
UROLOGICAL SURVEY

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STONE DISEASE

Diabetes Mellitus and Hypertension Associated With Shock Wave Lithotripsy of Renal and Proximal Ureteral Stones at 19 Years of Followup

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Purpose: SWL has revolutionized the management of nephrolithiasis and it is a preferred treatment for uncomplicated renal and proximal ureteral calculi. Since its introduction in 1982, conflicting reports of early adverse effects have been published. However, to our knowledge the long-term medical effects associated with SWL are unknown. We evaluated these adverse medical effects associated with SWL for renal and proximal ureteral stones.

Materials and Methods: Chart review identified 630 patients treated with SWL at our institution in 1985. Questionnaires were sent to 578 patients who were alive in 2004. The response rate was 58.9%. Respondents were matched by age, sex and year of presentation to a cohort of patients with nephrolithiasis who were treated nonsurgically.

Results: At 19 years of followup hypertension was more prevalent in the SWL group (OR 1.47, 95% CI 1.03, 2.10, $p = 0.034$). The development of hypertension was related to bilateral treatment ($p = 0.033$). In the SWL group diabetes mellitus developed in 16.8% of patients. Patients treated with SWL were more likely to have diabetes mellitus than controls (OR 3.23, 95% CI 1.73 to 6.02, $p < 0.001$). Multivariate analysis controlling for change in body mass index showed a persistent risk of diabetes mellitus in the SWL group (OR 3.75, 95% CI 1.56 to 9.02, $p = 0.003$). Diabetes mellitus was related to the number of administered shocks and treatment intensity ($p = 0.005$ and 0.007).

Conclusions: At 19 years of followup SWL for renal and proximal ureteral stones was associated with the development of hypertension and diabetes mellitus. The incidence of these conditions was significantly higher than in a cohort of conservatively treated patients with nephrolithiasis.

Editorial Comment

This provocative study underscores the need for long-term studies of the impact of our interventions, be they medical or surgical. Specifically, it raises concerns of the development of hypertension and diabetes mellitus following shockwave lithotripsy. The data related to the development of diabetes is particularly compelling, with a high odds ratio (3.75) that persists despite controlling for body mass index, and demonstrates a dose-dependency (correlation with number and intensity of shocks) that supports the hypothesis that a true biological effect exists. Deterioration in pancreatic endocrine function has been reported in up to 30% of patients undergoing SWL for pancreatic stones, though whether this reflects underlying pancreatic disease or the effects of the SW has not been determined. It is also unclear whether the effects noted in this study are peculiar to the shock path and focal area of the Dornier HM-3, or if similar effects may be anticipated with current lithotripter designs.

The data pertaining to hypertension is less compelling. Though more patients who underwent SWL developed hypertension, shockwave lithotripsy had no impact on the final prevalence of hypertension. In other words, the differences seen can be attributed to baseline differences in the rate of hypertension. It is plausible that other differences at baseline, in particular differences in stone size (those observed had smaller stones) reflect a bias that patients treated with SWL were further along in their disease process. Lastly, no dose-response correlation was noted with regards to number or intensity of shockwave and the development of hypertension, making it less likely that a true biological effect exists.

It is important to also note a few weaknesses in study design. The method of follow-up was not consistent in the study – patients treated with SWL were followed by questionnaire while the control group was followed by chart review, though the authors acknowledge that less than 20% of their patients return to their institution for follow-up. No information was gathered regarding subsequent SWL or other therapies for stone disease in either group during the 13 year follow that may confound the analyses conducted.

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Effect of Dietary Modification on Urinary Stone Risk Factors

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Kidney Int. 2005; 68: 2264-73

Background: This study was undertaken to ascertain the effect of dietary modification on urinary stone risks, and to determine whether the response depends on the prevailing urinary calcium.

Methods: A retrospective data analysis was conducted from our stone registry involving 951 patients with calcareous stones undergoing ambulatory evaluation, whereby 24-hour urine samples were collected during random diet and after dietary modification composed of restriction of calcium, oxalate, sodium, and meat products. Samples were analyzed for stone risk factors. Urinary calcium was also obtained after overnight fast and following a 1 g-calcium load. Changes produced by dietary modification from the random diet were evaluated in 356 patients with moderate-severe hypercalciuria (> 6.88 mmol/day, group I), 243 patients with mild hypercalciuria (5.00-6.88 mmol/day, group II), and 352 with normocalciuria (< 5.00 mmol/day, group III).

Results: Urinary calcium postcalcium load and the percentage of patients with absorptive hypercalciuria type I were highest in group I, intermediate in group II, and lowest in group III. During dietary modification, urinary calcium declined by 29% in group I, 19% in group II, and 10% in group III. Urinary oxalate did not change. Urinary saturation of calcium oxalate declined by only 12% in group I, 6% in group II, and nonsignificantly in group III, owing to various physicochemical changes in urinary biochemistry, which attenuated the effect of the decline in urinary calcium. Urinary saturation of brushite declined in all 3 groups due to the fall in urinary calcium, phosphorus, and pH. This reduction was more marked in the hypercalciuric groups than in the normocalciuric group. Urinary saturation of monosodium urate also decreased from a decline in urinary sodium and uric acid.

Conclusion: Secondary rise in urinary oxalate occurring from calcium restriction can be avoided by concurrent dietary oxalate restriction. Dietary modification (restriction of dietary calcium, oxalate, sodium, and meat products) is more useful in reducing urinary saturation of calcium oxalate among patients with hypercalciuria than among those with normocalciuria.

Editorial Comment

The pendulum swings once more. Dietary restriction of calcium may play a select role in recurrent stone management. This study suggests that those who stand to benefit most from calcium restriction are those with urinary CA > 275 mg/day and those with calcium phosphate supersaturation. The authors correctly note that the addition of potassium citrate supplementation to dietary restriction of calcium may be important to have a

significant impact on calcium oxalate saturation, as limiting dairy products alone will decrease the alkali load leading to lower pH and citrate levels. They also emphasize that calcium restriction should be part of a broad dietary intervention that also limits oxalate intake so as to avoid a compensatory increase in urinary oxalate due to increased bowel absorption. Though a diagnosis of absorptive hypercalcuria type I (AH1) was determined by a calcium load test, the authors did not stratify response to calcium restriction based on this diagnosis. However, almost 75% of patients with urinary CA > 275 mg/day were diagnosed with AH1. The authors propose that the use of a calcium-sparing diuretic and potassium citrate supplementation are additional important considerations to prevent a negative calcium balance with subsequent impact on bone density.

