, and intraoperative and postoperative data were reviewed.
Results: A total of 66 patients had a history of abdominal aortic disease (54), vena caval disease (9) or both (3). Of the patients 85% had 3 or greater comorbidities, 88% had an American Society of Anesthesiologists score of 3 or greater and 88% were on chronic anticoagulation therapy. A total of 27 patients (41%) had undergone prior surgical treatment for vascular pathology. Laparoscopic renal surgery, which was transperitoneal in 25 cases and retroperitoneal in 41, included radical nephrectomy in 20, partial nephrectomy in 17 and cryoablation in 29. Open conversion was performed in 3 patients (5%). There were 3 intraoperative (5%) and 9 postoperative (14%) complications. One patient died of pulmonary sepsis. There was no statistically significant difference in perioperative outcomes between the aortic and vena caval disease groups. The retroperitoneal approach was associated with less blood loss and shorter operative time ($p = 0.0003$ and 0.004, respectively).
Conclusions: Laparoscopic surgery for renal tumor in the presence of aortic or vena caval disease is safe and feasible. Considerable prior laparoscopic experience is necessary when treating these patients at high risk.

Editorial Comment

Since the first report of laparoscopic surgery in urology by Clayman et. al. in 1991, the development of new laparoscopic procedures has been steadily increasing, as well as, the complexity of patients' co-morbidity and surgical techniques. The authors demonstrate that patients with severe major vascular pathology may undergo laparoscopic surgery with insufflation of the abdomen without causing immediate conversion to open surgery. In this series, intraoperative parameters, such as blood loss, ORT, the conversion rate and the complication

rate, were comparable to those in other reported series. The results indicate that laparoscopic renal procedures are safe in patients with aortic and/or vena cava disease, and the type of major vessel disease did not have an impact on the laparoscopic procedure. Moreover, laparoscopic procedure difficulty was not increased in patients with a vena cava filter.

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IMAGING

MRI in the histologic characterization of testicular neoplasms

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Objective: The purpose of our study was to investigate the potential role of MRI in the preoperative characterization of the histologic type of testicular tumors and, more specifically, to differentiate seminomatous from nonseminomatous testicular neoplasms.
Materials and Methods: Twenty-one patients with histologically proven germ cell testicular tumors underwent MRI of the scrotum on a 1.5-T unit. T2- and T1-weighted sequences before and after i.v. administration of gadolinium chelate were performed. MRI studies were retrospectively reviewed by two radiologists and findings were correlated with the histopathologic diagnosis. An attempt was made to differentiate seminomatous from nonseminomatous testicular tumors on the basis of signal intensity and homogeneity of the lesions, presence of fibrovascular septa, tumor encapsulation, and patterns of contrast enhancement. Interobserver agreement was assessed using weighted kappa statistics.
Results: MRI findings correctly characterized 19 (91%) of 21 testicular neoplasms (nine seminomatous and 10 nonseminomatous testicular tumors), with excellent interobserver agreement. The presence of an intratesticular lesion of predominantly low signal intensity on T2-weighted images, with septa enhancing more than tumor tissue after contrast material administration, was more suggestive for the diagnosis of a seminoma. Tumors that were markedly heterogeneous both on unenhanced and contrast-enhanced images were indicative of a nonseminomatous neoplasm. Conclusion: Our study shows that MRI provides a credible preoperative differentiation of seminomatous from nonseminomatous testicular tumors, with excellent interobserver agreement.

Editorial Comment

Imaging plays an important role in the evaluation of testicular masses. Ultrasound is still the first imaging modality to be used since adds essential information in distinguish intratesticular from extratesticular

lesions. US is also useful for adequate characterization of the vast majority of benign intra-scrotal lesions. The combination of clinical findings and sonography is usually sufficient for adequate management of the most scrotal masses since sonography is nearly 100% sensitive for detection of testicular tumors. On sonography, seminoma appears usually as a homogeneous hypoechoic lesion. The entire testis is replaced by tumor in more than half the cases and small cystic areas can be found in about 10% of tumors. Non-seminomatous tumors often have an inhomogeneous echotexture, irregular or ill-defined margins, echogenic foci (hemorrhage or calcification) and cystic necrosis. Both tumors present increased flow on color Doppler US. Sometimes some benign intratesticular lesions resemble malignant tumor on US. The authors of this manuscript confirm previous reports that MRI is an excellent technique for adequate differentiation of seminomatous from non-seminomatous testicular tumors (1). Although this information is essential for determining adequate treatment and prognosis an attempt to pre-operatively differentiate seminomatous from non-seminomatous testicular tumors perhaps is not essential since both are treated with orchiectomy. As already pointed out by the authors, it would be more interesting further investigation regarding the value of MRI in differentiating benign from malignant intratesticular lesions. The results of this study, however, further strength the utility of MRI, which should be used whenever sonographic findings are inconclusive or inconsistent with the clinical findings.

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Prostate cancer: identification with combined diffusion-weighted MR imaging and 3D 1H MR spectroscopic imaging—correlation with pathologic findings

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Purpose: To retrospectively measure the mean apparent diffusion coefficient (ADC) with diffusion-weighted magnetic resonance (MR) imaging and the mean metabolic ratio (MET) with three-dimensional (3D) hydrogen 1 ((1)H) MR spectroscopic imaging in regions of interest (ROIs) drawn over benign and malignant peripheral zone (PZ) prostatic tissue and to assess ADC, MET, and combined ADC and MET for identifying malignant ROIs, with whole-mount histopathologic examination as the reference standard.
Materials and Methods: The institutional review board approved this HIPAA-compliant retrospective study and issued a waiver of informed consent. From among 61 consecutive patients with prostate cancer, 38 men (median age, 61 years; range, 42-72 years) who underwent 1.5-T endorectal MR imaging before radical prostatectomy and who fulfilled all inclusion criteria of no prior hormonal or radiation treatment and at least one PZ lesion

(volume, > 0.1 cm(3)) at whole-mount pathologic examination were included. ADC maps were generated from diffusion-weighted MR imaging data, and MET maps of (choline plus polyamine plus creatine)/citrate were calculated from 3D (1)H MR spectroscopic imaging data. ROIs in the PZ identified by matching pathologic slides with T2-weighted images were overlaid on MET and ADC maps. Areas under the receiver operating characteristic curves (AUCs) were used to evaluate accuracy.
Results: The mean ADC +/- standard deviation, (1.39 +/- 0.23) x 10(-3) mm(2)/sec, and mean MET (0.92 +/- 0.32) for malignant ROIs differed significantly from the mean ADC, (1.69 +/- 0.24) x 10(-3) mm(2)/sec, and mean MET (0.73 +/- 0.18) for benign ROIs (P < .001 for both). In distinguishing malignant ROIs, combined ADC and MET (AUC = 0.85) performed significantly better than MET alone (AUC = 0.74; P = .005) and was also better than ADC alone (AUC = 0.81), although the difference was not statistically significant (P = .09).
Conclusion: The combination of ADC and MET performs significantly better than MET for differentiating between benign and malignant ROIs in the PZ. (c) RSNA, 2008.

