International Braz J Urol
Official Journal of the Brazilian Society of Urology
Vol. 30 (6): 514-534, November - December, 2004

UROLOGICAL SURVEY

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EDITORIAL COMMITTEE

STONE DISEASE

Rapid Communication: Relative effect of urinary calcium and oxalate on saturation of calcium oxalate

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Kidney Int. 2004; 66: 2032-7

Background: The study compared the effect of urinary calcium with that of oxalate on urinary saturation [relative saturation ratio (RSR)] of calcium oxalate.

Methods: A retrospective data analysis was conducted on urinary stone risk analysis from 667 patients with predominantly calcium oxalate stones. Urinary RSR of calcium oxalate was individually calculated using Equil 2. A "theoretical" curve of the relationship between urinary RSR of calcium oxalate and concentration of calcium or oxalate was obtained at two stability constants for calcium oxalate complex, while varying calcium or oxalate and using group mean values for urinary constituents.

Results: At the stability constant of 7.07 x 10(3), the increase in RSR of calcium oxalate was less marked with calcium than with oxalate. However, at the stability constant of 2.746 x 10(3) from the Equil 2 that is considered the "gold standard," calcium and oxalate were equally effective in increasing RSR of calcium oxalate. The above theoretical curves (relating RSR with calcium or oxalate) were closely approximated by the actual curves constructed with data from individual urine samples. Urinary saturation of calcium oxalate was equally dependent on urinary concentrations of calcium and oxalate ($r = 0.75$ unadjusted and 0.57 adjusted for variables, and $P < 0.0001$ for calcium; $r = 0.73$ unadjusted and 0.60 adjusted, $P < 0.0001$ for oxalate).

Conclusion: Among calcium oxalate stone-formers, urinary calcium is equally effective as urinary oxalate in increasing RSR of calcium oxalate.

Editorial Comment

It has long been held that urinary oxalate is a more important contributor to calcium oxalate stone formation than urinary calcium. This perception stems from work published in 1972 by Nordin, Peacock and Wilkinson (1) in which the relationship of urinary calcium and oxalate concentration on urinary saturation calcium oxalate was determined using the stability proposed by Robertson of 7.07 x 10(3). Their work showed that although urinary saturation of calcium oxalate initially increased with increasing urinary calcium concentration, saturation reached a plateau at moderate calcium concentration; in contrast, saturation of calcium oxalate continued to rise with increasing urinary oxalate concentration, thereby supporting a more pronounced effect of urinary oxalate than calcium on urinary saturation of calcium oxalate. Although Robertson later adjusted his stability constant, in line with a lower stability constant proposed by Finlayson (2), the relationships between urinary calcium and oxalate and urinary saturation of calcium oxalate were never re-assessed.

Pak and colleagues reexamined the relative contribution of urinary calcium and oxalate on urinary saturation of calcium oxalate using retrospective data from predominantly calcium oxalate stone formers in their stone registry. First, they constructed theoretical curves relating urinary calcium and oxalate concentrations to urinary saturation of calcium oxalate using average values for urinary analyses derived from the population of patients studied and varying the urinary calcium and oxalate concentrations from zero to 2 standard deviations above the mean of the patient-derived values. When the higher original Roberson stability constant was used, urinary saturation reached a plateau at relatively lower concentrations of urinary calcium than urinary oxalate. On the other hand, when the lower Finlayson stability constant was used (as is used in the Equil 2 computer

program, considered the gold standard for calculating saturation of stone-forming salts), saturation increased with both urinary calcium and oxalate concentrations, with the 2 curves departing only at high concentrations, at which point the curves reached a plateau at relatively lower calcium than oxalate concentrations. Furthermore, when actual urinary saturations were plotted against urinary calcium and oxalate concentrations for the patients in the database using the 2 stability constants, the "actual" values closely approximated the "theoretical" values derived using the lower Finlayson stability constant. Of significance, the calcium and oxalate curves were nearly superimposable.