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ENDUROLOGY & LAPAROSCOPY

Robot Assisted Laparoscopic Partial Nephrectomy: Initial Experience

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J Urol. 2006; 176: 36-39

Purpose: Advances in laparoscopy have made laparoscopic partial nephrectomy a technically feasible procedure but it remains challenging to even experienced laparoscopists. We hypothesized that robotic assisted laparoscopic partial nephrectomy may make this procedure more efficacious than the standard laparoscopic approach.

Materials and Methods: Ten patients with a mean age of 58 years and mean tumor size of 2.0 cm underwent robotic assisted laparoscopic partial nephrectomy and another 10 with a mean age of 61 years and mean tumor size of 2.18 cm underwent laparoscopic partial nephrectomy, as performed by a team of 2 surgeons (MS and ST) between May 2002 and January 2004. Demographic data, intraoperative parameters and postoperative data were compared between the 2 groups.

Results: There were no significant differences in patient demographics between the 2 groups. Intraoperative data and postoperative outcomes were statistically similar. In the 10 patients who underwent robotic assisted laparoscopic partial nephrectomy there were 2 intraoperative complications. There was 1 conversion in the laparoscopic partial nephrectomy group.

Conclusions: Robotic assisted laparoscopic partial nephrectomy is a safe and feasible procedure in patients with small exophytic masses. The robotic approach to laparoscopic partial nephrectomy does not offer any clinical advantage over conventional laparoscopic nephrectomy.

Editorial Comment

Advances in laparoscopy allowed surgeons to perform complex reconstructive and ablative surgical procedures. Laparoscopic partial nephrectomy is the best example to depict these innovations where accuracy, speed and surgeon's expertise must work in concert. Robotic surgery may bring some advantages to the novice laparoscopists when performing laparoscopic radical prostatectomies but for nephron-sparing nephrectomies does not appear to help. Although the authors acknowledge the need of randomization of larger number of patients for clinical

validation, this study is a pioneer comparing laparoscopic partial nephrectomy (LPN) versus robotic assisted laparoscopic partial nephrectomy (RALPN). Interestingly, the authors believe that the distance between the surgeon and the sterile surgical field may have decreased the threshold to convert the RALPN to a hand assisted or open procedure. Other potential disadvantages of the robotic system are cost, training, equipment malfunction and setup time. Additionally, while LPN can safely be performed with a primary surgeon and an assistant, RALPN is a procedure that must be done with 2 experienced surgeons. In conclusion, RALPN is not ready for primetime yet.

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Comparison of Laparoscopic Partial Nephrectomy and Laparoscopic Hand Pain During Hand Assisted Laparoscopic Nephrectomy - An Ischemic Event?

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Purpose: The etiology of hand discomfort during hand assisted laparoscopic nephrectomy may be ischemic in nature. We determined if pneumoperitoneal pressure sustained to the hand during hand assisted laparoscopic nephrectomy poses an occupational risk, contributing to local hand hypoxia and resultant extremity pain.

Materials and Methods: A total of 442 measurements of hand oxygen saturation were made during hand assisted laparoscopic nephrectomy. A Nellcor(r) OxiMax(tm) Max-1(r) oxygen sensor was attached to the left index finger of each surgeon and hand assisted laparoscopic nephrectomy was performed using a LapDisc(r) at 15 mm Hg pneumoperitoneal pressures. Local hand oximetry readings and a numerical pain distress scale (range 0 to 10) were recorded every 2 minutes. To control for motion artifact oximetry readings were taken during hand motion and at rest. The Student t test was used to compare differences in local hand oxygen saturation and hand pain in and between study groups.

Results: A history of hand pain during hand assisted laparoscopic nephrectomy was significantly associated with local hypoxia during operative motion and at rest ($p=0.023$ and 0.012 , respectively), even with an adequate fascial incision and standard pneumoperitoneal pressures. During hand assisted laparoscopic nephrectomy hand pain was most significantly associated with local hypoxia after 24 minutes ($p=0.0002$), when local oxygen saturation was 56% to 88%.

Conclusions: A cohort of urologists is predisposed to ischemic hand pain during hand assisted laparoscopic nephrectomy. The etiology of this pain may be hypoxic in nature, attributable to pneumoperitoneal pressure decreasing perfusion and causing venous congestion or regional local ischemia. Circumferential antebrachial constriction from the LapDisc(r) does not seem to be a significant contributing factor in the presence of an adequate fascial incision. Hand pain secondary to ischemia is most significant after 24 minutes at 15 mm Hg. Future studies in more subjects are called for to validate these findings to elucidate which surgeons are predisposed to this potential occupational hazard and what perioperative measures can be taken to avoid hand pain during hand assisted laparoscopic nephrectomy.

Editorial Comment

Hand assisted procedures allowed less experienced laparoscopic surgeons to offer a less invasive approach to their patients with results comparable to purely laparoscopic surgery; i.e.; radical nephrectomy.

Unfortunately, the causes of hand numbness and/or pain have never been completely elucidated, i.e. fascial length and compression, pneumoperitoneum, etc.

Interestingly, this paper demonstrated that after 24 minutes of pneumoperitoneum (15 mm of Hg) the surgeon's hand would suffer hypoxia that may trigger symptoms of discomfort and pain. For surgeons that would occasionally perform this type of surgery may not suffer the effects of local hypoxia but for those who would routinely perform hand-assisted procedures that would last more than 24 minutes should be aware of this occupational risk and take precautions to prevent from chronic problems.

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IMAGING

Prophylaxis of Contrast Material-Induced Nephropathy in Patients in Intensive Care: Acetylcysteine, Theophylline, or Both? A Randomized Study

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Purpose: To prospectively compare the protective effect of acetylcysteine, theophylline, and both agents combined in patients who are admitted to the intensive care unit with at least one risk factor for contrast material-induced nephropathy and who receive at least 100 mL of iodinated contrast medium.

Materials and Methods: Institutional ethics review board approval and informed consent were obtained. A total of 91 patients (mean age, 58.5 years \pm 14.8 [standard deviation]; 31 women, 60 men; 150 examinations) were admitted to the intensive care unit with at least one risk factor for contrast-induced nephropathy and received either (a) 200 mg theophylline 30 minutes before contrast medium administration (group T), (b) 600 mg acetylcysteine twice daily on the day of and (if possible) the day before the examination (group A), or (c) both agents combined (group AT). The primary endpoint for this study was the incidence of contrast-induced nephropathy (chi² test).