Editorial Comment

Magnetic resonance imaging (MRI) combined to 3D-magnetic resonance spectroscopic imaging (MRSI) is the only non-invasive technique with the potential to provide useful information regarding the detection, localization, staging and prognosis of prostate cancer. The combination of these techniques (MRI+MRSI) has improved the diagnostic assessment of prostate cancer beyond the morphologic information provided by conventional MR imaging. To further improve the specificity and sensitivity of MRI+MRSI, other complimentary techniques such as dynamic contrast enhanced MR imaging and diffusion-weighted MR imaging (DWI) has been used in last years. DWI is used to detect the state of molecular translational motion of water in the tissue. In prostate cancer, densely packed malignant epithelial cells, causes restricted diffusion of water relative to that of normal tissue. Since apparent diffusion coefficient (ADC) reflects primarily diffusion coefficient of extra-cellular water, ADC values tend to be lower for tumors compared to normal tissue (benign tissue: ADC values > 1.3 cm2/s; cancer tissue: ADC values < 1.3 cm2/s). Contrary to cancer in BPH, extra-cellular space volume is higher, thus ADC values are higher as well. The authors of this retrospective study, nicely shows that the association of the measurements of the mean ADC values (DWI) with the mean metabolic ratio (MRSI) performs significantly better than the mean metabolic ratio alone for the discrimination of normal and malignant prostatic tissue of the peripheral zone. Since 2004, we have been using in our institution MRI+MRSI, DWI and dynamic contrast enhancement for all patients evaluated for detection or staging prostate cancer. We agree with the authors' statement that MRSI+DWI are much better than the isolated use of any of these techniques. Unfortunately this combination does not prevent false positive results found particularly in patients with focal prostatic atrophy (1).

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PATHOLOGY

Small cell carcinoma of the prostate. A morphologic and immunohistochemical study of 95 cases

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Small cell carcinoma of prostate is rare, with the literature consisting of case reports and small series. The current work analyzes the morphology and immunohistochemistry of 95 cases of prostatic small cell carcinoma diagnosed at our institution. Specimens included 55 needle biopsies, 27 transurethral resections, 4 radical prostatectomies, and 9 biopsies from metastatic sites (some patients with > 1 procedure). Patients ranged in age from 44 to 92 years old (mean: 69 y). Although serum prostate-specific antigen (PSA) in some cases was very high (up to 1896 ng/mL), the median value was only 4.0 ng/mL. Of cases with available information, 33/78 (42%) had a history of usual prostatic adenocarcinoma. The interval between the diagnosis of small cell carcinoma and prior usual prostatic cancer ranged from 1 to 300 months (median 25 mo). Pure small cell carcinoma was seen in 54/95 (57%) of cases with the remaining cases admixed with prostate adenocarcinoma. In cases with adenocarcinoma, there was a sharp demarcation between small cell carcinoma and adenocarcinoma in 20.5% of cases; in the remaining cases there was gradual merging of the 2 components. In mixed cases, small cell carcinoma predominated (median: 80% of the tumor); the Gleason score of the adenocarcinoma was > or = 8 in 85% of these cases. In 61 cases (64%), small cell carcinoma was classic "oat cell" morphology with remaining the "intermediate cell" variant. Of the 95 cases: necrosis was seen in 40% (2% to 95% of the tumor); giant bizarre cells in 19%; Indian filing in 21%; rosette formation in 29%; focal vacuolated cytoplasm in 18%; and desmoplasia in 20%. Most (88%) of small cell carcinoma were positive for at least 1 neuroendocrine marker. In the small cell carcinoma component, 14/73 (19%) were positive for PSA, 17/61 (28%) positive for prostein (P501S), and 15/59 (25%) positive for prostate-specific membrane antigen, although often very focally. Stains for thyroid transcription factor-1 were positive in 23/44 (52.3%) cases. In this, the largest study of prostatic small cell carcinoma, we highlight the presence of morphologic features that may result in its underdiagnosis. Other more classic histologic features of small cell carcinoma along with rosettes are critical for its accurate diagnosis. P501S and prostate-specific membrane antigen were better in identifying the prostatic origin of small cell carcinoma than PSA, although the majority (60%) of prostatic small cell carcinomas were negative for all 3 markers.

Editorial Comment

The variant small cell carcinoma of the prostate must be recognized by the pathologist. These rare tumors have an aggressive course and the average survival of patients is less than a year. Most of these tumors show neuroendocrine differentiation demonstrated by immunohistochemistry with markers like NSE, synaptophysin, or chromogranin. Due to these unique features small cell carcinomas are not histologically graded.

Approximately half of the tumors are associated with conventional prostate adenocarcinoma. It is important to note that neuroendocrine differentiation may occur during progression of prostate conventional carcinomas. Therefore, the tumor may be a conventional adenocarcinoma in the prostate and small cell carcinoma in a metastatic site. In this very large series of Wang and Epstein's the median value of serum prostate-specific antigen was 4.0 ng/mL. In mixed cases, small cells predominate and the Gleason score of the conventional component is high (> or = 8 in 85% of the cases).

A review of the literature of genitourinary small cell carcinoma, Mackey et al. (1) found cisplatin chemotherapy to be beneficial for bladder tumors but only surgery was prognostic for prostate small cell

carcinomas. Others suggest treating small cell carcinoma of the prostate with the same combination chemotherapy used to treat small cell carcinoma in other sites like, for example, “oat cell carcinoma” of the lung (2-4).