These findings suggest that urinary calcium and oxalate contribute equally to the tendency toward calcium oxalate stone formation. As such, recent studies downplaying the role of dietary calcium in stone formation and advising against calcium restriction for stone prevention should be viewed cautiously. Indeed, urinary calcium, among stone risk factors, has most consistently been shown to be associated with risk of calcium stone formation. Although these findings in no way minimize the contribution of oxalate to calcium oxalate stone formation, both dietary calcium and oxalate should be taken into account when recommending dietary measures for stone prevention and efforts to reduce both levels in the urine may result in reduced stone formation rates.

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Fluid absorption during ureterorenoscopy

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Background and Purpose: Ureterorenoscopy (URS) is a common minimally invasive diagnostic and therapeutic modality for ureteral and renal pathology. Fluid absorption during routine URS has not been studied prospectively, despite the fact that fluid absorption during other endoscopic urologic procedures can be substantial.

Patients and Methods: During URS in 15 male and 8 female patients with a mean age of 54 years (range 19 - 81 years), volumetric balance was performed by measuring all fluids instilled into the urinary tract (irrigation fluid and contrast medium) and fluids collected from the urinary tract (irrigation fluid, contrast medium, and urine output) and by estimating urine output from creatinine concentration in the urine and in the fluids collected from the urinary tract. Fluids from the urinary tract were assessed by measuring drainage fluid and the preoperative and postoperative weights of the drapes and bedsheets. Of the procedures, 11 were right-sided and 12 were left-sided. The indications for URS were urolithiasis (N = 18) and diagnosis (hematuria in 2, ureteral or renal filling defect in 2, flank pain and hydronephrosis in 1).

Results: The mean total operative time was 55 minutes (range 20 - 95 minutes), and the mean URS time was 37 minutes (range 8 - 83 minutes). The mean volume of irrigation fluid used was 2531 mL (range 552 - 5580 mL). The mean estimated urine output during the procedure was 62 mL (range 7 - 201 mL). The mean estimated systemic fluid absorption during URS was 54 mL (range 4 - 137 mL). There were two intraoperative complications (ureteral perforations) but no postoperative complications.

Conclusions: Routine URS is associated with minimal systemic fluid absorption, even if ureteral perforation occurs. Estimated absorption of as much as 137 mL was seen; however, evaporative losses and unaccounted for losses of fluid likely account for a substantial portion of this fluid discrepancy. This result suggests that irrigation with fluids other than normal saline, such as sterile water, during URS is likely safe.

Editorial Comment

As ureteroscope design and instrumentation have improved, ureteroscopic procedures have become more ambitious; it is increasingly common to treat larger and more complex renal calculi with ureteroscopy, particularly as the limitations of shock wave lithotripsy have become better defined. However, with more complex ureteroscopic cases have come longer operative times and greater potential for complications. Among the potential problems with lengthy ureteroscopic cases are sepsis and systemic absorption of irrigation fluid similar to that seen in TURP syndrome and that reported in some PCNL cases.

Cybulski and colleagues attempted to quantitate systemic fluid absorption during routine ureteroscopy (both diagnostic and therapeutic) by applying volumetric balance studies of input and outflow fluids, estimating urine output by creatinine concentration measurement of the urine and outflow fluid. Among 18 ureteroscopic cases with a mean ureteroscopy time of 37 minutes, mean systemic fluid absorption was only 54 cc, which correlated strongly with actual ureteroscopy time. Among 2 cases of ureteral perforation, fluid absorption was approximately twice the average. The authors concluded that fluid absorption during routine ureteroscopy is minimal and use of sterile water irrigation fluid may be safe, but deserves further study.

This is an important study, the first of its kind to quantitate systemic fluid absorption during ureteroscopy and show that the risk of significant fluid absorption and the associated consequences are minimal during routine cases. However, it is important to keep in mind that the average ureteroscopy time in this series was quite short, only 37 minutes. Most of the more complex ureteroscopic procedures performed today (for stones as large as 2 cm or more), are associated with lengthier ureteroscopy times. It is not known if fluid absorption is a linear process, correlating directly with ureteroscopy time, or if the rate of absorption may accelerate with time. Second, in the current series, a ureteral access sheath was used in all cases. It has been shown in both a cadaver study (1) and in a clinical series (2) that use of a ureteral access sheath reduces intrarenal pressure, which in all likelihood will reduce the chance of fluid absorption from the collecting system. Whether fluid absorption is greater in cases performed without an access sheath remains to be seen, but the use of a ureteral access sheath may increase the margin of safety for lengthy ureteroscopic procedure for exactly this reason. Thus, although this important study shows that fluid absorption during routine ureteroscopic cases is minimal, extrapolation to longer more complex cases is not advisable, and the use of water should be discouraged. Having personally reviewed several medicolegal cases of deaths due to use of sterile water irrigation during prolonged ureteroscopic cases, I suggest that the advantage gained in visibility with the use of sterile water irrigation is not worth the risk.