Results: Groups T, A, and AT were comparable with regard to baseline creatinine levels and the amount of contrast medium administered. The incidence of contrast-induced nephropathy in groups T, A, and AT was 2%, 12%, and 4%, respectively, and was significantly lower in group T than in group A ($P = 0.047$). There was no significant difference in the incidence of contrast-induced nephropathy between groups A and AT ($P = 0.148$) or between groups T and AT ($P = 0.53$). For group A, serum creatinine did not change after 12, 24, or 48 hours compared with baseline. Creatinine levels in group T decreased 12 hours (1.19 mg/dL \pm 0.58; $P = 0.008$) and 48 hours (1.16 mg/dL \pm 0.55; $P = 0.034$) after contrast material injection compared with baseline (1.25 mg/

dL \pm 0.61). In group AT, creatinine significantly decreased 24 hours (1.21 mg/dL \pm 0.74; P = 0.003) and 48 hours (1.17 mg/dL \pm 0.69; P < 0.001) after contrast material injection compared with baseline (1.28 mg/dL \pm 0.74). Group A had significantly higher maximal increases in creatinine than groups T and AT (P = 0.014). Conclusion: For prophylaxis of contrast-induced nephropathy in patients who are admitted to the intensive care unit and who receive 100 mL or more of contrast medium, theophylline is superior to acetylcysteine.

Editorial Comment

Although contrast-induced nephropathy is relatively rare in patients with no risk factors, it is considered an important clinical issue since it is the third most frequent cause of acute renal failure. The frequency of contrast-induced nephropathy strongly depends on a number of risk factors: pre-existing renal dysfunction (nephropathies associated with diabetes and multiple myeloma), dehydration, congestive heart failure and use of concurrent nephrotoxic medication (including aminoglycosids and amphotericin B). For this reason, several strategies are currently proposed in order to prevent this complication, such as the use of non-contrast based imaging techniques, the reduction of the total amount of contrast material injected, the use of iso-osmolar or low-osmolar contrast agents and hyperhydration. Recently several preventive measures to avoid contrast-induced nephropathy have been proposed which include administration of N-acetylcysteine, theophylline, or fenoldopam, sodium bicarbonate infusion, and peri-procedure hemofiltration/hemodialysis. This is a very interesting and unique prospective randomized study showing that in 150 patients who were admitted to the intensive care unit and who received at least 100 mL of contrast medium, theophylline an “easy to handle” agent was superior to acetylcysteine with regard to prevention of contrast material-induced nephropathy.

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Comparison of 16-MDCT and MRI for Characterization of Kidney Lesions

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Objective: The objective of our study was to compare the diagnostic performance of 16-MDCT with that of MRI in the characterization of kidney lesions.

Subjects and Methods: Twenty-eight patients with kidney lesions detected with sonography and requiring further evaluation were examined. MDCT was performed in the unenhanced, arterial, and portal venous phases. MRI was performed at 1.5 T with T2- and T1-weighted and dynamic gadolinium-enhanced sequences. Consensus reading was done by two radiologists. Image quality was rated on a four-point scale. Classification of lesions as surgical or nonsurgical was done with five levels of confidence, and it was required that a definite diagnosis be assigned to each lesion. The 1997 TNM classification was used for staging. Statistical analysis was done by receiver operating characteristic analysis or paired Student's t test. Histologic or follow-up findings at least 12 months after the primary diagnosis served as the standard of reference.

Results: The image quality of MDCT (mean grade, 2.79 on a 0-3 scale) was superior to that of MRI (1.93; p < 0.01). The area under the curve for differentiating surgical from nonsurgical lesions was 0.979 for MDCT and 0.957 for MRI with resulting sensitivity and specificity values of 92.3% and 96.3% for MDCT and 92.3% and

91.3% for MRI. Sensitivity and specificity for definite classification of the lesions were 93.8% and 68.4% for MDCT and 93.8% and 71.4% for MRI.

Conclusion: Both MDCT and MRI are excellent for differentiating surgical from nonsurgical kidney lesions. Both methods have low specificity for the differentiation of benign from malignant lesions.

Editorial Comment

In this interesting original study, the authors compared the performance of state of the art, 16 channel-MDCT and 1.5 T MRI in the characterization of renal lesions previously detected by ultrasound in the same patient group. Due the presence of artifacts on MR examinations, MDCT proved superior to MRI with regard to image quality. Both MDCT and MRI however proved excellent for differentiating surgical from nonsurgical kidney lesions (sensitivity and specificity of 92.3% and 96.3% for MDCT and 92.3% and 91.3% for MRI). It is also interesting to note that both MDCT and MRI correctly depicted 15 of 16 renal cell carcinomas (sensitivity, 93.3%) but both technique had similar limitation for depiction of benign lesions (specificity, 68.4% and 71.4% respectively). This occurred because both methods were unable to differentiate between oncocytoma and renal cell carcinoma. This study confirms the classic limitation of imaging methods regarding the criteria for identification of enlarged lymph node as metastatic disease from renal cancer. In this series the authors reports that both MDCT and MRI interpretation led to overstaging 3 and 4 lesions respectively, due to the presence of enlarged lymph node(> 15 mm), currently criteria for interpreting as malignant but with reactive changes at histological examination. In our experience, MDCT and fast MR imaging has similar specificity for the detection, characterization and staging of solid renal masses larger than 1.0 cm in diameter. Similarly to the authors' experience, we consider MDCT superior for the detection of very small solid renal lesions (< 1.0 cm), but fast MRI and sometimes high-resolution ultrasound, are in some cases superior for the evaluation of complicated renal cystic masses. MRI and occasionally ultrasound better demonstrates internal septations, thickening of the cyst wall and/or septa. MRI better demonstrates areas of abnormal enhancement. In both situations, these additional findings will transform a nonsurgical into a surgical cystic mass (1).

Reference

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UROGENITAL TRAUMA

Predictors of the Need for Nephrectomy after Renal Trauma

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Background: Initial management of solid organ injuries in hemodynamically stable patients is nonoperative. Therefore, early identification of those injuries likely to require surgical intervention is key. We sought to identify factors predictive of the need for nephrectomy after trauma.

Methods: This is a retrospective review of renal injuries admitted over a 12-year period to a Level I trauma center.

Results: Ninety-seven patients (73% male) sustained a kidney injury (mean age, 27 +/- 16; mean Injury Severity Score, 13 +/- 10). Of the 72 blunt trauma patients, 5 patients (7%) underwent urgent nephrectomy, 3 (4%) had repair and/or stenting, and 89% were observed despite a 29% laparotomy rate for associated intraabdominal injuries in this group. Twenty-five patients with penetrating trauma underwent eight nephrectomies (31%), one partial nephrectomy, and two renal repairs. Regardless of the mechanism of injury, patients requiring nephrectomy were in shock, had a higher 24-hour transfusion requirement, and were more likely to have a high-grade renal laceration (all $p < 0.05$). Bluntly injured patients requiring nephrectomy had more concurrent intraabdominal injuries ($p < 0.0001$). Overall, patients after penetrating trauma were more severely injured, had higher 24-hour transfusion requirements, and a higher nephrectomy rate (all $p < 0.05$). Despite a higher injury severity in the penetrating group, however, mortality was higher in the bluntly injured group ($p < 0.0001$). Univariate predictors for nephrectomy included: revised trauma score, injury severity score, Glasgow Coma Scale score, shock on presentation, renal injury grade, and 24-hour transfusion requirement. No patient with a mild or moderate renal injury required nephrectomy, whereas 6 of 12 (50%) grade 4 injuries and 7 of 8 (88%) grade 5 injuries required nephrectomy. Multiple logistic regression analysis confirmed penetrating injury, renal injury grade, and Glasgow Coma Scale score as predictive of nephrectomy.