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Pseudocarcinomatous epithelial hyperplasia in the bladder unassociated with prior irradiation or chemotherapy

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Pseudocarcinomatous epithelial hyperplasia in the bladder is a little known phenomenon, recognized to be associated with prior irradiation and/or chemotherapy. Whether this process can occur outside of this setting has not been studied. We identified 8 of these cases mimicking invasive urothelial carcinoma from our consultation files from 07/04 to 07/06 with no prior history of radiation or chemotherapy. The mean age at diagnosis was 65 years (range, 42 to 81 y), with 5 of the 8 males. Seven patients had a potential etiology for these changes that could either have resulted in localized ischemia or injury to the urothelium. These included case 1: atrial fibrillation, hypertension, congestive heart failure, gastrointestinal bleeding, and coronary artery vascular disease; case 2: coronary angioplasty, atrial fibrillation, hyperlipidemia, and amputation of arm for ischemia; case 3: hypertension, uncontrolled diabetes, hyperlipidemia, and atrial fibrillation; case 4: underlying arteriovenous malformation of the bladder; cases 5 to 6: history of indwelling Foley catheter; and case 7: history of radical prostatectomy for prostate cancer but no radiation. One patient had no potential contributing factors. All 8 patients presented with gross hematuria. At cystoscopy, 7 patients had polypoid lesions with 1 appearing nonpolypoid. Histologically, all cases showed epithelial proliferation of urothelium with cells having prominent eosinophilic cytoplasm. This process that mimicked invasive cancer within the lamina propria was marked in 3 cases (38%). Moderate nuclear pleomorphism was seen in 6 cases (75%). Only 1 case revealed mitotic figures. Ulceration was seen in 1 case. All cases showed some degree of hemorrhage with hemosiderin deposition identified in 3 cases (38%). Fibrin deposition was present in 1 case within the stroma, 3 cases in the vessels, and 4 cases in both. Five cases show stromal fibrosis. Edema and vascular congestion were common features (90% and 100%, respectively).

Six out of 8 cases were accompanied by moderate to marked acute and chronic inflammation. The original diagnosis included nested variant urothelial carcinoma (1 case), atypical suspicious for invasive carcinoma (5 cases), hemangioma (1 case), and eosinophilic cystitis (1 case). Patients were followed for a mean of 16.5 months (range, 10 to 34 mo), and none developed bladder cancer. As a rare response to ischemia and chronic irritation, pseudocarcinomatous epithelial proliferations in the bladder may be confused with invasive urothelial carcinoma. Pathologists must be aware of the histologic changes mimicking cancer, and recognize that it can occur outside of the setting of prior irradiation or chemotherapy.

Editorial Comment

Irradiation and/or chemotherapy induce well known lesions in the urinary bladder. They include: acute cystitis with desquamation of the urothelial cells, hyperemia, edema in the lamina propria, atypical epithelial and/or stromal cells, hyalinization and thrombosis of the vessels, and prominent telangiectatic vessels that explain the hematuria that often occurs. Late complications of radiation injury include ulcers, marked contraction of the bladder because of fibrosis, and ureteral strictures that may lead to severe pyelonephritisd and death (1).

A pitfall for the pathologist in radiation cystitis is pseudocarcinomatous proliferation of the urothelium simulating invasive urothelial carcinoma. In 2000, Baker and Young (2) reported 4 cases with this lesion. It is a reactive process and the authors point out some clues for the correct diagnosis: absence of mitotic figures, preservation or decrease of the nuclear-to-cytoplasmic ratio, prominent vacuolar change, and squamoid appearance of the epithelium.

The report of Lane and Epstein's is very important because it adds to pseudocarcinomatous epithelial hyperplasia in the bladder causes unassociated with prior irradiation or chemotherapy that must be known by the pathologist. One patient had no potential contributing factor, but 7 patients had ischemia and/or chronic irritation as possible causes for this reactive lesion mimicking invasive urothelial carcinoma. We had the opportunity to see in our Institution a biopsy of the urinary bladder of a 44-year-old male showing pseudocarcinomatous hyperplasia unassociated with prior irradiation or chemotherapy. This reactive lesion was associated to chronic cystitis due to a rectalvesical fistula secondary to diverticulitis.

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INVESTIGATIVE UROLOGY

Beneficial effect of taurine on testicular ischemia-reperfusion injury in rats

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Objectives: To evaluate the effect of taurine, a potent antioxidant, on testicular ischemia-reperfusion injury due to excess reactive oxygen species produced by neutrophils after testicular torsion-detorsion.
Methods: A total of 60 adult male Sprague-Dawley rats were randomly divided into three groups, each containing 20 rats. The control group underwent a sham operation of the left testis. In the torsion-detorsion group, the left testis was rotated 720 degrees counterclockwise for 2 hours. The treatment group underwent the same surgical procedure as the torsion-detorsion group, but taurine was administered intravenously at repair of the testicular torsion. One half of the rats in each group underwent orchiectomy 4 hours after detorsion for measurement of myeloperoxidase activity, an indicator of neutrophil accumulation in the testis, and for evaluation of tissue malondialdehyde, an indicator of intratesticular reactive oxygen species content. The remainder were killed at orchiectomy 3 months after detorsion for analysis of testicular spermatogenesis.
Results: Unilateral testicular torsion-detorsion caused a significant increase in myeloperoxidase activity and the malondialdehyde level and a significant decrease in testicular spermatogenesis in the ipsilateral testes. The decrease in ipsilateral testicular spermatogenesis involved a reduction in testicular weight, mean seminiferous tubular diameter, number of germ cell layers, and mean testicular biopsy score. The rats treated with taurine had a significant decrease in myeloperoxidase activity and malondialdehyde level and a significant increase in testicular spermatogenesis in the ipsilateral testes compared with the torsion-detorsion group.
Conclusions: The results of our study have shown that the administration of taurine exerts a beneficial effect on testicular ischemia-reperfusion injury. This effect might be partly the result of a reduction in reactive oxygen species generation by diminishing neutrophil recruitment to the testis.