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ENDOUROLOGY & LAPAROSCOPY

Laparoscopic transuterine fetal vesicostomy: a feasibility study

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Purpose: We evaluate the feasibility of applying minimally invasive techniques for fetal vesicostomy. We also evaluate whether transuterine fetal vesicostomy can be performed laparoscopically.

Materials and Methods: A total of 25 pregnant ewes were time dated at approximately 90 days of gestation. With the animals under general anesthesia a low open abdominal incision was made and the uterus was brought out through the incision. With a 14 gauge needle the amniotic sac was filled with 1 to 2 L warm glycine. Three to 4, 5/12 blunt tip balloon trocars were placed in the uterus. Using laparoscopic techniques, a low transverse incision was made in the fetal abdomen, the bladder was opened at the dome and 2 running sutures were placed approximating the fetal abdominal wall to the edge of the fetal bladder. The trocar sites in the uterus were closed, and the maternal abdominal incision was closed.

Results: Of the 25 pregnant ewes the technique was developed in the initial 15. In the subsequent 10 animals the complete procedure was accomplished successfully. Following these 10 procedures 5 abortions occurred on postoperative day 2, and there was 1 intrauterine fetal demise. Three fetuses were alive and delivered by cesarean section on postoperative days 10, 30 and 31. In the first fetus in which we used an interrupted suture for the vesicostomy a large hernia was noted at the vesicostomy site. The other 2 fetuses had a patent, well healed vesicostomy and were alive at cesarean section delivery on postoperative days 10 and 31. The last fetus was allowed to deliver at term by standard vaginal delivery. The fetus was alive and well, and the vesicostomy had strictured down to a pinhole in size, which was not unexpected as it was not an obstructed model.

Conclusions: Although technically challenging, transuterine laparoscopic fetal vesicostomy is technically feasible in the ewe model. Continued evaluation of this technique should include intensive fetal monitoring and the use of tocolytics to decrease the incidence of spontaneous abortion.

Editorial Comment

Fetal bilateral hydronephrosis with oligohydramnios is an indication for evaluation and potential fetal intervention. Currently, when fetal lungs are immature with good renal function, vesical decompression can be performed in utero percutaneously with the placement of a shunt (stent) but the results are suboptimal due to malfunction of the stents often requiring manipulation or replacement.

The authors studied the feasibility of laparoscopic technique to perform transuterine fetal vesicostomy using an animal model.

Interesting technical aspects should be noted; i.e., the exchange of the amniotic fluid with warm glycine to optimize visualization and cauterization, the use of blunt tip balloon trocar to prevent fluid leakage through port sites and closure of port sites with endoscopic gastrointestinal anastomosis staplers. Clearly, the development of this technique required several steps including a significant number of animals culminating with 1 strictured and 2 well healed patent vesicostomies. The authors should be congratulated for the well designed and pioneering study.

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Transperitoneal or extraperitoneal laparoscopic radical prostatectomy: does the approach matter?

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J Urol. 2004; 172 (6 Pt 1): 2218-23

Purpose: The greater accuracy of apical dissection and reconstruction in our first 100 patients undergoing transperitoneal laparoscopic radical prostatectomy (TLRP) was not matched by a proportionate increase in the rate of return to normal continence compared with our prior open prostatectomy experience. We postulated that greater bladder dysfunction due to the almost total bladder dissection mandated by TLRP might be responsible and this might be rectified by the adoption of laparoscopic radical prostatectomy using an extraperitoneal approach (ELRP).

