
UROLOGICAL SURVEY

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STONE DISEASE

Obesity, weight gain, and the risk of kidney stones

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Context: Larger body size may result in increased urinary excretion of calcium, oxalate, and uric acid, thereby increasing the risk for calcium-containing kidney stones. It is unclear if obesity increases the risk of stone formation, and it is not known if weight gain influences risk.

Objective: To determine if weight, weight gain, body mass index (BMI), and waist circumference are associated with kidney stone formation.

Design, Setting, and Participants: A prospective study of 3 large cohorts: the Health Professionals Follow-up Study (N = 45,988 men; age range at baseline, 40-75 years), the Nurses' Health Study I (N = 93,758 older women; age range at baseline, 34-59 years), and the Nurses' Health Study II (N = 101,877 younger women; age range at baseline, 27-44 years).

Main Outcome Measures: Incidence of symptomatic kidney stones.

Results: We documented 4827 incident kidney stones over a combined 46 years of follow-up. After adjusting for age, dietary factors, fluid intake, and thiazide use, the relative risk (RR) for stone formation in men weighing more than 220 lb (100.0 kg) vs men less than 150 lb (68.2 kg) was 1.44 (95% confidence interval [CI], 1.11-1.86; P = .002 for trend). In older and younger women, RRs for these weight categories were 1.89 (95% CI, 1.52-2.36; P<.001 for trend) and 1.92 (95% CI, 1.59-2.31; P<.001 for trend), respectively. The RR in men who gained more than 35 lb (15.9 kg) since age 21 years vs men whose weight did not change was 1.39 (95% CI, 1.14-1.70; P = .001 for trend). Corresponding RRs for the same categories of weight gain since age 18 years in older and younger women were 1.70 (95% CI, 1.40-2.05; P<.001 for trend) and 1.82 (95% CI, 1.50-2.21; P<.001 for trend). Body mass index was associated with the risk of kidney stone formation: the RR for men with a BMI of 30 or greater vs those with a BMI of 21 to 22.9 was 1.33 (95% CI, 1.08-1.63; P<.001 for trend). Corresponding RRs for the same categories of BMI in older and younger women were 1.90 (95% CI, 1.61-2.25; P<.001 for trend) and 2.09 (95% CI, 1.77-2.48; P<.001 for trend). Waist circumference was also positively associated with risk in men (P = .002 for trend) and in older and younger women (P<.001 for trend for both).

Conclusions: Obesity and weight gain increase the risk of kidney stone formation. The magnitude of the increased risk may be greater in women than in men.

Editorial Comment

Many urologists have long suspected that obese individuals are at increased risk of kidney stone formation, with the risk of stone disease assumed to be due to across-the-board overindulgence in substances known to be associated with stone formation, such as dairy products, animal protein and salt. Taylor and colleagues confirmed the suspicion of increased stone risk with obesity in 3 prospective cohort studies that used food frequency questionnaires and assessed the rate of incident stone formation. They determined that the relative risk (RR) of incident stone formation correlated positively with weight, weight gain and body mass index (BMI) in over 240,000 individuals comprising 3 large independent cohorts of men (Health Professional follow-up Study), younger women (Nurses' Health Study II) and older women (Nurses' Health Study I). Furthermore, this correlation held when adjusting for age and dietary and medication factors known to be associated with stone risk.

The mechanism by which obesity increases stone risk is not known. Several studies have linked obesity and insulin resistance with an increased risk of uric acid stone formation as a result of a defect in renal ammoniogenesis (1). Of note, this association was found to be independent of diet. Hyperinsulinemia has also been shown to have a hypercalciuric effect that could potentially increase the risk of calcium stones (2). Other investigators found higher urinary uric acid levels in obese stone formers compared with non-obese stone formers (3). Taken together, these studies suggest both diet-dependent and diet-independent mechanisms for the increased rate of stone formation. Given the increased difficulty in surgically treating stones in obese patients, efforts should be made not only to correct underlying metabolic risk factors in these patients, but also to encourage weight control.

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Treatment of complete staghorn stones: a prospective randomized comparison of open surgery versus percutaneous nephrolithotomy

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J Urol. 2005; 173: 467-73

Purpose: We studied the role of open surgery versus percutaneous nephrolithotomy (PCNL) in the treatment of complete staghorn stones in a prospective randomized manner.

Materials and Methods: A total of 79 patients with 88 complete staghorn stones, defined as filling the entire collecting system or at least 80% of it, were prospectively randomized for PCNL (43) or open surgery (45). Intraoperative and postoperative morbidity, operative time, hospital stay, and stone clearance at discharge home and followup were compared for both methods. Patients with significant residuals in both groups were subjected to extracorporeal shock wave lithotripsy (Dornier Medical Systems, Inc., Marietta, Georgia) on an outpatient basis. Followup was completed for all cases with a mean duration +/- SD of 4.9 +/- 2.5 months (range 3 to 14). Renal function was evaluated by Tc-mercaptoacetyltriglycine renogram before and after treatment in both groups.

Results: Intraoperative complications in terms of bleeding requiring blood transfusion, and pleural, vascular or ureteral injuries were recorded in 7 patients (16.3%) in the PCNL and 17 (37.8%) in the open surgery groups, a difference of significant value ($p < 0.05$). Major postoperative complications including massive hematuria requiring blood transfusion, septicemia, urinary leakage and wound infection were observed in 8 patients (18.6%) in the PCNL group and in 14 (31.1%) in the open surgery group, a difference of no significant value. PCNL was associated with shorter operative time (127 +/- 30 vs 204 +/- 31 minutes, $p < 0.001$), shorter

hospital stay (6.4 +/- 4.2 vs 10 +/- 4.2 days, $p < 0.001$) and earlier return to work (2.5 +/- 0.8 vs 4.1 +/- 1 weeks, $p < 0.001$). On the other hand both treatment groups were comparable in regard to stone-free rates at discharge home (49% vs 66%) and at followup (74% vs 82%). At followup renal function improved or remained stable in 91% and 86.7% in the PCNL and open surgery groups, respectively.

Conclusions: PCNL is a valuable treatment option for complete staghorn stones with a stone-free rate approaching that of open surgery. Moreover, it has the advantages of lower morbidity, shorter operative time, shorter hospital stay and earlier return to work.

Editorial Comment

In 1997, the AUA Nephrolithiasis Clinical Guidelines Panel performed an extensive literature review to determine the optimal treatment of staghorn calculi (1). At that time, not a single prospective, randomized, trial compared any of the treatment options: SWL, PCNL, combination therapy and open surgery. Based on their review, they recommended PCNL, with or without adjuvant SWL, as preferred treatment for staghorn calculi, because it combined high stone free rates with relatively low morbidity. A new Guidelines Panel recently completed an update of the review process, and changed their recommendation for treatment of most staghorn calculi to PCNL-based therapy because of poorer stone free rates in recent series of combination PCNL/SWL, likely due to heavy reliance on SWL and less on flexible nephroscopy for stone clearance (unpublished). In their review, a single prospective, randomized trial compared SWL with PCNL monotherapy and showed clear superiority of PCNL (2). Open surgery series in the updated review were few, and a decline in success rates is thought to be due to reservation of open surgery for patients with only the most complex staghorn calculi and those requiring extensive reconstruction of the collecting system, as well as to less experience in this technique in the era of minimally invasive surgery.