Editorial Comment

Taurine (2-aminoethanesulfonic acid) is a major intracellular free beta-amino acid found in most mammalian tissues and is supposed to exerts cytoprotective properties such as antioxidation, intracellular calcium flux regulation, membrane stabilization, osmoregulation, and antiapoptosis. Exogenous administration of taurine has been shown to have a preventive and therapeutic effect on ischemia-reperfusion injury of the heart, liver, brain, and other organs. The authors investigated by the first time the role of taurine in testicular ischemia-reperfusion injury, by evaluating its effect on testicular spermatogenesis in a rat testicular ischemia-reperfusion injury model.

The authors demonstrated the beneficial effect of taurine on testicular ischemia-reperfusion injury. One part of the beneficial effect could be a result of a reduction of reactive oxygen species generation by diminishing the neutrophil recruitment to the testis.

The treatment with taurine (200 mg/kg) significantly rescued ipsilateral testicular spermatogenesis in the present study; nevertheless, the saved spermatogenesis was not restored to its normal value. Since the authors did not study the effect of taurine at different doses or different administration times, the effect of taurine could be affect by these aspects. So, additional studies taking into account these factors could led to elucidation of taurine´s optimal effect.

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Microarray analysis of exstrophic human bladder smooth muscle

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BJU Int. 2008; 101: 100-5

Objective: To compare the genetic profiles of 'healthy' bladder smooth muscle cells (SMCs) and exstrophic SMCs (ESMCs) to identify genes that are over- and under-expressed in ESMCs, thus providing a molecular evaluation of the quality and therapeutic potential of ESMC tissue.
Patients, Material and Methods: Classical bladder exstrophy is a rare disorder, occurring in 1 in 30,000 live births. Studies have shown that exstrophic bladders are developmentally immature at birth. After surgical closure, the bladder typically undergoes abnormal remodelling (such as over-expression of collagen III) throughout early development. We hypothesized that the predominant genetic differences between normal SMCs and ESMCs are in the developmental genes. This hypothesis was tested by the use of microarray analysis. Bladder SM biopsies were taken from 'healthy' subjects undergoing bladder surgeries for other conditions (for example, urinary reflux) and patients with bladder exstrophy. Cells were expanded in vitro, and total RNA was isolated and hybridized to the Affymetrix U133A GeneChip (Affymetrix Inc., Santa Clara, CA, USA) by the Wake Forest University School of Medicine Affymetrix core facility, using standard protocols.
Results: We created a genetic signature consisting of 961 genes that are over-expressed and 432 genes that are under-expressed in ESMCs. Analysis of these signatures identified an over-expression of inflammatory genes and an under-expression of developmental genes.
Conclusion: Our data is in concordance with previous studies and histological data showing that ESMCs are developmentally immature relative to healthy bladder SM. The clinical implication of the ESMC genetic signature is that it provides a list of targets that can be (i) manipulated ex vivo and/or in vivo to induce differentiation (the completion of development) and (ii) used as biomarkers to explain the variability of the clinical symptoms after surgical closure.

Editorial Comment

This is another pioneer study from this group of investigators, which opened new windows on understanding and treatment of bladder exstrophy-epispadias complex (BEEC).

The authors used the microarray technique to identify the global genetic differences between bladder exstrophic smooth muscle cells (ESMCs) and normal bladder smooth muscle (SM) cells from patients who underwent surgery for other conditions (not age matched). The authors were able to create a genetic signature consisting of 961 genes that were over-expressed and 432 genes that were under-expressed in ESMCs.

The analysis of these signatures identified an over-expression of inflammatory genes and an under-expression of developmental genes.

The authors emphasized that the data on inflammatory genes shows the importance of keeping the bladder sterile after birth and would argue that an antibiotic should be given after birth. Also, the authors think that it is important to note any possible pathogen exposure before surgery as a way to identify patients that can potentially be at greater risk of complications, such as retention of inflammatory gene expression after in vitro expansion and fibrotic tissue that could be identified during development. The data on inflammatory over-expression could also explain why some patients have symptoms during childhood and others are asymptomatic. Concerning the inflammatory issue, the authors demonstrated the importance of keeping the bladder sterile after birth and argued that an antibiotic should be given after birth. They also think that it is important to note any possible pathogen exposure before surgery as a way to identify patients that can potentially be at greater risk of complications.

Concerning developmen, the present microarray analysis shows that ESMCs are developmentally immature relative to healthy SMCs. This issue was already demonstrated previously, nevertheless, the present data is data is original because it gives a molecular explanation, identifying the presence of key developmental pathways such as IL-6 and Wnt. This is further validated by the under-expression data set, which was comprised of several biosynthetic processes.

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RECONSTRUCTIVE UROLOGY

Tissue engineering of urethra using human vascular endothelial growth factor gene-modified bladder urothelial cells

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Acquired or congenital abnormalities may lead to urethral damage or loss, often requiring surgical reconstruction. Urethrocutaneous fistula and strictures are common complications, due to inadequate blood supply. Thus, adequate blood supply is a key factor for successful urethral tissue reconstruction. In this study, urethral grafts were prepared by seeding rabbit bladder urothelial cells (UCs) modified with human vascular endothelial growth factor (VEGF(165)) gene in the decellularized artery matrix. A retroviral pMSCV-VEGF(165)-GFP vector was cloned by insertion of VEGF open reading frame into the vector pMSCV-GFP (murine stem cell virus [MSCV]; green fluorescent protein [GFP]). Retrovirus was generated using package cell line 293T. Rabbit UCs were expanded ex vivo and modified with either MSCV-VEGF(165)-GFP or control MSCV-GFP retrovirus. Transduction efficiency was analyzed by fluorescence-activated cell sorting. The expression of VEGF(165) was examined by immunofluorescence, reverse transcript-polymerase chain reaction, Western blot, and enzyme-linked immunosorbent assay (ELISA). Decellularized rabbit artery matrix was seeded with genetically modified UCs and was subsequently cultured for 1 week prior to subcutaneous implantation into nude mice. Four weeks after implantation, the implants were harvested and analyzed by fluorescence microscopy, and by histologic and immunohistochemical staining. Ex vivo transduction efficiency of UCs was greater than 50% when concentrated retrovirus was used. The modified cells expressed both VEGF and GFP protein. Furthermore, the VEGF-modified UCs secreted VEGF in a time-dependent manner. Scanning electron microscopy and histochemical analysis of cross sections of the cultured urethral grafts showed that the seeded cells were attached and proliferated on the luminal surface of the decellularized artery matrix. In the subcutaneously implanted vessels, VEGF-modified cells significantly enhanced neovascularization and the formation of a urethral layer compared to GFP-modified cells. These results indicate that VEGF gene therapy may be a suitable approach to increase the blood supply in tissue engineering for treatment of urethral damage or loss.