Materials and Methods: A total of 100 patients undergoing TLRP were compared with 100 undergoing ELRP. The groups were subdivided into halves to investigate the influence of any learning curve effect. All patients had clinical stage T3aN0M0 or less prostate cancer and they were operated on by a single surgeon.

Results: Mean operative time (238.9 vs. 190.6 minutes), blood loss (310.5 vs. 201.5 ml), postoperative hospitalization (3.8 vs. 2.6 nights) and catheterization duration (11.3 vs. 10.1 days) were significantly greater in the TLRP group. After the first 50 cases were excluded in each group statistical significance persisted only for operative time (218.3 vs. 184.2 minutes) and hospitalization (3.5 vs. 2.5 nights). The pad-free rate was significantly lower 3 months following ELRP (80% vs. 56%, p = 0.02). The overall 12-month pad-free rate for TLRP and ELRP was 90% and 96%, respectively. The overall 12-month erection rate for TLRP and ELRP was 61% and 82%, respectively.

Conclusions: ELRP is superior to TLRP with respect to operative time, hospitalization and early continence.

Editorial Comment

Since Guillonneau & Vallancien first described their successful series of transperitoneal laparoscopic radical prostatectomy this procedure disseminated world-wide.

Recently, few other centers developed the extraperitoneal technique mimicking the open approach. Although the anatomical features are more familiar to the surgeon the working operative space is more limited. Conversely, the ELRP can be performed with the patient in supine position and potentially decreases the incidence of ileus since the peritoneum is not violated.

Important points discussed in this manuscript: 1) LRP should be taught by a mentor/proctorship program, 2) Surgeons performing LRP must have enough experience with radical prostatectomies anatomical variations and its complications (more than 50 cases yearly), 3) According with the authors bladder mobilization in the TLRP group affected patients early urinary continence recovery compared to the ELRP. The authors tried to remove other factors out of the equation, i.e.; learning curve, prior obstructive problems and surgeries. The overall rate of positive margins were the same revealing that the dissection was performed uniformly in terms of technique but question remains if the last group of ELRP patients with higher clinical stage prostate cancer and higher positive margin rate had more incontinence than the rest. Certainly the observations are intriguing and provoking but better delineation of the pathophysiology is needed.

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IMAGING

Differentiation of renal clear cell carcinoma and renal papillary carcinoma using quantitative CT enhancement parameters

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AJR Am J Roentgenol. 2004; 183: 1387-91

Objective: The purpose of our study was to evaluate quantitative multiphasic CT enhancement patterns of malignant renal neoplasms to enable lesion differentiation by their enhancement characteristics. We used a new method to standardize enhancement measurement in lesions on multiphasic CT not being influenced by intrinsic factors like cardiac output.

Conclusion: The new correction method is a simple tool for excluding intrinsic influences on the enhancement of lesions. Quantitative enhancement evaluation with this method of the influence of intrinsic factors enables accurate differentiation between renal clear cell carcinoma and renal papillary carcinoma.

Editorial Comment

The authors present an interesting and standardized method of measurements of the attenuation of renal tumors on computed tomographic studies, which are designed to eliminate the influence of intrinsic factors on the measured attenuation values of these lesions. This method was able to differentiate the most common malignant renal tumors accurately and was performed using multiphasic CT (unenhanced, corticomedullary, and nephrographic phases). In this study, the author used an enhancement correcting method in the corticomedullary phase, which allowed them to differentiate renal clear cell carcinoma from renal papillary carcinoma with an accuracy rate of 95.7. In other words this study showed a high enhancement in the corticomedullary phase in renal clear cell carcinoma with a slight washout in the nephrographic phase; it showed a low enhancement in many renal papillary carcinomas - sometimes less than 12 H in the corticomedullary phase - but in the nephrographic phase, the enhancement of renal papillary carcinoma was clearly higher than 12 H.

Several recent papers have dealt with the CT capabilities of distinguishing the histological type of renal cell carcinoma. The reason for this effort is related to the potential effect of this differentiation in the preoperative and operative strategies. As we know the papillary sub-type of renal cell carcinoma has better prognosis than the clear cell carcinoma. This information might be useful in the management of patients with high surgical risks. Because renal papillary carcinoma are usually hypovascular they may also show less propensity for bleeding during surgical resection or during conservative treatments such radiofrequency ablation or cryotherapy.