Conclusion: Overall, injury severity, severity of renal injury grade, hemodynamic instability, and transfusion requirements are predictive of nephrectomy after both blunt and penetrating trauma. Nephrectomy is more likely after penetrating injury.

Editorial Comment

This study confirms the well-established concept that most renal injuries are AAST grade 1-3, and can be safely managed non-operatively. Predictors for nephrectomy were shock, higher AAST grade of renal injury (4 - 5), ongoing transfusion requirement, and associated intraabdominal injuries. Grade 5 injuries, by definition are potentially life-threatening with avulsion of the renal hilum or a completely shattered kidney. That the nephrectomy rate in this study for Grade 5 kidney injuries approached 90% is not surprising. In unstable kidney trauma patients with ongoing blood loss, nephrectomy is part of a “damage control” approach to stabilize the patient, get them off the OR table, and quickly into the ICU for resuscitation.

Clearly, opening up Gerota’s fascia and releasing the tamponade effect of the retroperitoneal hematoma may result in uncontrollable bleeding and subsequent nephrectomy. Thus, there are 2 main ways to avoid unnecessary nephrectomy: 1) For the stable trauma patient, image the abdomen with CT with delayed images in order to properly stage the kidney injury. With an accurate kidney injury stage and location of the retroperitoneal hematoma, patients can then be selected for surgery or expectant management. 2) Retroperitoneal hematomas that are not zone 1, stable, non-expanding, non-pulsatile, and contained do not demand exploration. Zone 1 hematomas, namely midline supramesocolic or midline inframesocolic, from a blunt or penetrating mechanism demand exploration. Zone 2, lateral perinephric hematomas should be selectively explored for penetrating trauma, and typically observed for blunt trauma (1).

In Davis et al, half of Grade 4 injuries ended up with nephrectomy. This is higher than prior reports, but again nephrectomy may have been performed as “damage control” in the face of instability and associated injuries. Prior reports, however, have demonstrated that most Grade 4 renal injuries can be managed expectantly, with the kidney being re-imaged by CT with intravenous contrast and delayed images (3 to 5 days after initial

injury) to assess for persistent urinary leakage. Worsened or unimproved leak warrants ureteral stent placement of urinoma drain placement.

Reference

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Damage Control Management of Experimental Grade 5 Renal Injuries: Further Evaluation of FloSeal Gelatin Matrix

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Background: We developed a porcine grade 5 renal laceration damage control model to evaluate the hemostatic efficacy of FloSeal gelatin matrix (Baxter Healthcare, Corp., Deerfield, Ill).

Methods: Ten commercial swine underwent celiotomy, contralateral nephrectomy, and cooling to 32 degrees C after a well-established hypothermia protocol to simulate a damage control scenario. Following prospective randomization, a complex grade 5 renal injury was uniformly produced on the remaining kidney. Control animals (group 1, n = 5) were treated with direct manual compression with a gelatin sponge. Experimental animals (group 2, n = 5) were treated by application of FloSeal gelatin matrix followed by direct compression with a gelatin sponge. Operative blood loss and efficacy of hemostasis were compared. Creatinine levels were obtained daily until postoperative day 7. Abdominal computed tomography was performed at 10 days.

Results: Use of FloSeal gelatin matrix hemostatic sealant resulted in significantly less mean blood loss than gelatin sponge bolster compression alone (202.4 mL vs. 540.4 mL, respectively, p = 0.016). Hemostasis was complete in 60% (three out of five) of experimental animals after 2 minutes, but was incomplete in all control animals. After an initial increase, serum creatinine approached baseline by postoperative day 7 in all animals. Axial imaging 10 days postoperatively revealed no evidence of significant delayed perirenal hemorrhage.

Conclusions: FloSeal gelatin matrix performed well as a rapidly deployable, effective hemostatic agent in a hypothermic grade 5 renal injury damage control model. The absence of delayed bleeding and nephrotoxicity suggests a possible increased role for FloSeal in the treatment of devastating renal injuries in damage control surgery.

Editorial Comment

This article illustrates nicely the concept of damage control and the use of a pig model. Damage control is the concept that an abdominal trauma surgery is abbreviated to control hemorrhage and fecal and urinary contamination, to not perform the definitive repair until a planned staged re-operation improves survival, and to resuscitate the patient in the ICU before any prolonged reconstructive surgery. Such a policy of staged, abbreviated operations, has clearly been shown to improve overall survival, and helps to avoid the lethal triad of cold (body temperature), coagulopathy and acidosis.

The use of fibrin sealants in urology has been particularly popular recently, due to its use in laparoscopic kidney surgery. With the expanding role of laparoscopy for partial nephrectomy, methods to better control urinary leak or bleeding have been explored. Aside from direct suturing of the collecting system and vessels, fibrin sealants have been the “suspenders” to the “belts” of suturing. The current commercially available sealants are Tisseel “fibrin sealant”, (by Baxter, a mix of fibrinogen aprotonin solution, Factor XIII, and human derived thrombin), FloSeal “gelatin matrix” (by Baxter, a mix of human derived thrombin and bovine derived gelatin matrix), and BioGlue “surgical adhesive” (by Cryolife, a mix of bovine serum albumin and gluteraldehyde).

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PATHOLOGY

Xp11.2 Translocation Renal Cell Carcinoma with Very Aggressive Course in Five Adult Patients

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Background: Renal cell carcinomas (RCC) associated with Xp11.2 translocations (TFE3 gene fusions) are rare tumors occurring predominantly in children and young adults. Although, thus far, only limited data is available, these tumors are believed to be rather indolent even when diagnosed at advanced stages.

Design: Five cases of TFE3-RCC were evaluated in patients aged 18 or older (mean age 31). Diagnosis was confirmed by IHC detection of increased TFE3 fusion protein. Morphology was examined by HE, IHC and electron microscopy (EM) and correlated with clinical picture.