Editorial Comment

The regeneration of urethral strictures remains a challenge with different approaches being taken to improve the long-term outcome. In most cases buccal mucosa is the current gold standard (1). However, other

approaches continue to be investigated so that a second surgical location can be avoided which would significantly decrease the patient's discomfort and other potential postoperative risks.

In recent years, these approaches have focused on efforts to simplify the surgical approach through the research of shelf-prepared material. In its initial stages, we began to use an organ specific acellular matrix and found during regeneration that certain growth factors change significantly over time (2). More recently, different approaches have been taken in order to overcome the well-known problem of back-drafts that occur during the regeneration process (3).

The authors have advanced the regeneration process with the use of a seeded acellular artery matrix using VEGF-expressing urothelials cells to improve the outcome for sustained urothelial reconstruction; the results have been positive and resulted in a faster angiogenesis of the acellular matrix so that an almost normal urethra has been created, which has been previously investigated for bladder regeneration (4). Basic fibroblast growth factor (bFGF), hepatocyte growth factor (HGF), platelet derived growth factor-BB (PDGF-BB), vascular endothelial growth factor (VEGF), insulin like growth factor-1 (IGF-1) and heparin binding epidermal growth factor (HB-EGF) are involved during angiogenesis and inhibited significantly graft shrinkage (5).

However, despite the fact that certain grown factors are a necessity, today we (as the authors critically self comment) still do not know which cells are influencing the surrounding tissue. The reported approach could be beneficial, if it is possible that the acting growth factors can be timed so that possible side effects are limited similar to the demonstrated turnover of tissue engineered urothelium cells (6). Conversely, we have been able to culture and stratify a multi-layer urothelium out of urothelium cells harvested from a bladder wash that might further improve regeneration (7). With these two different strategies, we must always bear in mind that the acellular matrix used should be as similar as possible to support the best regeneration that also further demonstrates its influence in the re-vascularization process (8).

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Early continence outcomes of posterior musculofascial plate reconstruction during robotic and laparoscopic prostatectomy

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Objectives: To detail the technique and evaluate in a preliminary study the effectiveness of posterior reconstruction of Denonvilliers' musculofascial plate (PRDMP) in enhancing early continence after robotic and laparoscopic radical prostatectomy (RP).
Patients and Methods: Thirty-two consecutive patients having robotic or laparoscopic RP with PRDMP (group 1). Thirty previous patients not having PRDMP were compared as historical controls (group 2). Continence, as measured by patient self-reporting of the number of pads used/24 h, was assessed at 3 days and 6 weeks after catheter removal, by telephone interview. 'Continent' was defined as the use of none or one pads, 'moderate incontinence' as two pads, and 'severe incontinence' as more than two pads. Intraoperative transrectal ultrasonography (TRUS) was used to measure the membranous urethral length before and after PRDMP.
Results: At 3 days after catheter removal, more patients in group 1 were continent than in group 2 (34% vs 3%, P = 0.007). At 6 weeks continence was again better in group 1 (56% vs 17%, P = 0.006). The mean length of the membranous urethra on TRUS measured before RP, after RP but before the musculofascial suture, and afterward, was 15.6, 12 and 14 mm, respectively. Thus, reconstruction restored the length of the transected membranous urethra by a mean of 2 mm.
Conclusions: PRDMP during robotic and laparoscopic RP leads to improved maintenance of membranous urethral length and significantly higher early continence rates.

Editorial Comment

At the end of the 21st century, the first reports about the external urethral sphincter or rabdosphincter can be found which discuss omega-shaped of striated muscle fibers innervated by the pudendal nerves (1,2). With further investigations it was demonstrated that the preservation of the levator ani fascia helps to protect the levator ani muscle, rhabdosphincter with its pudendal nerve branches (3). With the reconstruction of the posterior fibrous raphe, early continence was revealed (4). The propagation of these findings for the robotic or laparoscopic radical prostatectomy (RP) results in similar findings as previously reported for the open RP (5).

Similar results seem to be achieved with the reported preservation of the periprostatic nerve courses as recently described by Hennenlotter et al. 2007, which might further avoid the discontinuation of the posterior fibrous raphe (6). Therefore it might be suggested that the careful preservation of the extracapsular nerve courses especially at the apex might be supportive for the sphincter function especially in the early postoperative phase.

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UROLOGICAL ONCOLOGY

Prediction of pathological stage is inaccurate in men with PSA values above 20 ng/mL

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Introduction: We hypothesized that either very low (0-2.5 ng/mL) or very high (>20 ng/mL) PSA values may limit the accuracy of pathological stage predictions. To test this hypothesis, we examined 5193 consecutive patients subjected to radical prostatectomy (RP) for localized prostate cancer (PCa).
Material and Methods: Patients were divided into three cohorts according to their pre-treatment PSA value: </=2.5 (n=331), 2.51-20 (n=4545) and >20 ng/mL (n=317). Subsequently in each cohort, the ability of PSA, clinical stage and biopsy Gleason sum was tested in multivariable logistic regression models predicting three separate endpoints: extracapsular extension (ECE), seminal vesicle invasion (SVI) and lymph node invasion (LNI). Predictive accuracy represented the performance benchmark. All models were adjusted for year of surgery and subjected to 200 bootstrap resamples to reduce overfit bias.
Results: For PSA </=2.5 ng/mL, predictive accuracy was 76.7%, 72.3% and 82.8% for respectively ECE, SVI and LNI. For PSA 2.51-20 ng/mL, the predictive accuracy for the same endpoints was 67.8%, 77.4% and 81.6%. Finally, for PSA > 20 ng/mL, predictive accuracy was 63.6%, 63.7% and 70.6%.
Conclusions: The ability to predict pathological stage in patients with PSA values in excess of 20 ng/mL significantly decreased, compared to patients with lower PSA values. Therefore, accurate staging of these patients may require alternative markers or staging schemes.