Further studies, with larger number of patients, is necessary to confirm the CT capabilities to differentiate the histological sub-types of renal cell carcinoma.

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Organ-confined prostate cancer: effect of prior transrectal biopsy on endorectal MRI and MR spectroscopic imaging

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Objective: Our aim was to determine the effect of prior transrectal biopsy on endorectal MRI and MR spectroscopic imaging findings in patients with organ-confined prostate cancer.

Materials and Methods: Endorectal MRI and MR spectroscopic imaging were performed in 43 patients with biopsy-proven prostate cancer before radical prostatectomy confirming organ-confined disease. For each sextant, two independent reviewers scored the degree of hemorrhage on a scale from 1 to 5 and recorded the presence or absence of capsular irregularity. A spectroscopist recorded the number of spectrally degraded voxels in the peripheral zone. The outcome variables of capsular irregularity and spectral degradation were correlated with the predictor variables of time from biopsy and degree of hemorrhage after biopsy.

Results: Capsular irregularity was unrelated to time from biopsy or to degree of hemorrhage. Spectral degradation was inversely related to time from biopsy ($p < 0.01$); the mean percentage of degraded peripheral zone voxels was 18.5% within 8 weeks of biopsy compared with 7% after 8 weeks. Spectral degradation was unrelated to the degree of hemorrhage.

Conclusion: In organ-confined prostate cancer, capsular irregularity can be seen at any time after biopsy and is independent of the degree of hemorrhage, whereas spectral degradation is seen predominantly in the first 8 weeks after biopsy. MRI staging criteria and guidelines for scheduling studies after biopsy may require appropriate modification.

Editorial Comment

This study provides several important information related to the performance and interpretation of endorectal MR and MR spectroscopic imaging of the prostate after transrectal biopsy. As we know a thickened and irregular prostate capsule is an important MRI sign of extra-prostatic tumor extension. The authors suggests that these capsular changes are common in organ-confined prostate cancer and are unrelated to time from biopsy and extent of post-biopsy hemorrhage and that these changes may represent a normal variant rather than a biopsy artifact. Another interesting finding was related to the presence of spectral degradation on MR spectroscopic studies. This spectral curve degradation was significantly more frequent within the first 8 weeks after transrectal biopsy and was caused by post-biopsy changes. It is well known that post- biopsy hemorrhage usually precludes an optimal result in the conventional endorectal MRI study performed for local staging of prostate cancer. Since post-biopsy changes precludes also an optimal spectroscopic evaluation of the metabolites, the authors recommend that a period of 8 weeks after biopsy is necessary before submit the patient to a MRI and MR spectroscopic evaluation. This information is very important because recent studies have shown that the ideal MRI protocol for local staging of prostate cancer is obtained with the association of conventional endorectal MRI and 3D-MR-spectroscopic techniques. 3D-MR-spectroscopic imaging offers important additional information to the conventional endorectal MRI exam such as: estimative of tumor volume, better prediction of an extra-prostatic disease and information about tumor aggressiveness. As the authors pointed out, this optimized post-biopsy interval for an adequate MRI and MR spectroscopic imaging should be balanced against patient anxiety, although this interval is probably negligible in terms of the natural history of prostate cancer.

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UROGENITAL TRAUMA

High-grade renal injuries in children - is conservative management possible?

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Urology. 2004; 64: 574-9

Objectives: To review our experience with the management of high-grade (grade IV and V) renal injuries to clarify the role of conservative management.

Methods: From 1991 to 2003, 79 consecutive patients (age range 2 to 14 years) with renal injuries were treated in an urban level I pediatric trauma center. Twenty children were identified as having high-grade renal injury (grade IV, 10 children and grade V, 10 children). The mechanism of injury was blunt trauma in 17 patients (85%) and penetrating trauma in 3 (15%).

Results: Of the 10 patients with grade IV injury, 8 (80%) were successfully treated conservatively with bedrest and catheter drainage. Two patients with persistent urine leaks required ureteral stenting, and one subsequently required open operative repair. The initial radiographic findings in both patients demonstrated complete renal fracture with retained vasculature to both renal segments. All 10 patients with grade V injury required open operative management and only 3 (30%) achieved long-term renal salvage.