The current authors performed a prospective, randomized trial comparing PCNL with open surgery for the treatment of complete staghorn calculi. They found that PCNL provided comparable stone free rates to open surgery but with reduced morbidity, shorter hospital length of stay and quicker recovery. These results validate the findings of the Guidelines Panel, and lend further credibility to the recommendation of PCNL-based therapy over open surgery by way of a non-biased comparison of the 2 modalities by a group of investigators with extensive experience in both approaches. Although open surgery has nearly vanished from practice in the U.S., the procedure is still performed in some countries with limited resources and equipment for newer minimally invasive techniques. With this trial, open surgery is relegated to an even more remote position in the armamentarium of surgical treatments for nephrolithiasis.

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ENDOUROLOGY & LAPAROSCOPY

Trends toward laparoscopic nephrectomy at a community hospital

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J Urol. 2005; 173: 547-51

Purpose: For proper indications at university hospitals laparoscopic nephrectomy is often considered the standard of care. At community hospitals past surveys have not demonstrated this change. We describe the changing practice patterns of performing laparoscopic nephrectomies in indicated patients at our community hospital. We reviewed our data on monitoring our training program.

Materials and Methods: A retrospective chart review was performed of 381 consecutive complete nephrectomies performed at our institution from February 2000 to December 2003, including 62 live donor nephrectomies. Patient age, pathological size, operative time, estimated blood loss, duration to solid food intake and duration of hospitalization were compared between open nephrectomy and laparoscopic nephrectomy groups using the Wilcoxon 2-sample test. Surgical practice and surgeon characteristics were also described.

Results: Patients who underwent laparoscopic nephrectomy demonstrated superior postoperative recovery with earlier return to solid diet and shorter hospitalization. The 2 groups were similar in regard to major complication rates. The number of laparoscopic nephrectomies increased annually, while the number of open nephrectomies decreased. The number of laparoscopic urologists increased annually. More importantly laparoscopic urologists performed an increasing number of nephrectomies, while nonlaparoscopic urologists faced a decrease in the number of nephrectomies performed. There appeared to be little evidence of hand assisted laparoscopic nephrectomy as a bridge to learning standard laparoscopic nephrectomy.

Conclusions: Our training paradigm has safely and effectively trained community urologists to perform laparoscopic nephrectomies. Laparoscopic nephrectomy is now considered a standard treatment option along with conventional open surgery and it should be offered to the patient in the medical setting. Although fellowship trained urologists can certainly add expertise to any program, community based hospitals do not have to depend on them.

Editorial Comment

Since Claymann and colleagues described the first laparoscopic radical nephrectomy (LRN) in 1991, the technology and techniques have evolved. Currently, LRN is considered the standard treatment option for renal cancer patients. Although academic investigators have documented the advantages of this minimally invasive procedure and its variations in surgical technique, interestingly, there is little data from the community surgeons' side. This manuscript demonstrates the feasibility, safety and learning curve of this surgical approach in the community setting.

The increase of laparoscopic cases from 8 in 2000 to 52 in 2003 that the authors described revealed a significant annual increase of nephrectomies (open, laparoscopic donor and radical) with less time of hospitalization and resumption of solid food intake without increasing the rate of complications.

The practice includes general, oncological and laparoscopy fellowship trained urologists. Even the urologists that did not receive formal fellowship training were able to take the minimally invasive approach utilizing the hand assist device.

Clearly this data shows that laparoscopic nephrectomies will be widely accepted as treatment of renal cancer and transplantation for potential donors in the community setting.

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Laparoscopic skills training using a webcam trainer

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J Urol. 2005; 173:180-3

Purpose: Many sophisticated and expensive trainers have been developed to assist surgeons in learning basic laparoscopic skills. We developed an inexpensive trainer and evaluated its effectiveness.

Materials and Methods: The webcam laparoscopic training device is composed of a webcam, cardboard box, desk lamp and home computer. This homemade trainer was evaluated against 2 commercially available systems, namely the video Pelvitrainer (Karl Storz Endoscopy, Culver City, California) and the dual mirror Simuview (Simulab Corp., Seattle, Washington). The Pelvitrainer consists of a fiberglass box, single lens optic laparoscope, fiberoptic light source, endoscopic camera and video monitor, while the Simuview trainer uses 2 offset, facing mirrors and an uncovered plastic box. A total of 42 participants without prior laparoscopic training were enrolled in the study and asked to execute 2 tasks, that is peg transfer and pattern cutting. Participants were randomly assigned to 6 groups with each group representing a different permutation of trainers to be used. The time required for participants to complete each task was recorded and differences in performance were calculated. Paired t tests, the Wilcoxon signed rank test and ANOVA were performed to analyze the statistical difference in performance times for all conditions.

Results: Statistical analyses of the 2 tasks showed no significant difference for the video and webcam trainers. However, the mirror trainer gave significantly higher outcome values for tasks 1 and 2 compared to the video ($p = 0.01$ and < 0.01) and webcam ($p = 0.04$ and < 0.01 , respectively) methods. ANOVA indicated no overall difference for tasks 1 and 2 across the orderings ($p = 0.36$ and 0.99 , respectively). However, by attempt 3 the time required to complete the skill tests decreased significantly for all 3 trainers (each $p < 0.01$).

Conclusions: Our homemade webcam system is comparable in function to the more elaborate video trainer but superior to the dual mirror trainer. For novice laparoscopists we believe that the webcam system is an inexpensive and effective laparoscopic training device. Furthermore, the webcam system also allows instant recording and review of techniques.

Editorial Comment

The lack of well defined training to optimize the learning curve for laparoscopic procedures is still a challenge. The old saying, see one, do one, teach one, does not seem to apply to laparoscopy, as the authors mentioned. The study evaluated dry lab training for laparoscopic skills using established tasks with different types of trainers: 1) Pelvitrainer (\$2,095) 2) Simuview (\$300), and 3) a homemade webcam system (\$30). Forty two participants without prior laparoscopic training were asked to execute 2 basic tasks: 1) peg transfer (task 1) and 2) pattern cutting (task 2). The participants were randomly assigned to different groups. The time required for participants to complete each task was recorded and differences in performance were calculated. Although the Simuview was effective, it showed significantly worse performance time compared to the other 2 systems,

since it did not provide magnification. The authors concluded that the homemade laparoscopic trainer offers easy setup and use with comparable quality to the fancier pelvic trainers allowing the user to record and play back sessions for personal review or to have a distant proctor assisting via the Internet.

Unquestionably, better educational and training tools need to be developed to decrease the learning curve and minimize complications in laparoscopic surgery. Certainly virtual simulation models as well as training programs and centers are in need not only to grant the initial training but also to provide assistance in the clinical setting.

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IMAGING

Significance of the pseudocapsule on MRI of renal neoplasms and its potential application for local staging: a retrospective study

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Objective: The purpose of our study was to evaluate the role of MRI in showing a pseudocapsule for local staging of renal tumors, and its potential application to select patients for partial surgery.

Materials and Methods: Eighty tumors (73 renal cell carcinomas [RCCs] and seven oncocytomas) were preoperatively evaluated by MRI. MRI findings were assessed with a special focus on perinephric fat and pseudocapsule. Correlations were performed with pathologic staging after surgery.

Results: At pathology, a pseudocapsule was recognized in 79 cases. Twenty-three RCC were staged pT3a (21 clear cell; two papillary). MR images exhibited a pseudocapsule in 90% of cases as a hypointense rim surrounding the tumor on T2-weighted images. MRI findings concerning isolated analysis of the pseudocapsule for differentiating stage T1/T2 from T3a were sensitivity: 86%, 50%; specificity: 95%, 92%; positive predictive value: 95%, 33%; negative predictive value: 88%, 92%; and accuracy: 93%, 89%, for clear cell and papillary types, respectively. For stage T3a, with both abnormalities of the pseudocapsule and perirenal fat, results were, for overall RCC sensitivity: 84%; specificity: 95%; positive predictive value: 91%; negative predictive value: 91%; and accuracy: 91%.