Editorial Comment

The authors of this multi-institutional survey investigate whether the current prognosticators and tables (e.g. Partin) are useful in very low and very high PSA levels. They analyzed the radical prostatectomy results of 5193 patients.
Altogether, the predictive accuracy was rather satisfactory even in the very low and the very high PSA ranges. In the latter, predictive accuracy declined.

It may be allowed to shed a critical view on the figures in detail, which may decrease the enthusiasm for prognosticators somewhat. Overall, extracapsular extension (ECE) was found in 20.4% and seminal vesicle invasion (SVI) in 10.6%. In the PSA range > 20 ng/mL, ECE was found in 30.6 % and SVI in 33.4 %. Otherwise, still of patients 13% had ECE and 10% had SVI in the PSA range below 2.5.

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Intravesical instillation of bacille Calmette-Guérin for superficial bladder cancer: cost-effectiveness analysis

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Objectives: Frequent recurrence of superficial bladder cancer is a major problem that impairs patients' quality of life. We studied the current treatment of superficial bladder cancer, including the economic aspects of intravesical instillation.
Methods: A total of 138 superficial bladder cancers were assessed. The tumor characteristics and treatments were investigated during a mean observation period of 86 months by univariate and multivariate analyses. The costs associated with intravesical instillation of bacille Calmette-Guérin (BCG) and its side effects were subjected to cost-effectiveness analysis.
Results: Tumor histologic examination revealed grade 1 in 21 lesions, grade 2 in 60 lesions, grade 3 in 40 lesions, and unclassified in 17 lesions. The pathologic stage was Stage Ta in 85 lesions, T1 in 47 lesions, and Tis in 6 lesions. Univariate and multivariate analyses showed that intravesical instillation of BCG was the most significant factor preventing recurrence, and intravesical chemotherapy had no impact on recurrence. The 5-year recurrence-free survival rate was 78% and 28% for tumors with and without BCG instillation, respectively. The cost-effectiveness ratio of BCG instillation was approximately 3900 dollars/5-yr recurrence-free period.
Conclusions: Our results have indicated that BCG is an effective adjuvant therapy after transurethral resection of superficial bladder cancer in the current medical environment.

Editorial Comment

The discussion on whether to give intravesical chemotherapy or immunotherapy is viable since many years. As these authors state "When prophylaxis with intravesical therapy is performed, it is necessary to strike a balance between more benefit with severe side effects versus less benefit with mild side effects." The authors shed another perspective onto this discussion in analyzing and comparing the overall costs (including costs of e.g. antibiotics) of intravesical chemotherapy and BCG immunotherapy against superficial bladder cancer in 138 consecutive patients.

The figures are based on the Japanese health care system. Still, they are meaningful for the treatment of superficial bladder cancer in toto.

The treatment of BCG related complications are 11% of the total BCG treatment costs. As BCG treated patients had significantly lower recurrence rates, the cost-effectiveness ratio was clearly in favor of BCG immunotherapy with 525 US$ per year.

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A multicentre, randomised prospective trial comparing three intravesical adjuvant therapies for intermediate-risk superficial bladder cancer: low-dose bacillus Calmette-Guerin (27 mg) versus very low-dose bacillus Calmette-Guerin (13.5 mg) versus mitomycin C

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Objective: The primary aim was to search for lower doses of Bacillus Calmette-Guerin (BCG) that are effective and have lower toxicity.
Methods: A low dose of BCG 27 mg was compared with BCG 13.5mg, using mitomycin C (MMC) 30 mg as the third arm of comparison. A total of 430 patients with intermediate-risk superficial bladder cancer were randomised into three groups. Instillations were repeated once a week for 6 wk followed by another six instillations given once every 2 wk during 12 wk.
Results: There was a significantly longer disease-free interval for BCG 27 mg versus MMC 30 mg (p=0.006). There were no statistically significant differences between BCG 27 mg and BCG 13.5mg (p=0.165) or between BCG 13.5mg and MMC 30 mg (p=0.183). Cox proportional hazards regression showed that disease-free interval in the multivariate analysis was significantly better for primary disease and treatment with BCG 27 mg. There were no significant differences among the three groups with regards to time to progression and cancer-specific survival time. Local and systemic toxicity were higher in both BCG treatment groups.
Conclusions: One third of the standard dose, BCG 27 mg, seems to be the minimum effective dose as adjuvant treatment for intermediate-risk superficial bladder cancer, being more effective than MMC 30 mg. One sixth of the standard dose, BCG 13.5mg, has the same efficacy as MMC 30 mg but it is more toxic.

Editorial Comment

This trial is based upon precious trials from the CUETO group on low dose BCG in superficial bladder cancer. Within these non-blinded trials low dose BCG had shown a reduction in side effects together with equal efficacy against tumor recurrences. As with most trials, data on progression suffer from the relatively low numbers of patients in each arm. Furthermore, the maintenance schedule with BCG was very different from other trials as a “slow-dose long-term schedule” was applied with 2-weekly instillations for 6 weeks following the typical 6 weeks induction course.

Still, there are meaningful results to be drawn from this trial, which are generally important for BCG immunotherapy. BCG immunotherapy is dose-dependent. One-third (27 mg) of the full dose (81 mg) may be equally effective, but one-sixth certainly was inferior to one-third. The Kaplan-Meyer curves still showed superior efficacy of all doses of BCG over MMC.