Results: HE showed clear cells, arranged in a pseudopapillary architecture, with retention of morphology in the metastatic tumor deposits. By IHC there was strong nuclear positivity for TFE3 in all cases and focal stain for AE3 and vimentin; stains for HMB45, calretinin, pankeratin and AE1 were all negative. By EM (2/5 cases examined) there were junctional complexes and rudimentary microvilli. In one case there were abundant lipid droplets and glycogen; in a second case, rare rhomboid crystals, similar to those seen in alveolar soft part sarcoma, were present. All patients (3 Caucasian, 2 Hispanic) presented with innocuous complaints, abdominal/flank pain and hematuria, and lacked any significant prior history. All but one patient presented with distant metastases at the time of diagnosis, and all patients were diagnosed with additional metastases or tumor recurrence within 5 months of presentation. Treatments included tumor resection, interleukin-2 therapy, combination chemotherapy, and radiation therapy, all with minimal success. Patients followed a rapidly terminal course, with a mean survival of 15 months post-diagnosis (range 10-20 months). One patient is currently undergoing chemotherapy at 13 months post-diagnosis (with brain metastasis), and another patient is alive at 6 months post-diagnosis, with metastases.

Conclusions: The patients presented here were older than typically described for TFE3-RCC. Although tumor morphology was similar to pediatric patients, these adult patients had a very aggressive clinical course compared to pediatric TFE3-RCC and even to conventional, adult-type RCC. Consistent use of antibodies against TFE3 in all tumors, regardless of patient age, may expand the spectrum of Xp11.2 translocation RCC with respect to age, clinical behavior and molecular abnormalities.

Editorial Comment

These carcinomas are defined by several different translocations involving chromosome Xp11.2. The t(X; 1) (p11.2; q21) translocation results in the fusion of TFE3 gene in chromosome X to PRCC gene in chromosome 1; the t(X; 17) (p11.2; q25) translocation results in the fusion of TFE3 gene in chromosome X with the ASPL gene in chromosome 17. This latter translocation is also seen in the alveolar soft part sarcoma.

These carcinomas predominantly affect children and adolescents and are believed to be rather indolent even when diagnosed at advanced stages. The most distinctive histopathologic appearance is that of a carcinoma with papillary architecture comprised of voluminous clear to eosinophilic cytoplasm, discrete cell borders, vesicular chromatin and prominent nucleoli. Scattered hyaline nodules and psammomatous bodies can be seen. The most distinctive immunohistochemical feature of these tumors is nuclear immunoreactivity for the chimerical (mutant) TFE3 protein (1).

The present study by Meyer et al. reported 5 patients of TFE3 renal cell carcinoma aged 18 or older (mean age 31). All but one patient presented with distant metastases at the time of diagnosis, and all patients were diagnosed with additional metastases or tumor recurrence within 5 months of presentation. The authors emphasize the fact that although tumor morphology was similar to children and adolescents, these adult patients had a very aggressive course. It is noteworthy a Brazilian female 58-year old recently reported with renal cell carcinoma associated with Xp11.2 translocation TFE3 (ASPL-TFE3) gene fusion (2). Metastases were seen in 3 of the 6 dissected lymph nodes, thus determining a final staging (TNM, 2002) pT1b, pN2, pMX (stage IV). After approximately 6 months of follow-up, the patient showed favorable outcome, without manifesting disease or any other signs or symptoms.

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Papillary Renal Cell Carcinoma: Assessment of Clear Cell Change and Clinicopathologic Correlation

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Mod Pathol Suppl 1. 2006; 19: 138A

Background: Papillary renal cell carcinoma with clear cell change and chromosome 3p21 aberration has been described. The significance of this finding, however, remains unclear. We perform the first study to investigate the significance of clear cell change and its clinicopathologic correlation.

Design: Nineteen cases of papillary renal cell carcinoma between 1992 and 2005 were retrieved from the slide archives in the Department of Pathology, Westchester Medical Center. Cytogenetic findings were obtained in 2 cases. All tumors were subclassified as type 1 or 2 and were evaluated for clear cell change and Fuhrman nuclear grade. American Joint Committee on Cancer TNM Staging of Renal Cell Carcinoma (2002) was used and clinical charts were reviewed retrospectively to obtain clinical stage.

Results: The patient age ranged from 11 to 77 years (mean 56). Sixteen patients were males and 3 were females. Tumor size ranged from 1.8 to 10 cm (mean 4.6 cm). All tumors contained clear cells ranged from 0 to 85%. Of the 12 tumors with 0 to 25% clear cells, 9 cases presented with stage I, 2 with stage II, and 1 with stage III disease. Seven tumors possessed clear cell change ranged from 30 to 85%. Of these 7 patients, 2 cases presented with stage I, 1 with stage II, 3 with stage III, and 1 with stage IV. Cytogenetics findings in a tumor with 30% clear cells revealed 49-50X,-X, der(3)add(3)(p21),+7,+17,-19,+21 and the case with 5% clear cells showed 57,XXY,+2,+3,+4,+7,+8,+12,+16,+17,+20. Nine cases (47%) were classified as type 1 and 10 cases (53%) type 2. Of the 9 type 1 tumors, 2 cases had grade 1 nuclei, 6 grade 2, and 1 grade 1. Six of these patients presented with stage I, 2 with stage 2, and 1 with stage IV. In comparison to type 1, 5 cases of type 2 lesions had a nuclear grade of 2 and 5 had grade 3 nuclei. Five patients presented with stage I, 1 with stage II, and 4 with stage III disease.

Conclusions: Type 2 papillary renal cell carcinomas have higher nuclear grade and stage than that of type 1 lesions. Type 2 lesions have poorer prognosis than type 1. Patients bearing tumors with greater than 30% clear cells present with higher stage of disease. Therefore, clear cell change may be a useful pathologic prognosticator in evaluating clinical behavior of these tumors.

Editorial Comment

Papillary renal cell carcinoma has a tendency to present at a lower stage, but with a distinct potential for progression and aggressive behavior (1). Papillary renal cell carcinomas comprise approximately 10% of renal cell carcinoma in large surgical series. The tumor is characterized by malignant epithelial cells forming varying proportions of papillae and tubules. The tumor papillae contain a delicate fibrovascular core and aggregates of foamy macrophages and cholesterol crystals may be present. Solid variants consist of tubules or short papillae resembling glomeruli.

Two morphological types of papillary renal cell carcinoma have been described (2). Type 1 tumors have papillae covered by small cells with scanty cytoplasm, arranged in a single layer on the papillary basement membrane. Type 2 tumor cells are often of higher nuclear grade with eosinophilic cytoplasm and pseudostratified nuclei on papillary cores. Type 1 tumors are more frequently multifocal. Sarcomatoid dedifferentiation is seen in approximately 5% of these tumors and has been associated with both type 1 and type 2 tumors. In series of papillary renal cell carcinoma containing both type 1 and 2 tumors, five year survivals for all stages range from 49% to 84% with tumor grade, stage at presentation and the presence of sarcomatoid dedifferentiation being correlated with outcome. Longer survivals have been demonstrated for type 1 when compared with type 2 on both univariate and multivariate analysis that included both tumor stage and grade.