Conclusion: The identification of the pseudocapsule offers an additional value for local staging by MRI. The presence of an intact pseudocapsule is a sign of lack of perinephric fat invasion. It is more likely to predict that the tumor can be removed by partial surgery.

Editorial Comment

The identification of a well defined pseudocapsule around a small tumor has recently been considered a very important finding for the local staging of a possible renal cell carcinoma. As we know this pseudocapsule represents a narrow area of fibrosis and normal renal parenchyma, which is displaced by the slow growing tumor. The demonstration of a well defined pseudocapsule by helical CT indicates that in the majority of

cases the renal tumor is confined to the kidney (stage T1), thus amenable to conservative surgery: open partial nephrectomy or laparoscopic partial nephrectomy (1). The identification of this pseudocapsule by CT has 95% accuracy for predicting that the tumor is confined to the kidney. The authors used in this study MR imaging findings for identification of the pseudocapsule and their results confirm the conclusion of the study using multidetector CT. The authors shows that the presence of pseudocapsule (thin, regular, linear band with hypo- intensity signal in both T1 and T2 –weighted images), is a reliable imaging sign to predict lack of perinephric fat invasion. Consequently, this sign is useful for differentiating stage T1/T2 from stage T3a, with a 92% positive predictive value .When there is disruption of this pseudocapsule and consequent opacification of the perirenal fat manifested as spiculation around the mass, the overall accuracy for predicting stage T3a is 91% .This finding is very useful for adequate surgical management of renal tumors since in many centers stage T3a tumor is considered a limitation for conservative renal surgery.

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CT urography of urinary diversions with enhanced CT digital radiography: preliminary experience

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Objective: The purpose of this study was to determine if 3D-rendered CT urography (CTU) depicts both normal and abnormal findings in patients with urinary diversions and if the addition of contrast-enhanced CT digital radiography (CTDR) improves opacification of the urinary collecting system.

Materials and Methods: Thirty CTU and contrast-enhanced CTDR examinations were performed in 24 patients who underwent cystectomy for bladder cancer. Indications for evaluation included hematuria, tumor surveillance, or suspected diversion malfunction. All examinations were evaluated without knowledge of the stage or grade of a patient's tumor and were compared with the clinical records. Opacification of the urinary collecting system was evaluated with 3D CTU alone, contrast-enhanced CTDR alone, and combined CTU and CTDR.

Results: Nine abnormalities were identified including distal ureteral strictures (n = 4), vascular compression of the mid left ureter (n = 1), scarring of the mid right pole infundibulum (n = 1), bilateral hydronephrosis and hydroureter (n = 1), urinary reservoir calculus (n = 1), and tumor recurrence invading the afferent limb of the neobladder (n = 1). Eight of the nine detected abnormalities were surgically or pathologically confirmed. All abnormalities were identified on all three imaging techniques but were best seen on 3D CTU and enhanced CTDR images. Incomplete opacification of the urinary collecting system occurred in 17 patients with CTU alone, 12 patients with contrast-enhanced CTDR alone, and nine patients with combined CTU and contrast-enhanced CTDR. Compared with CTU alone, the combined technique of 3D CTU and contrast-enhanced CTDR improved opacification by a statistically significant difference (p = 0.037).

Conclusion: CTU with 3D rendering can accurately depict both normal and abnormal postoperative findings in patients with urinary diversions. Adding enhanced CTDR can improve visualization of the urinary collecting system.

Editorial Comment

Radiologic evaluation of urinary diversion has 4 main objectives: the detection of postoperative complications, the detection of newly developed urothelial tumors, to monitor upper tract distention and to detect metastasis. Various surgical techniques that are used in continent and noncontinent diversions alter the normal anatomy and make the radiologic interpretation difficult. An accurate interpretation can be made only if radiologists become familiar with the various surgical procedures and the appearances of various postoperative anatomic changes.

The type of imaging procedure and the frequency of imaging is dictated by the urologist preference. In most cases, early complications require urgent radiographic evaluation, usually with intravenous urography or CT. Late complications of urinary diversion are more often insidious, and several imaging techniques have been used: intravenous urography, contrast enhanced CT, pouchograms, fluoroscopic loopogram or CT loopogram. The authors present their results where a multidetector 3D-CT urography associated with a digital scout view of the abdomen and pelvis after intravenous contrast injection (enhanced CTDR), was performed in 24 patients treated by cystectomy or cystoprostatectomy with subsequent urinary diversion. They compared the 2 types of images in the opacification of the urinary collecting system and evaluated whether one technique was superior or complementary to the other for the detection of any type of abnormalities. These patients presented with ileal conduits, right colonic pouches and ileal neobladders. The combined imaging technique of CTU and enhanced CTDR allowed total opacification of the urinary tract in 21 (70%) of 30 cases studied. They found that the middle and distal left ureteral segments and the left ureteroenteric anastomosis were the most common sites that failed to opacify on either CTU alone, enhanced CTDR, or combined CTU and enhanced CTDR. Even with this drawback, there are numerous advantages of CTU over IV urography and fluoroscopic loopogram. The advantages include better evaluation of distal ureter narrowing, tumor recurrence, better detection and localization of urinary calculi and fistulae, identification and characterization of small renal masses, and detection of extra urinary disease. Main limitations of loopogram include: incapacity of retrograde opacification of the upper urinary tract, incapacity to evaluate renal function, and limitation to detect renal masses, tumor recurrence or extra urinary disease. We have used the same technique presented by the authors, for the evaluation of 16 patients with urinary diversions. Similarly, we have observed more difficulties for adequate opacification of the distal portion of the left ureter. In order to improve this visualization, we have added recently, a 250-mL saline bolus during excretory phase. This modification in the technique allowed us to obtain improved opacification of the distal portion of left ureter in 37% of patients. This modification was also useful for better demonstration of narrow fistulas in 2 patients. This is a very good, very well written and nicely illustrated paper. As a radiologist, I found it extremely useful for understanding all the surgical details of the more common surgical procedures used for urinary diversion. There is no doubt that multidetector CTU with 3D rendering has the potential to be the imaging technique of choice for the initial evaluation of patients with urinary diversion.

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UROGENITAL TRAUMA

Renovascular injury: an argument for renal preservation

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Background: Renovascular injury is uncommon among children. This study hypothesized that preservation of the severely injured kidney can be achieved safely without renal insufficiency, postinjury hypertension, or the need for hemodialysis.

Methods: Retrospective chart review of renal injuries seen between 1997 and 2001 at a level 1 pediatric trauma center was conducted. Severity of injury was graded by the American Association for the Surgery of Trauma Organ Injury Severity Scale. The outcome variables included the need for hemodialysis, impaired renal function (creatinine), and postinjury hypertension.

Results: In this study, 34 children presented with grade 1, 2, or 3 injury (74%), whereas 13 children presented with grade 4 or 5 renovascular injury (28%). The children with unilateral renovascular injury who underwent either nephrectomy or renal preservation had comparable outcomes with no hypertension, hemodialysis, or renal insufficiency in either group.

Conclusions: The treatment outcomes were not different between the patients who underwent renal preservation and those who had immediate nephrectomy. The authors conclude that renal preservation should be attempted for all children with grade 4 or 5 renovascular injury.