Conclusions: Most children with grade IV renal injury can be treated conservatively. Patients with complete renal fracture or significant urinary extravasation on initial radiographic imaging may be less likely to undergo spontaneous resolution. Patients with a persistent urinary leak can be successfully treated with internal drainage. Grade V injuries are associated with an increased risk of requiring open operative intervention, and the renal preservation rates are low.

Editorial Comment

Information on pediatric renal trauma has lagged behind information reported about adults. Now several excellent papers have been published which attempt to establish the “proper” amount of surgery for children with renal trauma.

The paper by Rogers et al. attempted conservative management even for Grade IV injury. Only 1 of their 10 patients required a stent and 1 required open repair. All 10 Grade V injury patients required surgery, and this was a nephrectomy in 7/10 patients. (It is not clear to me that the remaining 3 patients truly had a Grade V injury by the description of the injuries provided in the paper). Conservative management was not without its problems. Patients had to stay at bed rest an average of 13 days, and required urinary catheterization an average of 9 days, although significant complications such as death or iatrogenic nephrectomy was avoided. Interestingly, 3 out of 3 cases of attempted vascular repair failed, further bolstering the opinion of most experts that significant unilateral renal vessel injury should be treated with nephrectomy (as repair never seems to work).

The conclusions from this study are:

1) Conservative management of even high-grade renal injuries (Grade IV) in children can be attempted.
2) Conservative management will fail only in a small percentage of the population.
3) Ureteral stents will need to be used in a small percentage.
4) Even severe penetrating renal injury might be treated nonoperatively in children.
5) Grade V renal injuries will likely still need surgery, and that surgery will likely be a nephrectomy.

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Pediatric renal injuries: management guidelines from a 25-year experience

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J Urol. 2004; 172: 687-90; discussion 690

Purpose: We defined the mechanism and cause of pediatric renal trauma, and developed guidelines for management based on the outcome analysis of operative vs. nonoperative management.

Materials and Methods: We retrospectively reviewed 374 pediatric renal injuries at San Francisco General Hospital, comparing operative vs. nonoperative management based on clinical presentation, type of renal injury, hemodynamic stability, associated injuries and the results of radiographic imaging.

Results: Blunt trauma accounted for 89% of pediatric renal trauma with a renal exploration rate of less than 2%. Penetrating trauma represented the remaining 11% with a renal exploration rate of 76%. Of grade IV renal injuries 41% were successfully managed nonoperatively based on computerized tomography and staging in hemodynamically stable children. Our overall renal salvage rate was greater than 99%.

Conclusions: Pediatric renal trauma is often minor and observation poses no significant danger to the child. In serious pediatric renal injuries early detection and staging based on clinical presentation and computerized tomography are critical for determining operative vs. nonoperative management. Regardless of the type of management the standard of care is renal preservation (less than 1% nephrectomy rate in this series).

Editorial Comment

The study by Buckley & McAninch is the largest pediatric renal trauma series ever reported. Although this center is now devoted to conservative management when appropriate, some of this series is 25 years old, and predates the time when conservative management was used widely by anyone. Interestingly, even though this series reports 374 patients, they had fewer Grade IV and V injuries than that reported in Roger's et al. smaller series of 79 patients (Urology. 2004; 64: 574-9)! In this series, 8/9 blunt Grade IV renal trauma patients were managed nonoperatively. The overall rate of exploration was higher than that seen now, however, because of the policy of exploring all penetrating trauma patients with gross hematuria, and all patients who are taken immediately to the operating room "in whom renal staging (imaging) was incomplete". To the credit of this group, only 1 patient (1%) got a nephrectomy.

The conclusions from this study are:

1) As has been reported elsewhere, blunt renal trauma patients can probably be imaged just like adults (that is, CT only with gross hematuria, major associated injuries, hypotension or deceleration).
2) Most pediatric renal injuries are minor and can be observed.
3) Major blunt renal injuries can be managed nonoperatively.
4) Nonoperative management of renal trauma may require a long hospitalization (average 14 days in McAninch and 13 days in Rogers).