Uropathologists are aware of the fact that some papillary renal cell carcinomas show clear cell differentiation. Torres-Cabala et al. (3) showed that some of papillary renal cell carcinomas with clear cell differentiation show 3p deletion that is a common finding in conventional clear cell carcinoma. They suggested that this finding might represent an early event in tumor progression to conventional clear cell carcinoma. The study of Dasgupta and Yeh is a further evidence that clear cell differentiation in papillary renal cell carcinomas may have prognostic implications. Patients bearing tumors with greater than 30% clear cells presented with higher stage of disease. Pathologists should report on presence of clear cell differentiation in papillary renal cell carcinomas.

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INVESTIGATIVE UROLOGY

Immunohistochemical Distribution of cAMP- and cGMP-Phosphodiesterase (PDE) Isoenzymes in the Human Prostate

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Eur Urol. 2006; 49: 740-5

Objectives: With the introduction of sildenafil citrate (VIAGRA trade mark), the concept of phosphodiesterase (PDE) inhibition has gained tremendous interest in the field of urology. Cyclic nucleotide second messengers cGMP and cAMP have been assumed to be involved in the control of the normal function of the prostate. The aim of the present study was to evaluate by means of immunohistochemistry the expression and distribution of some cAMP- and cGMP-PDE isoenzymes in the prostate.

Material & Methods: Cryostat sections (10µM) of formaldehyde-fixated tissue segments excised from the transition zone of human prostates were incubated with primary antibodies directed against the PDE isoenzymes 3, 4, 5, and 11. Then, sections were exposed to either fluorescein isothiocyanate- (FITC) or Texas Red- (TR) labeled secondary antibodies and visualization was commenced by means of laser fluorescence microscopy.

Results: TR-immunofluorescence indicating the presence of PDE4 (cAMP-PDE) was abundantly observed in the fibromuscular stroma as well as in glandular structures of the transition zone. In contrast to the distribution of PDE4, immunoactivity indicating PDE5 (cGMP-PDE) and 11 (dual substrate PDE) was mainly observed in glandular and subglandular areas. No immunostaining for PDE3 (cGMP-inhibited PDE) was detected.

Conclusion: Our results confirm the presence of PDE isoenzymes 4, 5 and 11 in the transition zone of the human prostate and present evidence that these isoenzymes are not evenly distributed. These findings are in support of the hypothesis that there might be a rationale for the use of PDE inhibitors in the pharmacotherapy of BPH and LUTS.

Editorial Comment

Lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) association is a very much discussed theme in urology practice and many papers have been published during the last few years. Prostatic obstruction may be clinically treated either by alpha-blockers (effect on bladder neck) or by 5-alpha-reductase inhibitors (reducing effect on gland volume) (1). Recent research (2,3) suggests that the combination of an alpha-blocker and a phosphodiesterase type 5 inhibitor may be useful in patients with (LUTS) associated with erectile dysfunction. The present paper demonstrates the pharmacological background for previous clinical findings.

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Is Pelvicaliceal Anatomy a Risk Factor for Stone Formation in Patients with Solitary Upper Caliceal Stone?

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Urology. 2006; 67: 1159-63

Objectives: To investigate the effect of pelvicaliceal anatomy on stone formation in patients with solitary upper caliceal stones.

Methods: The records of patients with solitary upper caliceal stones between 1996 and 2004 were reviewed. After the exclusion of patients with hydronephrosis, major anatomic abnormalities, noncalcium stones, metabolic abnormalities, history of recurrent stone disease, multiple stones, and previous renal surgery, 42 patients (24 male, 18 female) and 42 healthy subjects (22 male, 20 female) with normal results on intravenous pyelography (IVP) were enrolled into the study. With a previously described formula, upper pole infundibulopelvic angle (IPA), infundibular length (IL) and width (IW), and pelvicaliceal volume of the stone-bearing and contralateral normal kidney of patients and bilateral normal kidneys of healthy subjects were measured from IVP.

Results: Forty-two stone-bearing and 126 normal kidneys (42 contralateral, 84 healthy) were assessed. The mean stone size was 153.47 mm² (range, 20 to 896 mm²). There were no statistically significant differences in terms of upper caliceal specifications between stone-bearing and normal kidneys. The mean (+/- standard deviation) pelvicaliceal volume of 42 stone-bearing and 126 normal kidneys was 2455.2 +/- 1380.2 mm³ and 1845.7 +/- 1454.8 mm³, respectively (P = 0.019). These values were 2114 +/- 2081.5 mm³ (P = 0.34) and 1709.5 +/- 989.1 mm³ (P = 0.001) for contralateral normal kidneys (n = 42) and normal kidneys of healthy subjects (n = 84), respectively.

Conclusions: Explanation of the etiology of the upper caliceal stone by the anatomic features is very difficult, and these caliceal anatomic variables (IPA, IL, IW) seem not to be a significant risk factor for stone formation in the upper calyx.

Editorial Comment

The study is interesting and demonstrated that there is any statistically significant difference between the stone-bearing and the normal kidneys of patients with upper caliceal stones and healthy individuals in terms of infundibulopelvic angle (IPA), infundibular length (IL) and width (IW) of upper caliceal system. Previous anatomical findings on pelvicaliceal features are well presented and discussed.

The mean pelvicaliceal volume of 42 stone-bearing was $2455,2 \pm 1380,2$ mm³ and contralateral kidneys was $2114 \pm 2081,5$, with no statistical difference between stone-bearing and contralateral normal kidneys ($p=0,34$). When comparing to bilateral kidneys of healthy individuals not bearing stones the difference was significant. Nevertheless, as the authors stated, these finding must be viewed with caution.

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UROLOGICAL ONCOLOGY

Is A Second Transurethral Resection Necessary For Newly Diagnosed Pt1 Bladder Cancer?

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J Urol. 2006; 175: 1258-61

Purpose: We evaluated the potential benefit of a second transurethral resection in patients with newly diagnosed pT1 transitional cell carcinoma of the bladder.

Materials and Methods: Between January 2001 and May 2003, 80 patients with stage T1 bladder cancer were included in this protocol in which all patients prospectively received second TUR within 2 to 6 weeks following the initial resection. Patients with incomplete resections were excluded from study. The pathological findings of the second TUR were reviewed.