Editorial Comment

In adults the consensus seems to be that major renovascular injury is probably going to result in nephrectomy (see article below). Those with complete avulsion are usually bleeding briskly and need speedy vascular control to save their life; those with renal artery thrombosis nearly always eventually require nephrectomy even if revascularization is attempted (see paper below) and it is starting to be seen that even venous lacerations have a high nephrectomy rate even in the best hands (1). This pediatric series of 13 patients with grade IV (7 patients) or grade V (6 patients) renovascular injury, supports observing these patients without nephrectomy if possible. Six children in this series who had no treatment seemed to do as well as 4 that had nephrectomy for their injury. Even one child with bilateral hilar injuries (usually listed as a reason to attempt vascular repair) was observed without vessel repair (although he later developed renovascular hypertension). Unfortunately, the authors do not specify the outcomes of those with grade IV injuries compared to grade V. Obviously those with grade V avulsions should be expected to do much worse! In any case, this paper is further evidence that you should at least initially consider expectant management of renal trauma - in a pediatric subset with nonexsanguinating renovascular trauma.

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Outcome after major renovascular injuries: a Western trauma association multicenter report

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J Trauma. 2000; 49: 1116-22

Background: Major renal vascular injuries are uncommon and are frequently associated with a poor outcome. In addition to renal dysfunction, posttraumatic renovascular hypertension may result, although the true incidence of this complication is unknown. The objective of this study was to describe the factors contributing to outcome after major renovascular trauma. We hypothesized that the highest percentage of renal salvage would be achieved by minimizing the time from injury to repair.

Methods: This was a retrospective chart review over a 16-year period conducted at six university trauma centers of patients with American Association for the Surgery of Trauma grade IV/V renal injuries surviving longer than 24 hours. Postinjury renal function with poor outcome was defined as renal failure requiring dialysis, serum creatinine greater than or equal to 2 mg/dL, renal scan showing less than 25% function of the injured kidney, postinjury hypertension requiring treatment, or delayed nephrectomy. Data collected for analysis included demographics, mechanism of injury, presence of shock, presence of hematuria, associated injuries, type of renal injury (major artery, renal vein, segmental artery), type of repair (primary vascular repair, revascularization, observation, nephrectomy), time from injury to definitive renal surgery, and type of surgeon performing the operation (urologist, vascular surgeon, trauma surgeon).

Results: Eighty-nine patients met inclusion criteria; 49% were injured from blunt mechanisms. Patients with blunt injuries were 2.29 times more likely to have a poor outcome compared with those with penetrating injuries. Similarly, the odds ratio of having a poor outcome with a grade V injury ($n = 32$) versus grade IV ($n = 57$) was 2.2 ($p = 0.085$). Arterial repairs had significantly worse outcomes than vein repairs ($p = 0.005$). Neither the time to definitive surgery nor the operating surgeon's specialty significantly affected outcome. Ten percent (nine patients) developed hypertension or renal failure postoperatively: three had immediate nephrectomies, four had arterial repairs with one intraoperative failure requiring nephrectomy, and two were observed. Of the 20 good outcomes for grade V injuries, 15 had immediate nephrectomy, 1 had a renal artery repair, 1 had a bypass graft, 1 underwent a partial nephrectomy, and 2 were observed.

Conclusion: Factors associated with a poor outcome following renovascular injuries include blunt trauma, the presence of a grade V injury, and an attempted arterial repair. Patients with blunt major vascular injuries (grade V) are likely to have associated major parenchymal disruption, which contributes to the poor function of the revascularized kidney. These patients may be best served by immediate nephrectomy, provided that there is a functioning contralateral kidney.

Editorial Comment

This is not the newest paper, but it is one of the best. It establishes that “conservative” management of adult renovascular injury probably means “nephrectomy instead of vascular repair”. In a multicenter series of 89 patients with renovascular injuries, 3 of 4 patients that had a primary repair had a “poor” result, while only 3 of 18 of those with a primary nephrectomy had a poor result. In general, an attempted bypass graft was 15 times more likely to result in a poor result for the patient than nephrectomy. These data again support at least a trial of nonoperative treatment of the patient, and failing that, a “conservative” approach by performing nephrectomy instead of vascular repair. In this dataset, some patients who were initially observed eventually needed the kidney to be removed, but this could be achieved after a few days when the patient was

stable. Two patients developed renovascular hypertension, but these patients had vascular repair instead of kidney removal.

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PATHOLOGY

Current practice of diagnosis and reporting of PIN and glandular atypia among genitourinary (GU) pathologists

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Background: Although there is a sizable body of literature relating to PIN and atypical glands suspicious for cancer, many areas remain unresolved and practice patterns are varied.

Design: A questionnaire was sent to 93 GU pathologists in countries around the world with the purpose to survey current practices of diagnosing and reporting prostate needle biopsies with PIN and atypia.

Results: The response rate was 69%. The term PIN was universally acknowledged for preneoplastic lesions. However, if cytological or architectural atypia were pronounced, 44% would use intraductal carcinoma.

PIN was graded by 83%, usually as low/high grade PIN (LGPIN/HGPIN) or, more commonly, as HGPIN only. Lesions that may qualify for LGPIN were never mentioned (58%) or only rarely mentioned in the descriptive part of the report (25%). Architectural patterns of PIN were usually not specified (81%) and those who specified never commented on their significance. The majority (75%) did not comment that HGPIN is premalignant and 63% would not recommend a repeat biopsy. With invasive cancer also present, 69% would still mention HGPIN. Basal cell stains were used in <5% of HGPIN cases (67%). HGPIN would be diagnosed by 56% in the absence of prominent nucleoli, most commonly based on prominent pleomorphism (53%), marked hyperchromasia (47%) or mitotic figures (28%). Among diagnostic criteria for HGPIN were different degrees of nucleolar prominence (52%), or nucleoli seen in at least 10% of cells (33%). Number of cores involved with HGPIN was specified by half of the respondents.

Lesions suspicious for but not diagnostic of carcinoma were reported as ASAP (47%) or atypia/atypical glands/suspicious (48%). Degree of suspicion of cancer in atypical acinar lesions was defined by 41%. Only 34% always recommended repeat biopsy, while 30% would do it depending on referring doctor and 13% depending on patient age.

Conclusions: For controversial areas relating to PIN and atypical glands, our survey provides information to general pathologists about how GU pathologists deal with these issues.

Editorial Comment

This is a timely topic for the urologists on how pathologists report PIN and ASAP. Atypical prostate epithelium was described as early as 1926 (1). Since then the lesion was referred as atypical hyperplasia, atypical lesions, dysplastic lesions, intraductal dysplasia, carcinoma in situ and premalignant lesion among many other denominations. In 1989 (2), during an international workshop sponsored by the American Cancer

Society in Bethesda, Maryland, in order to unifying such diverse names, it was suggested that the best denomination for such lesions would be prostatic intraepithelial neoplasia (PIN). In 1987, Bostwick & Brawer (3) had described 3 histologic grades for PIN. In the workshop of 1989 it was suggested to refer to grade 1 as low-grade PIN and to grades 2 and 3 as high-grade PIN. Most pathologists do not report grade 1 (low-grade) PIN. The main reasons are: 1) there is a lack of reproducibility in its diagnosis (4); and, 2) the finding of low-grade PIN on needle biopsy does not confer an increased likelihood of finding prostate cancer in a given individual on subsequent biopsy (5).

The term atypical small acinar proliferation (ASAP) has been proposed for lesions that contain insufficient cytological or architectural atypia to establish a definitive diagnosis of cancer (6). According to Iczkowski et al. (6) the major causes for the report of ASAP are: 1) small size of the focus (70% of cases); disappearance on step levels (61%); and, 3) lack of significant cytologic abnormalities. It is very important for the urologist to understand that ASAP is not an entity. The term atypical small acinar proliferation may be misunderstood as adenosis, PIN or other conditions. In order to avoid this problem and considering that ASAP is an indication for rebiopsy, I have advised the pathologists to use the term suspicious but not diagnostic for adenocarcinoma instead of ASAP.