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Serial markers of bone turnover in men with metastatic prostate cancer treated with zoledronic Acid for detection of bone metastases progression

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Objectives: This study assessed the usefulness of serial measurements of bone turnover markers in men with metastatic prostate cancer treated with zoledronic acid to detect disease progression.
Methods: Serum measurements of total alkaline phosphatase (tALP), bone-specific alkaline phosphatase (bALP), cross-linked N-terminal (NTx) and cross-linked C-terminal (CTx) telopeptides of type I collagen, amino-terminal procollagen propeptides of type I collagen (PINP), C-terminal telopeptides of type I collagen (ICTP), and prostate-specific antigen (PSA) were performed in 77 prostate cancer patients suffering from bone metastases and treated with zoledronic acid up to 15 mo. Fifty patients were with and 27 patients without objective evidence of metastatic bone progression during the administration of zoledronic acid.
Results: The baseline bone marker concentrations were not significantly different between the groups. After administration of zoledronic acid all bone markers except of ICTP decreased compared with baseline. CTx showed the greatest decrease. In patients with metastatic bone progression PINP, tALP, bALP, and ICTP were significantly higher at weeks 24, 36, 48, and 60 after starting treatment with zoledronic acid compared with patients without progression. In addition to the information of prostate-specific antigen as a monitoring parameter, the bone formation marker showed a better distinction between patients with and without disease progression.
Conclusions: Selected bone turnover markers provide valuable information regarding progression of bone metastasis in men with metastatic prostate cancer under bisphosphonate therapy. The clinical impact should be confirmed in prospective randomised studies.

Editorial Comment

Many patients with prostate cancer ultimately suffer from bone metastases. In this trial, bone turnover markers were analyzed with regard to their predictive value upon progression in patients with bone metastases.

Basically, PSA was the most important marker to predict progression. All patients received zoledronic acid resulting in an initial reduction of bone turnover markers. Interestingly, if these initial levels were taken as baseline, a subsequent increase was a significant predictor of bone progression.

Thus, bone turnover markers could become an important tool in the monitoring of patients with advanced prostate cancer.

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NEUROUROLOGY & FEMALE UROLOGY

Predictors of success with postoperative voiding trials after a mid urethral sling procedure

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Purpose: We identified predictors of passing a voiding trial after incontinence surgery with a mid urethral sling and examined if successful performance on a voiding trial was maintained.
Materials and Methods: A total of 89 women scheduled for incontinence surgery were enrolled from July 2005 until April 2006. Voiding trials were performed the day of discharge from the hospital, with a two-thirds volume void after a 300 mL fill considered passing. Those who passed underwent a second voiding trial 3 hours later.
Results: Of the participants 60 (67.4%) underwent tension-free vaginal tape surgery, 29 underwent transobturator tape (32.6%) and 64 (71.9%) underwent concurrent vaginal repairs. A total of 59 (67.0%) participants passed the first voiding trial. Univariate analysis identified 12 potential predicting variables for passing the first voiding trial. From these 12, model building via backward stepwise logistic regression found maximum flow on preoperative uroflowmetry to be the only significant predictive variable ($p = 0.0002$). Of the 59 women who passed the initial voiding trial 9 (16.4%) failed the second voiding trial. None of the 11 participants who had maximal flow rates greater than 30 cc per second failed the first or second voiding trial, whereas 17 of 22 subjects (77.3%) who had maximal flow rates less than 15 cc per second failed either of these trials.
Conclusions: Maximum flow rates on preoperative uroflowmetry were the best predictor of passing an initial voiding trial after undergoing a mid urethral sling procedure for incontinence. However, the ability to maintain performance on a second voiding trial, even only 3 hours after passing an initial trial, is not assured.

Editorial Comment

The authors prospectively studied a cohort of patients with regard to their ability to successfully void on the day of their discharge after anti-incontinence surgery. The patients were asked to complete two "fill-pull" trial of voids using 300 cc's of instilled fluid to see if they could go home without their urinary catheter. Successful voids were characterized by at least two-thirds of the bladder instillate being voided out over a ten-minute period. The investigators subsequently reviewed the patients' clinical histories and urodynamic evaluations and based on 51 potential predictors noted that the maximum flow rates were the best predictor of passing the first voiding trial. Nevertheless, voiding well the first time did not guarantee that the patient would pass the second voiding test.

I found this an interesting contribution to the literature if only to remind surgeons of the challenge of postoperative voiding function. Successful initial voiding does not rule out subsequent urinary retention: the

authors noted that approximately 16% of their population failed the second voiding trial and ultimately ended up with a catheter upon discharge to home. In addition, their flow diagram reveals that approximately one-third of their patients had to leave the hospital with a catheter. We have all shared in the muted appreciation of a postoperative patient who must go home with a catheter after her surgery.

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Does uroflow predict ISD?

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Neurourol Urodyn. 2008; 27: 40-4

Aim: The term superflow has been given to abnormally high flow rates in women, and has been thought to be indicative of intrinsic sphincteric deficiency (ISD), as ISD is associated with low urethral pressure. Pelvic organ prolapse (POP) damages the sphincteric mechanism extrinsic to the urethra. The aim of this study was to determine if ISD can be predicted from voiding flow rates in women with symptomatic POP.

Methods: The charts of 82 patients who had undergone surgery for repair of symptomatic vaginal prolapse were reviewed. Uroflow and urodynamic endpoints were compared between dry and stress incontinent patients, and correlations between abdominal leak point pressures (LPP) and pressure/flow data evaluated.

Results: Average maximum flow (Q(max)) at uroflow was greater than at urodynamics with no significant difference in voided volumes. Twenty eight patients were found to have urodynamic stress incontinence (SUI), and an additional 19 to have "occult" stress incontinence. Patients with SUI had higher flow rates at urodynamics than continent patients. Voiding detrusor pressures and flow rates were not different when categorized by LPP cutoffs of 100 and 60 cm/w. Abdominal leak point pressure did not significantly correlate with any uroflow or urodynamic pressure/flow parameter.

Conclusions: Flow rates, whether determined by uroflow testing or at urodynamics, are not predictive of ISD as defined by a low abdominal leak point pressure, in patients with symptomatic POP. Either the effect of ISD on flow rates is a non-linear complex relationship or LPP does not adequately define ISD.

Editorial Comment

The authors examine the correlation of catheter free uroflow to the presence of intrinsic sphincter deficiency during urodynamic evaluation in a population of patients with symptomatic pelvic organ prolapse. This population was selected in that it was conjectured that the pelvic organ prolapse group would offer the truest evaluation of urethral sphincter function since the impact of the external sphincter mechanism would be minimized secondary to their anatomic pathology. The authors found that catheter free uroflow rates were not correlated to leak point pressures in this select population of women (symptomatic pelvic organ prolapse and stress urinary incontinence).