Results: Of the 80 patients who underwent second resection, 18 (22.5%) had macroscopic tumors before resection. However, with the addition of microscopic tumors, overall residual disease was determined in 27 (33.8%) patients. Of the 27 patients 7 had pTa, 14 had pT1, 3 had pT1+pTis and 3 had pT2 disease. Residual cancers were detected in 5.8%, 38.2% and 62.5% in G1, G2 and G3 tumors, respectively. The risk of residual tumor directly correlated with the grade of the initial tumor ($p = 0.009$).

Conclusions: Although second TUR dramatically changed the treatment strategy in a small percentage of cases, we strongly recommend performing second TUR in all cases of primary pT1 disease, especially in high-grade cases.

Editorial Comment

This paper highlights the usefulness of a second transurethral resection in superficial bladder cancer by providing own data and a review of the meanwhile large body of literature evidence.

In their own data the authors found at least 18.8% residual tumor at second TUR with an increasing rate up to 33.8% in large and/or multifocal tumors. In the literature, up to 74% of T1G1-3 tumors had residual disease. A second TUR is highly recommended at least in large tumors and all T1 tumors.

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Guidelines on TaT1 (Non-muscle Invasive) Bladder Cancer

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http://www.uroweb.org/files/uploaded_files/guidelines/05%20TaT1%20Bladder%20Cancer.pdf

No abstract available

Editorial Comment

These guideline represent and evolutional development from the “old” EAU bladder cancer guidelines, which were well received worldwide. They incorporate recommendations for such major steps in superficial bladder cancer treatment as postoperative single shot instillation with chemotherapy and maintenance therapy with BCG.

The most important information, which led to these steps forward, came from recently published metaanalyses, which were prepared in close cooperation predominantly from members of the guidelines group.

Specifically, the following changes appear as of highest importance and are commented below. Guidelines for superficial and invasive bladder cancer are generated from different groups and are distinct.

Use of histological classification - However, until the 2004 WHO classification has been validated by more clinical trials, tumors should be graded according to both the 1973 and the 2003 WHO classification.

Fluorescence cystoscopy - This investigational method has not yet been implemented on a regular basis in daily practice.

Second resection is recommended in most intermediate and all high-risk tumors.

Single-shot postoperative instillation of chemotherapy is strongly recommended.

Intravesical BCG is superior to intravesical chemotherapy in reducing recurrences and is the only drug to interfere with progression of SBC. BCG immunotherapy is indicated in intermediate risk and high-risk bladder cancer. The use of maintenance therapy of at least 1 year is strongly recommended.

An algorithm for predicting tumor recurrence and progression is extensively provided in these guidelines.

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NEUROUROLOGY & FEMALE UROLOGY

Is There A Role For Periurethral Collagen Injection In The Management Of Urodynamically Proven Mixed Urinary Incontinence?

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Urology. 2006; 67: 725-9; discussion 729-30

Objectives: To investigate the effectiveness of periurethral collagen injection (PCI) in patients presenting with symptoms of mixed urinary incontinence (MUI) and urodynamically demonstrated sphincter deficiency and detrusor overactivity.

Methods: A retrospective review was performed on all patients undergoing PCI from February 1999 to February 2003, during which those with MUI were treated with PCI as first-line therapy. The inclusion criteria were MUI symptoms, detrusor overactivity on urodynamic study, stress urinary incontinence due to sphincter deficiency (determined from physical examination, stress test, urodynamic study with Valsalva leak point pressure, and cystography findings, without urethral hypermobility). The primary outcome measures were the Urogenital Distress Inventory (UDI), Incontinence Impact Questionnaire, and quality-of-life score and the need for anticholinergic medications or additional surgery. Comparisons were performed using the Wilcoxon signed ranks test and paired t test.

Results: Of the 56 patients who underwent PCI, 43 presented with symptoms of MUI, and 16 of these (29%) had both detrusor overactivity and stress urinary incontinence on urodynamic study. The mean follow-up after PCI (without additional PCI) was 18 months (range 6 to 39). The mean age was 65 years (range 40 to 84). The mean Valsalva leak point pressure was 54 +/- 40 cm H₂O (range 18 to 146). Ten patients had undergone previous anti-incontinence procedures, and anticholinergic medications had failed in six. The questionnaire scores, indicating severe MUI/poor quality of life before PCI, improved after PCI: UDI question 1, 2.3 +/- 0.8 versus 1.3 +/- 1.0 (P = 0.021); UDI question 2, 2.1 +/- 1.2 versus 1.4 +/- 1.0 (P = 0.068); UDI question 3, 2.9 +/- 0.4 versus 1.8 +/- 1.2 (P = 0.010); and quality-of-life question, 8.6 +/- 2.1 versus 5.2 +/- 3.5 (P = 0.026). The mean injected volume/patient was 8.5 cm³ (range 5 to 17) within a mean of 1.9 treatments (range 1 to 3). Four patients continued taking anticholinergic medications and one proceeded to sling placement.

Conclusions: The use of PCI as the primary/initial intervention in patients with MUI may be the preferred approach, particularly in patients with an elevated risk of anticholinergic medication side effects or when voiding dynamics preclude sling placement.

Editorial Comment

The authors describe a retrospective review involving the performance of periurethral collagen injection for patients plagued with mixed urinary incontinence. The detrusor overactivity was diagnosed on urodynamics as an increase in detrusor pressure and/or a sensation of urgency with or without incontinence during the filling phase of the study.

The authors found a significant improvement in both the symptoms of stress urinary incontinence and overactive bladder (urinary frequency and urinary urge incontinence). These findings somewhat echo those found by McGuire & Savastano (1) from greater than 2 decades ago. This mirror success rate does give some merit to the argument of detrusor overactivity having a definite urethral component in its etiology. Based on the findings of these authors, injectable therapy seems to be a very reasonable option for patients with mixed urinary urge incontinence and has a higher success than those patients tried with pharmacologic therapy alone.

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Treatment for Unsuccessful Tension-Free Vaginal Tape Operation by Shortening Pre-Implanted Tape

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J Urol. 2006; 175: 2196-9; discussion 2199-200

Purpose: We studied the efficacy of shortening the pre-implanted suburethral tape in patients with recurrent urodynamic stress incontinence after a TVT operation.

Materials And Methods: A total of 14 women, including 6 with ISD, were treated for recurrent urodynamic stress incontinence after the initial TVT operation by performing the shortening procedure under local anesthesia. Urodynamics, a 1-hour pad test, introital ultrasonography of the urethra and a cotton swab test were done before the procedure and 1 year postoperatively.