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Differences in clinical outcome between primary Gleason grades 3 and 4: an analysis of 228 patients with a pathological Gleason score 7

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Mod Pathol. 2005; 18 (suppl. 1): abstract #665, 144A

Background: In radical prostatectomy specimens, Gleason score 7 is among the most commonly assigned scores to prostate carcinoma accounting for 30-50% of the cases. Gleason score 7 is different from other more differentiated prostate carcinomas (tumors of Gleason scores 5 and 6), with a significantly worse outcome and higher rate of recurrence.

Design: Five hundred and four patients underwent radical prostatectomy for prostate cancer. Two hundred and twenty-eight of the patients (45%) had a Gleason score of 7. Cases were analyzed for a variety of clinical and pathologic parameters.

Results: Among 228 prostatic adenocarcinomas with Gleason score 7, 91(40%) had a primary Gleason grade of 4 and 137 (60%) had a primary grade of 3. Patients of the former group were more likely to have a higher pathological stage ($P = 0.004$), a higher rate of PSA recurrence ($P = 0.008$), and a higher incidence of vascular invasion ($P = 0.039$). In multiple logistic regression controlling for tumor stage ($P = 0.046$), surgical margin status ($P = 0.0003$), vascular invasion ($P = 0.033$), and preoperative PSA ($P = 0.015$), the primary Gleason grade was not an independent predictor of PSA recurrence ($P = 0.141$).

Conclusions: Among patients with Gleason score 7, primary Gleason grade 4 carries the likelihood of higher tumor stage, higher rate of PSA recurrence and higher incidence of vascular invasion. It does not however independently predict a worse outcome after controlling for other known prognostic parameters that are associated with disease progression.

Editorial Comment

There are evidences showing that Gleason grade 4/5 may be superior to the Gleason score as a predictor of PSA progression following surgery (1,2). There are several ways to evaluate grade 4/5: primary Gleason grade 4 or 5, secondary Gleason grade 4 or 5, % of Gleason grade 4, % of Gleason 5 and combined % of Gleason grade 4 and 5 (3).

Reporting of percentage Gleason grade 4/5 is cumbersome: there is the question of the reliability of the estimate (interobserver agreement) and how to quantitate percentage 4/5 cancer (4). It is our opinion that the easiest and straightforward way to evaluate the importance of grade 4/5 is to consider it either as the primary or secondary grade. In the present study of Hattab et al., grade 4 was considered either as the primary or the secondary grade in cases of Gleason score 7.

In a recent quite similar study done in our Institution, we found that Gleason score ≥ 7 or Gleason predominant grade 4/5 were more likely to have higher preoperative PSA, more extensive tumors, extraprostatic extension (pT3a) and seminal vesicle invasion (pT3b). However, only patients with Gleason predominant grade 4/5 had a statistical tendency for a shorter time to biochemical progression following radical prostatectomy (5).

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INVESTIGATIVE UROLOGY

Compositional changes of collagen and glycosaminoglycans in the tunica albuginea and corpus cavernosum from the human penis during the fetal and postnatal periods

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J Urol. 2005; 173: 1039-43

Purpose: We investigated the composition of collagen and glycosaminoglycans (GAGs) in the corpus cavernosum (CC) and tunica albuginea (TA) of normal human penises.

Materials and Methods: Penises were obtained from a 6-month-old child (group 1), a 2-year-old child (group 2), 18 to 34-year-old adults (group 3), 37 to 53-year-old adults (group 4) and 22 fetuses at 17.2 to 33.3 menstrual weeks (group 5). Total GAG and collagen concentrations were expressed per mg dry tissue and proportions of GAG species were determined by agarose electrophoresis and ion exchange chromatography.

Results: The GAG concentration in group 1 CC and TA was 1.32 and 0.52 microg/mg, respectively, and thereafter it increased noticeably. TA collagen concentration followed a similar pattern. TA had more collagen than CC in groups 3 (mean $\pm$ SD 93.41 $\pm$ 6.17 vs 53.77 $\pm$ 11.18 microg/mg, $p < 0.001$) and 4 (89.94 $\pm$ 5.53 vs 55.39 $\pm$ 5.89 microg/mg, $p < 0.01$). In these groups TA and CC differed markedly in the proportion of hyaluronan, heparan sulfate and dermatan sulfate. In TA group 4 had slightly less hyaluronan and more chondroitin sulfate than group 3 but in CC the GAG proportions were similar. Collagen content in the whole fetal penis correlated with gestational age ($r = 0.78$, $p < 0.001$).

Conclusions: Collagen and the GAG concentration in the human penis undergo extensive modifications during development and shortly after birth but from ages 2 to approximately 46 years changes are limited to the proportion of GAG species in TA from older individuals. Reflecting diverse biomechanical roles, the extracellular matrix of CC and TA are markedly different.

Editorial Comment

It is well known that depending on function and biomechanical properties, extracellular matrix (ECM) differs noticeably among tissues. The present paper demonstrated that proportions of hyaluronan, heparan sulfate and dermatan sulfate are different in corpus cavernosum and tunica albuginea of human penis, indicating the different properties of these structures. In terms of tissue engineering, their compositions should be taken into account when choosing the ideal material for surgical reconstruction of penile tissues.

Interestingly, this paper demonstrates that the most significant ECM developmental changes in the penis occur between 17 and 33 weeks of gestation, which were reflected by important increase in collagen concentrations. Surprisingly, collagen and glycosaminoglycans concentrations in the corpus cavernosum and tunica albuginea remain unchanged from ages 2 to 36-53 years, suggesting that the hormonal alterations that markedly affect penile morphology and function with the onset of adolescence have little or no effect on the overall collagen and GAG composition of penile erectile tissues.

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Maternal gestational protein-calorie restriction decreases the number of glomeruli and causes glomerular hypertrophy in adult hypertensive rats

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Am J Obstet Gynecol. 2005; 192: 945–51

Objective: This work analyzed the renal function and structure in offspring rats that were submitted to maternal protein-calorie restriction during prenatal or lactation periods.

Study design: Kidneys from adult offspring were studied. Animals from mothers that were submitted to food restriction were separated in 3 groups: control, prenatal restriction, and lactation restriction. Blood pressure, microalbuminuria, and glomerular filtration rate were determined. Kidney cortical remodeling was analyzed with stereology; volume-weighted glomerular volume and the number of glomeruli were estimated.

Results: Adult prenatal restriction offspring showed enhanced microalbuminuria, decreased glomerular filtration rate, and hypertension; their kidneys showed a smaller number of hypertrophied glomeruli than control and lactation restriction animals.

Conclusion: Maternal prenatal protein-calorie restriction in rats causes kidney disease in adult offspring, which is characterized by hypertension and renal dysfunction and suggests secondary kidney remodeling because of an impairment of glomerulogenesis.

Editorial Comment

This is one more important study from the State University of Rio de Janeiro on the effects of maternal protein and energy malnutrition during prenatal or lactation periods.

After an extensive study using different methodologies, the authors found that rats prenatally submitted to undernutrition became hypertensive and proteinuric. On the other hand, the effects on the renal function and blood pressure are not evident when the protein-calorie restriction takes place after birth.