An excellent article from a noted leader in the field. The introduction and discussion section alone are worth reading for the commentary and description of the continence control mechanisms. I found it interesting that in review of the tables and the results section there was no notation of variability of voiding pattern: pure Valsalva voiders; combined detrusor contraction with Valsalva voiding; and voiders who empty their bladder by

relaxing the pelvic floor. All who have evaluated female voiding dysfunction have found the noted voiding patterns at times to be very confounding with regards to analysis secondary to their variability (1).

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PEDIATRIC UROLOGY

Passerini-Glazel feminizing genitoplasty: modifications in 17 years of experience with 82 cases.

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Objectives: To describe modifications of Passerini-Glazel feminizing genitoplasty and report on long-term functional outcome.
Methods: Modifications include vaginal dissection and disconnection from the urethrovaginal sinus as the initial stage of the procedure; large dissection of the neurovascular bundle on both dorsal and lateral faces of the clitoris; plication of the skin around the reduced clitoris; and suturing the lateral edge of the proximal portion of the mucocutaneous plate with the labia majora's medial edge to a plane deeper than the subcutaneous tissue. These modifications reduce bleeding and operating time, better preserve clitoral sensitivity, form the clitoral prepuce, and create labia minora.
Results: Eighty-two patients underwent modified Passerini-Glazel feminizing genitoplasty. Mean operating time was 120min (range: 100-180). Forty-six patients (46 of 82, 56%) were assessed at a mean follow-up of 5 yr (range: 2-9). There were no cases of clitoral vascularization defect or urethrovaginal fistula. The urethral meatus was never hypospadic. The vaginal introitus was large and elastic in all cases. Vaginal caliber at the internal suture line was as large as the vaginal introitus and the distal native vagina in 20 (43.5%) of the 46 girls. All mothers and patients reported satisfaction with external genital appearance.
Conclusions: These long-term results suggest that our modifications of one-stage Passerini-Glazel feminizing genitoplasty facilitate the procedure and produce good cosmetic results.

Editorial Comment

In this manuscript, consecutive cases from 1988-2005 were reviewed. 82 primary cases were done by the Passerini-Glazel feminizing genitoplasty technique with some modifications. There were 22 remaining cases that had undergone surgery elsewhere and the primary cases were operated in an average age of two years while the secondary cases were operated at an average age of 13 years. The manuscript has a good description of the procedure and excellent diagrams for those who might be less familiar with the procedure. Complication rates of the procedures seem acceptable and the long-term follow up that was done. 56% of the patients underwent general anesthesia months to years after surgery showing good results.

Modifications of the procedures recommended by the authors were:

1. to dissect the urogenital sinus from the vagina first before it is separated from the corporal cavernosal bodies
2. complete removal of the corporal spongiosum minimizes bleeding and operating time
3. it is important to separate the posterior vaginal wall from the inferior urethral wall for a length of about 1 cm, which allows mobilization of the native urethra and avoids vaginal stenosis
4. to reduce vaginal stenosis at the suture line they recommend aggressive removal of the distal dysplastic segment of the vagina
5. make a U-shaped inverted skin flap in the perineum to rotate in and become part of the vaginal exterior suture line
6. make incisions in the corporal cavernosal bodies at 3 and 9 o'clock to minimize neurovascular bundle compromise
7. if the glans clitoris needs to be reduced they recommend a wedge from the ventral midline rather than two lateral triangles as was originally described

This procedure is helpful in difficult urogenital sinus cases and this manuscript and its illustration will be beneficial to surgeons who undertake these procedures.

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Lymphatic-sparing laparoscopic varicocelectomy versus microscopic varicocelectomy: is there a difference?

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Objectives: The ideal operation for the adolescent varicoceles has been debated for many years as new techniques or advances in existing technology develop. It is well acknowledged that the Palomo procedure has a negligible recurrence rate but a very high postoperative hydrocele rate compared with a microscopic varicocelectomy (MV). We sought to determine whether lymphatic-sparing laparoscopic varicocelectomy (LSLV) could provide similar negligible recurrence rates as the Palomo approach with the negligible postoperative hydrocele rate seen with MV.

Methods: We performed a retrospective chart review of patients who underwent either an MV (n = 31) or LSLV (n = 28). In the MV group, the artery and the lymphatics were spared, whereas in the LSLV group, the artery and veins were taken en masse. Statistical analysis included paired Student t-test and Chi-square test for continuous and categorical variables, respectively.

Results: Preoperative testis volumes were not different nor were the postoperative testis volumes between groups. Mean operating time was significantly longer in the MV than the LSLV group (140 minutes versus 51 minutes, P <0.01). With a mean time since surgery of 2 years, we observed only one patient with a recurrent varicocele (MV group); only one patient developed a hydrocele requiring hydrocelectomy (LSLV group).

Conclusions: Our early data indicate that LSLV and MV are comparable in preventing varicocele recurrence and formation of hydroceles. The primary difference between the procedures is the surgical time, with the LSLV being much faster to perform.

Editorial Comment

This study is a comparison between 31 patients with a microscopic varicocelectomy technique in 28 patients with a lymphatic-sparing laparoscopic varicocele technique over a 28-month period. Indications for the surgery were either pain or testicular hypotrophy defined as a 20% volume difference between testicles. Postoperative checks were at one week, six months and every 6-12 months thereafter. Testicular ultrasounds were encouraged postoperatively. Age and grade of varicoceles and bilateralism were not statistically significant between the groups. There were no immediate postoperative complications. There were no testis volume differences postoperatively on the 64% of patients who had ultrasounds and the left testis volume increased postoperatively in both groups. Only one recurrent varicocele was seen in the microscopic group and none in the laparoscopic group. There was one patient in the laparoscopic group who developed a hydrocele postoperatively that has subsequently been repaired.

Several techniques reported in the literature correct varicoceles. The microscopic technique has had the lowest varicocele recurrence and hydrocele development rates. This study shows that a laparoscopic lymphatic-sparring technique has as good of results as the microscopic group. It is good to know that the laparoscopic technique can have similar success rates and the major advantage of the laparoscopic technique in the study is shorter operating times by an hour-and-one-half. It may be that in the future laparoscopic techniques may be more familiar to urologists than the microscopic techniques, but only time will tell.

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