Results: All 14 patients completed the shortening procedure. Mean patient age was 47.2 years (range 43 to 66). Mean time between initial TVT and the shortening procedure was 4 months (range 3 to 14). Ten patients (71.4%) were objectively cured and treatment failed in 4 (2 with ISD and 2 with a fixed urethra). Mean operative time was 17 minutes (range 10 to 25). No intraoperative surgical complications were observed. The 1-hour pad test showed a decrease from a median of 9.0 gm to 1.0. Median postoperative hospital stay was 1 day (range 1 to 4). Spontaneous voiding with adequate post-void residual urine was noted in all patients before discharge home.

Conclusions: Shortening a pre-implanted TVT tape for the treatment of recurrent urodynamic stress incontinence is a safe, effective and minimally invasive option requiring only a short hospital stay. However, ISD and an immobile urethra seem to be risk factors for failure. Long-term followup is needed to determine if this surgery achieves long-lasting results.

Editorial Comment

The authors describe a method to address recurrent urinary incontinence after failed TVT by transvaginal plication of the in situ TVT tape. The authors managed to objectively cure 10 out of the 14 patients (71.4%) with this maneuver while 4 continued with recurrent stress incontinence.

Addressing of recurrent urinary incontinence after TVT has been a topic of discussion in the literature. The above method as described appears to be quite technically facile with a very reasonable salvage success rate. The authors, while performing the transvaginal procedure, did not have any difficulty in locating the in situ sling. Secondary to the actual nature of the TVT procedure, the in place tightening of sutures cannot be performed as described by Choe (1). Repeat transvaginal tape (2) may be considered but carries with it the duplicate expense for the repeat tape. Though multiple options exist for the failed TVT (including repeat TVT

procedure, suburethral sling using an alternative material, versus injectable) this procedure appears to be inexpensive, straight forward, with an acceptable level of success.

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PEDIATRIC UROLOGY

Prediction of Vesicoureteral Reflux after a First Febrile Urinary Tract Infection in Children: Validation of a Clinical Decision Rule

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Arch Dis Child. 2006; 91: 241-4

Aims: To test the reproducibility of a highly sensitive clinical decision rule proposed to predict vesicoureteral reflux (VUR) after a first febrile urinary tract infection in children. This rule combines clinical (family history of uropathology, male gender, young age), biological (raised C reactive protein), and radiological (urinary tract dilation on renal ultrasound) predictors in a score, and provides 100% sensitivity.

Methods: A retrospective hospital based cohort study included all children, 1 month to 4 years old, with a first febrile urinary tract infection. The sensitivities and specificities of the rule at the two previously proposed score thresholds (≤ 0 and ≤ 5) to predict respectively, all-grade or grade ≥ 3 VUR, were calculated.

Results: A total of 149 children were included. VUR prevalence was 25%. The rule yielded 100% sensitivity and 3% specificity for all-grade VUR, and 93% sensitivity and 13% specificity for grade ≥ 3 VUR. Some methodological weaknesses explain this lack of reproducibility.

Conclusions: The reproducibility of the previously proposed decision rule was poor and its potential contribution to clinical management of children with febrile urinary tract infection seems to be modest.

Editorial Comment

The authors attempt to validate a previously proposed decision-rule that can be used to decide when to obtain a VCUG in children who have had a first febrile UTI. This is potentially valuable, as any method of limiting the number of catheterized studies in young children would be beneficial. The proposed decision-rule takes into account the age, gender, family history, C-reactive protein and dilation noted on ultrasound. These are all clinically relevant features of the child presenting with a febrile UTI.

Unfortunately, the current study population did not support the use of the decision-rule. In order not to miss a positive VCUg, only 3 of the 143 patients would have been excluded. Nineteen could have been excluded if the clinician would be willing to miss 8% of the refluxing patients, including 1 of the 14 with at least grade 3/5 reflux. Moreover, it is well known that VCUGs themselves are only about 80% sensitive. Hence, the reported analysis is likely an overly positive estimate of the benefits of the decision-rule.

Hanging over this study is the possibility (that this author does not agree with) that diagnosing reflux, is itself of no value. Some have proposed giving temporary prophylactic antibiotics to all patients with febrile UTIs. Others have suggested that prophylactic antibiotics themselves are of no value; if so, why bother diagnosing reflux? In clinical practice, most clinicians still want to diagnose reflux. Therefore, a decision-rule like the one proposed would be of great value. At this time, unfortunately, none exists.

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Testicular Growth from Birth to Two Years of Age, and the Effect of Orchidopexy at Age Nine Months: A Randomized, Controlled Study

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Acta Paediatr. 2006; 95: 318-24

Aim: To study whether surgical treatment at age 9 mo in boys with congenitally unilaterally palpable undescended testes (cryptorchidism) is followed by improved growth of the previously retained testes compared to non-treatment.

Methods: At the age of 6 mo, 70 boys were randomized to surgical treatment at 9 mo and 79 boys to treatment at 3 y of age. The boys were then followed at 12 and 24 mo. Ultrasonography was used to determine testicular volume.

Results: After orchidopexy, the previously retained testes resumed growth and were significantly larger than the non-operated testes at 2 y (0.49 ml vs 0.36 ml, $p < 0.001$). Testicular growth after orchidopexy was also demonstrated by a higher mean ratio between the previously retained and the scrotal testes of the individual boys at 2 y: 0.84 for the surgically treated group, compared to 0.63 for the untreated group ($p < 0.001$).

Conclusion: Surgery at 9 mo has a beneficial effect on the growth of previously undescended testes.

Editorial Comment

The authors performed an excellent, randomized study of surgery at 9 months vs. delayed surgery (planned for 3 years of age) for undescended testes. They report that 1) undescended testes are slightly smaller than their descended contralateral matches are shortly after birth; 2) these testes lose considerable ground during the first 6 months of life; 3) those operated on grow much better than those non-operated on during the first 24 months of life.

This is the first randomized trial of early surgery in these patients and demonstrated a clear benefit in terms of testicular size. It is extremely important from that standpoint and it is rewarding for most surgeons in that it supports early surgery. On the other hand, there are a number of questions that the study raises. First, the size measurements were difficult to blind. Those still undescended clearly were notable at the time of the ultrasound and there might well be observer bias. Second, one has to wonder if the increased size is at all

related to lymphatic obstruction. Doing a proper orchiopexy may well require damaging most lymphatics, resulting in a large testis in the first year or 2 postoperatively. This type of enlargement might not be discernable on ultrasound. Third, the study results are reported after 24 months, so we do not know if those children operated on later might have the same increase in growth and therefore, there may not be any benefit to early surgery. Fourth, we do not know if the larger testis is any better functionally. Indeed, most studies suggest that the undescended testis contributes little to ultimate fertility. This is an early report of a much larger study and we can expect that the answers to some of these questions will be forthcoming.

Overall, the authors are to be congratulated on a careful randomized study of this complex problem. We eagerly look forward to further reports from this study.

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