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RECONSTRUCTIVE UROLOGY

Urethral reconstruction after erosion of slings in women

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Curr Opin Urol. 2004; 14: 335-8

Purpose of Review: The purpose of this review is to summarize the recent peer review literature and provide expert opinion about the diagnosis and treatment of sling erosions.

Recent Findings: The incidence of sling erosion depends partly on the composition of the sling. Synthetic slings, particularly those made of woven polyester and other tightly woven material erode 15 times more often than autologous, allograft and xenograft slings. The presenting symptoms for all types of sling erosions include

urinary retention, urge and mixed incontinence, but synthetic sling erosions often present with additional symptoms, including vaginal discharge, vaginal pain/pressure, suprapubic pain, and recurrent urinary tract infection. The diagnosis is made by cystoscopy. For synthetic sling erosions, it is generally agreed that the entire sling and as much foreign material (bone anchors, screws and sutures) as possible should be removed and the urethra repaired. For non-synthetic sling erosions, incision or partial excision of the sling and urethral closure suffices. The success rate for urethral repair ranges from 89 to 100%, but unless an anti-incontinence procedure is performed concomitantly, the likelihood of postoperative incontinence ranges from 44 to 83%. When synchronous anti-incontinence surgery was performed the anatomical success rate was 96% and the continence rate 87%.

Summary: Erosions of urinary slings are rare, but synthetic slings erode 15 times more often than non-synthetic slings. The anatomical success rate is very high after a single operation, but unless a concomitant anti-incontinence operation is performed, the likelihood of postoperative sphincteric incontinence is very high.

Rising awareness of the complications of synthetic slings

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Curr Opin Urol. 2004; 14: 317-21

Purpose of Review: This article will review the current literature on the complications of synthetic suburethral slings used in the treatment of stress urinary incontinence and the management of these complications.

Recent Findings: Loosely applied mid-urethral synthetic slings are becoming the treatment of choice in the management of stress urinary incontinence. Despite the ease of carrying out these procedures there is still a learning curve and, whilst the current literature shows there has been a significant reduction in the complication rate in recent years with the use of modern synthetic slings, they still occur and can be a significant cause of morbidity. There has been interest in developing better imaging techniques for both establishing early diagnosis and in assisting in the treatment of complications; magnetic resonance imaging of the urethra has been one of the modalities that has been investigated. Further work is needed to predict those who are more likely to develop complications during the placement of suburethral slings; the use of urodynamic procedures has shown equivocal results. Inevitably with more experience the techniques have evolved for the management of complications, such as the treatment of urethral obstruction with transvaginal sling incision.

Summary: Synthetic materials for slings provide an effective and safe method for treating urinary stress incontinence in women, and have delivered improved efficacy; nevertheless, although the incidence of complications has significantly reduced in recent years, they still represent a significant and not unsubstantial morbidity.

Editorial Comment

Both papers by well-known opinion leaders outline the problems, which may occur with sling operations in the treatment of stress urinary incontinence. Especially synthetic slings tend to erode the urethra 15 times more often than biological materials. Although allograft and xenograft slings seem to be the better solution when it comes to complications of the adjacent urethra remnant traces of donor desoxyribonucleic acid fragments or small protein structures are present and their long-term effect on the recipient is still unknown. Bhargava & Chapple stress the fact that complications from synthetic sling materials have declined in recent years and the management of complications has improved due to an increasing experience with these problems. However, sling complications still represent a “significant and not unsubstantial morbidity”.

Should we abandon sling operations in women with stress urinary incontinence? By no means. The majority of the patients can be successfully treated if the indication for the operation was appropriate. The fact that some of the sling operations can be done under regional or local anesthesia and with a short operating time should not make such a procedure the operation of choice for all women with stress urinary incontinence. An additional important fact is the type of sling material used. Whenever possible a material taken from the patient to be operated such as rectus fascia or fascia lata is the material of choice because it considerably reduces both urethral erosions and possible systemic side effects of cadaveric or xenograft materials.

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UROLOGICAL ONCOLOGY

Cancer progression and survival rates following anatomical radical retropubic prostatectomy in 3,478 consecutive patients: long-term results

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J Urol. 2004; 172: 910-4

Purpose: We updated a long-term cancer control outcome in a large anatomical radical retropubic prostatectomy (RRP) series. We also evaluated the perioperative parameters that predict cancer specific outcomes following surgery.

Materials and Methods: From May 1983 to February 2003, 1 surgeon (WJC) performed RRP in 3,478 consecutive men. Patients were followed with semiannual serum prostate specific antigen (PSA) tests and annual digital rectal examinations. We used Kaplan-Meier product limit estimates to calculate actuarial 10-year probabilities of biochemical progression-free survival, cancer specific survival and overall survival. Multivariate Cox proportional hazards models were used to determine independent perioperative predictors of cancer progression.

Results: At a mean followup of 65 months (range 0 to 233) actuarial 10-year biochemical progression-free, cancer specific and overall survival probabilities were 68%, 97% and 83%, respectively. On multivariate analysis biochemical progression-free survival probability was significantly associated with preoperative PSA, clinical tumor stage, Gleason sum, pathological stage and treatment era. Cancer specific survival and overall survival rates were also significantly associated with clinicopathological parameters.

Conclusions: RRP can be performed with excellent survival outcomes. Favorable clinicopathological parameters and treatment in the PSA era are associated with improved cancer control.

Editorial Comment

This paper is very valid as it describes the long-term outcome of a very large cohort of patients after radical prostatectomy. Notably, all patients have been operated by a single surgeon (W. Catalona), thus certifying best results by a high-volume urologist. The most interesting results are given as PSA progression-free survival data (defined as detectable PSA > 0.2 ng/mL) and are therefore comparable to other, especially nonsurgical data (see following comment). Biochemical progression was 20% at 5 and 32% at 10 years. A closer look into the Kaplan Meier curves reveals more truth: in very low-risk patients with PSA < 2.6 ng/mL around 10%

showed PSA progression after 150 months, for PSA 2.6 - 4 ng/mL roughly 20% and PSA 4 -10 ng/mL roughly 25% had biochemical progression after 150 months. Notably, these patients are considered low risk. With PSA > 10 less than 50% of patients remained progression free after 150 months. Another look is worthwhile on the curve showing Gleason grades and biochemical progression. In Gleason 2-6 around 20% of patients have failed after 100 months of follow-up, with a continuously decreasing curve. Altogether these data give a clear view on the advantages and especially, the limits of radical prostatectomy and should be considered if this procedure is advocated to men with prostate cancer.

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Prostate cancer in a large prostate is associated with a decreased prostate specific antigen failure rate after brachytherapy

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J Urol. 2005; 173: 79-81

Purpose: A large prostate has been found to correlate with improved prostate cancer survival in men undergoing radical prostatectomy. In the current study we analyzed the relationship of prostate size and prostate specific antigen (PSA) failure in men undergoing brachytherapy for localized prostate cancer.

Materials and Methods: We studied data on 613 men who had undergone I radioactive seed implantation. Average patient age +/- SD was 65 +/- 7.2 years. Average prostate volume ultrasonically measured at seed insertion was 40 +/- 15 ml. All patients had a minimum of 2 years of followup.

Results: Men with a large prostate had increased freedom from failure compared to men with a small prostate. Failure time in men with an intermediate size prostate was between that for large and small prostates. This difference in failure rates was significant (log rank test $p = 0.0002$). We further analyzed our data with Cox regression. Large prostate size significantly correlated with increased time to PSA failure ($p = 0.013$) and it was independent of the significant effects of Gleason score, PSA, disease stage ($p < 0.001$), minimal radiation dose covering 90% of prostate volume ($p = 0.008$) and hormone treatment, including androgen ablation ($p = 0.001$).

Conclusions: Some investigators have postulated that paracrine signals acting to regulate epithelial proliferation in benign prostatic hypertrophy have beneficial influences on coexistent prostate cancer. Our finding that the effect of prostate size is independent of Gleason score, PSA and disease stage supports the paracrine signal mechanism. If a circulating substance, such as a cytokine, might be responsible for improved survival, this substance might be useful for treating prostate cancer. Moreover, since we found that prostate size is independent of PSA, Gleason score and tumor stage for predicting outcome, we hypothesize that patients with a small prostate treated with brachytherapy might benefit from hormone treatment and larger radiation doses. These measures are now generally reserved for men with more advanced tumors, higher PSA and increased Gleason scores.

Editorial Comment

On first approach the data on the treatment of prostates of different sizes by brachytherapy are given. In a closer look this paper bears outcome data of one of the largest cohorts of permanent interstitial seed (LDR) brachytherapy treated patients with a long term follow up of 140 months. Therefore, this paper should be read

carefully and be compared to the above cited on.

Again, outcomes for low, intermediate and high-risk patients are given as PSA-progression-free survival data (defined as 3 consecutive PSA increases, ASTRO criteria).

In low-risk patients around 95% had no progression after 140 months. For intermediate risk patients roughly 12% and for high-risk patients roughly 45% had biochemical progression after 140 months. Interestingly, the curves do not show any further decrease and remain linear 75 months after treatment. With these 2 papers in mind, brachytherapy can no longer be considered an inferior therapeutic option to radical prostatectomy in men with localized prostate cancer.

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FEMALE UROLOGY

Preoperative pressure-flow studies: useful variables to predict the outcome of continence surgery

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BJU Int. 2004; 94: 1296-9

Objective: To determine whether the acceleration of flow rate (AFR), pressure flow variables and urethral pressure profilometry (UPP) measurements might have a role in evaluating women with urodynamic stress incontinence (USI), to predict the surgical outcome and de novo detrusor overactivity after Burch colposuspension.

Patients and Methods: Women with a urodynamic diagnosis of USI (209) who had a modified Burch colposuspension were assessed retrospectively. The AFR, the opening (ODP) and closing detrusor pressure (CDP), DP at maximum flow rate and UPP values were calculated for each woman before surgery.

Results: The preoperative AFR was significantly higher in women who developed de novo detrusor overactivity after surgery. The women who had persistent USI after colposuspension had significantly lower preoperative ODP and CDP than women who were continent after colposuspension. Other variables were not significantly different between the groups of women.

Conclusions: The AFR and ODP appear to be useful preoperative measures to predict the outcome of continence surgery and the emergence of de novo detrusor overactivity.

Editorial Comment

The authors review a population of patients who underwent Burch colposuspension and analyze urodynamic variables (acceleration of flow rate, pressure flow variables and urethral pressure profiles) both preoperatively and postoperatively. The findings were then used to examine their predictive power for surgical outcome and de novo detrusor overactivity. The authors found that acceleration of flow rate and opening detrusor pressure appears to have promise as a preoperative gauge in the incidence of de novo detrusor overactivity while urethral pressure profiles did not provide any particularly illuminating factor.

The authors should be commended for their thorough review of urodynamic variables to help assist the surgeon in predicting and potentially avoiding inadvertent outcomes from anti-incontinence surgery. Their discussion of acceleration of flow rate is interesting for this urodynamic test does not have an extremely popular

penetration as a preoperative urodynamic study. That the authors noted that the urethral pressure profiles were not particularly useful is not overly surprising in view that past authors have found no significant difference in resting urethral pressure profile and functioning urethral profile before and after anti-incontinence surgery (1). In addition, the potential puzzling nature of urethral pressure profiles pre and post operatively has been discussed by others (2).

The authors should be complimented on their discussion section, especially their thoughts on the association of opening and closing detrusor pressure and successful surgery. I recommend this paper highly to those surgeons actively performing active anti-incontinence operations as well as those with an active interest in urodynamics.

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Randomized, double-blind placebo- and tolterodine-controlled trial of the once-daily antimuscarinic agent solifenacin in patients with symptomatic overactive bladder

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Objective: To assess in a phase 3a trial the efficacy of solifenacin succinate, a once-daily oral antimuscarinic agent in development at 5-mg and 10-mg dosage strengths, for the treatment of overactive bladder (OAB) (Yamanouchi Pharmaceutical Co. Ltd, Tokyo, Japan) compared with placebo in patients with symptoms of OAB, i.e. urgency, incontinence, and frequency, with additional objectives being to assess the safety and tolerability of solifenacin and to compare the efficacy and safety of solifenacin with tolterodine 2 mg twice daily.

Patients and Methods: The study was an international, multicentre, randomized, double-blind, tolterodine- and placebo-controlled trial conducted at 98 centres. Adult patients with symptomatic OAB for > or = 3 months were eligible; after a single-blind 2-week placebo run-in period patients were randomized equally to a 12-week double-blind treatment with either tolterodine 2 mg twice daily, placebo, solifenacin 5 mg or 10 mg once daily. Efficacy variables included change from baseline in the mean number of urgency, incontinence and urge incontinence episodes, and change from baseline in voids/24 h and mean volume voided/void.

Results: In all, 1281 patients were enrolled, 1081 randomized and 1077 treated; 1033 were evaluated for efficacy. Compared with placebo, the change from baseline (-1.41, -32.7%) in the mean number of urgency episodes per 24 h was statistically significantly lower with solifenacin 5 mg (-2.85, -51.9%) and 10 mg (-3.07, -54.7%; both $P < 0.001$), but not with tolterodine (-2.05, -37.9%; $P = 0.0511$). There was a statistically insignificant decrease in episodes of incontinence with tolterodine (-1.14; $P = 0.1122$) but a significant decrease in patients

treated with solifenacin 5 (-1.42; $P = 0.008$) and 10 mg (-1.45; $P = 0.0038$). Compared with placebo (-1.20, -8.1%) the mean number of voids/24 h was significantly lower in patients receiving tolterodine (-1.88, -15%; $P = 0.0145$), solifenacin 5 (-2.19, -17%) and 10 mg (-2.61, -20%; both $P < 0.001$). The mean volume voided/void was also significantly higher with all three active treatments ($P < 0.001$). Solifenacin was well tolerated; compared with placebo (4.9%), dry mouth (the most common side-effect), mostly mild, was reported in 18.6% of patients receiving tolterodine, 14.0% receiving 5 mg and 21.3% receiving 10 mg solifenacin.

Conclusion: Solifenacin 5 and 10 mg once daily improved urgency and other symptoms of OAB, and was associated with an acceptable level of anticholinergic side-effects. Solifenacin demonstrated significantly favourable efficacy to side-effect ratio in treating symptomatic OAB.

Editorial Comment

The authors present data on a once a day antimuscarinic agent (solifenacin) and compared variable doses as well as the b.i.d. dose of tolteradine and placebo in an international multi-center, randomized double-blind trial. The investigators used the twice daily tolteradine as opposed to the once a day dose as the latter formulation was not commercially available at the time of the initiation of the study. The authors found that the solifenacin, both the 5 mg and 10 mg dose, was well tolerated and effective for treating the symptoms of overactive bladder.

As all urologists have realized, the armamentarium for the treatment of overactive bladder continues to expand at an aggressive pace. Solifenacin is a once a day antimuscarinic with greater M3 selectivity than M2 selectivity. Secondary to this greater M3 selectivity, the potential for bothersome side effects such as xerostomia may be diminished. A question arises when reviewing this affinity in the setting of pathophysiologic changes in the roles of M2 and M3 receptors in the abnormal micturitional state. With diabetes, denervation injury or bladder outlet obstruction there could be a change in the sensitivity of the muscarinic receptors. In addition, the aging process can have a similar effect as the disease states. Hedge et al. reported that in the denervated rat bladder there is significant increase in the M2 receptor density without a change in the M3 so the role of M2 receptors for detrusor contraction may be heightened in a denervation (1). In addition, the M3 specific antagonists may be at a disadvantage due to the M2 up regulation in the diseased bladder state. The feline model has demonstrated greater potency of M2/M3 antagonists on the bladder when compared with an M3 selective antagonist in the diseased bladder (2). The potential for disadvantage of the M3 selective agents in the denervated bladder over the M2 receptors has been noted by others as well (3). It is for the above reasons that it will be of significant clinical and economic interest to note if these M3 selective agents will be able to assist patients in an equal or superior way over other broadly selective antimuscarinic agents.

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PEDIATRIC UROLOGY

Timing of follow-up voiding cystourethrogram in children with primary vesicoureteral reflux: development and application of a clinical algorithm

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Background and Objectives: Of children diagnosed with urinary tract infection, 30% to 40% have primary vesicoureteral reflux (VUR). For the majority of these children, treatment involves long-term prophylactic antibiotics (ABX) and a periodic voiding cystourethrogram (VCUG) until resolution of VUR as detected by VCUG. Radiation exposure and considerable discomfort have been associated with VCUG. To date, no clear guidelines exist regarding the timing of follow-up VCUGs. The objective of this study was to develop a clinically applicable algorithm for the optimal timing of repeat VCUGs and validate this algorithm in a retrospective cohort of children with VUR.

Methods: Based on previously published data regarding the probability of resolution of VUR over time, a decision-tree model (DTM) was developed. The DTM compared the differential impact of 3 timing schedules of VCUGs (yearly, every 2 years, and every 3 years) on the average numbers of VCUGs performed, years of ABX exposure, and overall costs. Based on the DTM, an algorithm optimizing the timing of VCUG was developed. The algorithm then was validated in a retrospective cohort of patients at an urban pediatric referral center. Data were extracted from the medical records regarding number of VCUGs, time of ABX prophylaxis, and complications associated with either. VUR in patients in the cohort was grouped into mild VUR (grades I and II and unilateral grade III for those $<$ or $=$ 2 years old), and moderate/severe VUR (other grade III and grade IV). Kaplan-Meier survival curves were created from the cohort data. From the survival curves, the median times to resolution of VUR were determined for the cohort, and these times were compared with the median times to VUR resolution of the data used for the DTM. The numbers of VCUGs performed, time of ABX exposure, and costs in the cohort were compared with those that would have occurred if the algorithm had been applied to both mild and moderate/severe VUR groups.

Results: Using an algorithm that results in a recommendation of VCUGs every 2 years in mild VUR would reduce the average number of VCUGs by 42% and costs by 33%, with an increase in ABX exposure of 16%, compared with a schedule of yearly VCUGs. For moderate/severe VUR, a VCUG performed every 3 years would reduce the average number of VCUGs by 63% and costs by 51%, with an increase in ABX exposure of 10%. Applying this algorithm to the retrospective cohort consisting of 76 patients (between 1 month and 10 years old) with primary VUR would have reduced overall VCUGs by 19% and costs by 6%, with an increase in ABX exposure of 26%. The patterns of VUR resolution, age distribution, and prevalence of severity of VUR were comparable between previously published results and the retrospective cohort.

Conclusions: Delaying the schedule of VCUG from yearly to every 2 years in children with mild VUR and every 3 years in children with moderate/severe VUR yields substantial reductions in the average numbers of VCUGs and costs, with a modest subsequent increase in ABX exposure.

Editorial Comment

The authors of this paper recognize that one of the critical issues in the current treatment algorithms for vesicoureteral reflux is the morbidity. These children must stay on antibiotics for long periods of time and they undergo voiding cystourethograms (VCUGs) annually. These x-rays are not only unpleasant, but result in significant radiation exposure. In an effort to reduce this morbidity, the authors considered, in a mathematical model, the effects of prolonging the interval between VCUGs. The authors based an analysis of their model on

published summary data from a Guidelines Panel on the rate of reflux resolution. The model the authors applied will reduce the number of unpleasant tests, as well as cost and radiation exposure. On the other hand, a negative effect of this approach will be the prolongation of antibiotic usage. In a retrospective analysis of the effect of this policy, VCUGs would have been reduced by 19%, costs by 6% (surprisingly little), but antibiotic use would have increased by 26%.

This is a creative and valuable contribution and should be presented to parents that way. I believe that this will be a viable option for many families. On the other hand, many families would likely prefer not to increase antibiotic usage. They at least would have the option in this respect.

The authors also acknowledge that there may be other changes in treatment policies that may affect this approach. In particular, the use of antibiotics is being questioned for older children and the use of endoscopic injection therapy for the treatment of reflux may obviate long periods of follow-up. So, although this approach is valuable for some families, it may not remain useful algorithm for long.

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Ureteroscopy for pediatric urolithiasis: an evolving first-line therapy

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Objectives: To present in a retrospective report a contemporary series of patients aged 14 years and younger who were treated for stones with ureteroscopy at our institution from 1991 to 2002. With the improvement and miniaturization of ureteroscopes and ancillary instruments, the endoscopic treatment of renal and ureteral calculi in children has become more feasible.

Methods: A retrospective chart review was performed of 23 patients aged 14 years and younger who had undergone ureteroscopy for the treatment of ureteral or renal calculi at our institution.

Results: A total of 27 stones were treated in 23 patients. Of the 27 stones, 18 were in the distal ureter, 5 in the mid ureter, 2 in the proximal ureter, and 2 in the renal pelvis. Ureteral dilation was performed in 4 (17.4%) of the 23 patients. The lithotripsy modalities used were holmium:yttrium-aluminum-garnet laser in 16 (69.6%), electrohydraulic lithotripsy in 3 (13%), a combination of holmium laser and electrohydraulic lithotripsy in 2 (8.7%), and basket extraction alone in 2 (8.7%) of 23 patients. Ureteral stents were placed in 21 (91.3%) of 23 patients. The average operative time was 46.9 minutes (range 15 to 92). In 21 (91.3%) of 23 patients, postoperative imaging was available and revealed that 20 (95.2%) of the 21 patients were rendered stone free. Two patients were lost to follow-up. No intraoperative complications occurred. One patient was treated postoperatively with intravenous antibiotics for transient fever.

Conclusions: Ureteroscopy is safe and effective in the management of ureteral and renal calculi in children. In our institution, it has emerged as a valid first-line therapy for the treatment of pediatric urolithiasis.

Editorial Comment

The authors make the point that there has been a shift in their clinical practice from shock wave lithotripsy to ureteroscopy for the treatment of stones in children. This shift occurred because of the efficacy and minimal

morbidity of ureteroscopy with modern instruments. In particular, small ureteroscopes and holmium: YAG laser lithotripsy have both made major contributions to the approach to these stones.

I believe that this is a valuable contribution. Although SWL is “non-invasive,” most children will require an anesthetic or at least heavy sedation requiring anesthesia monitoring for the procedure. Newer machines with smaller focal areas and less power mean that fewer children have been stone free after an initial trial of therapy. This has certainly been our experience. At the same time, holmium laser lithotripsy has been highly effective and most patients are stone free shortly after the procedure. This combination has lead to a change in practice pattern in our institution as well. The authors have outlined this change nicely.

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