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PATHOLOGY

Characterization of minute adenocarcinomas of prostate at radical prostatectomy

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Urology. 2004; 64: 733-7

Objectives: To characterize minute prostate cancer seen at radical prostatectomy. With aggressive screening and more extensive biopsy sampling, we have increasingly seen these cancers at radical prostatectomy.

Methods: We examined radical prostatectomy specimens submitted in total for minute cancer.

Results: During the past 1.5 years, 78 prostates (5.2%) had either no cancer (2 cases) or contained between one and six foci of organ-confined carcinoma (76 cases) measuring 6 mm or less, with a Gleason score of 6 or less. The mean prebiopsy serum prostate-specific antigen level was 5.8 ng/mL, and 84.6% of the patients had undergone biopsy because of an elevated prostate-specific antigen level. Of these patients, 40% had had either benign or atypical diagnoses on prior biopsies, and 43% had only minute (0.5 mm or less) foci of carcinoma on biopsy. The radical prostatectomy specimens had a mean of two cancer foci measuring, on average, 3 mm in the greatest dimension. In 85% of the cases, the side of the positive biopsy matched the side of the carcinoma found at radical prostatectomy; 81.5% of cases had high-grade prostatic intraepithelial neoplasia immediately adjacent to the cancer.

Conclusions: The incidence of minute carcinoma of the prostate has increased from 0.5% in 1988 to 5.2% in the current study. The patients often had moderately increased prostate-specific antigen levels and minute foci of carcinoma on biopsy. These small tumors at radical prostatectomy are usually discovered by fortuitous biopsy that is often preceded by other biopsies with noncancerous diagnoses. Patients with the above clinical and biopsy findings should be counseled about the possibility of finding only minute foci of carcinoma at radical prostatectomy and may want to consider watchful waiting.

Editorial Comment

The incidence of “minute” (minimal, insignificant) cancer at radical prostatectomies has substantially increased in the last years. The main reason is aggressive screening and more extensive biopsy sampling. It is important to note that “minute” (minimal, insignificant) cancer in radical prostatectomy does not mean “latent” (dorment, indolent) carcinoma. It represents a low volume (incipient) cancer that can progress either as a “latent” or a “clinical” cancer. It is important to counsel the patients about the possibility of finding only minute foci of carcinoma at radical prostatectomy including the possibility of not finding a tumor at all.

According to the authors of the study, patients having clinical and biopsy findings for minute cancers may want to consider watchful waiting. In this respect, urologists consider age an important variable but the cut point is controversial. Carter et al. (1) informed men older than 65 years that expectant management was a reasonable option for management of cancer regardless of the presence or absence of co-morbidity. The recommended follow-up for those men managed expectantly was semiannual total and free PSA measurement with digital rectal examination, and annual surveillance transrectal ultrasound directed prostate biopsies.

Reference

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Characteristics of insignificant clinical T1c prostate tumors. A contemporary analysis

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Background: The authors examined the cases of men who had undergone radical prostatectomy for low-volume clinical T1c prostate carcinoma that was judged to be "insignificant" on the basis of previously established preoperative clinicopathologic parameters. Pathologic findings subsequently were analyzed for correlations with extent of disease in an attempt to validate the contemporary usefulness of existing parameters for predicting the "significance" of prostate tumors.

Methods: A series of 237 men who had undergone radical prostatectomy for T1c disease between December 2000 and August 2003 was evaluated. Insignificant prostate carcinoma as assessed on biopsy was defined according to the 1994 Epstein criteria, which were as follows: prostate-specific antigen density < 0.15 ng/mL, Gleason score < or = 6, fewer than 3 cores containing prostate carcinoma, and < or = 50% involvement of any core with prostate carcinoma. Postsurgical pathologic findings were analyzed for potential correlations with the Epstein criteria.

Results: According to the Epstein needle biopsy criteria, organ-confined prostate carcinoma was detected in 91.6% of all patients, whereas the remaining 8.4% of patients were found to have non-organ-confined disease. Comparison of pathologic findings and Epstein biopsy criteria revealed that alteration of the original criteria did not improve the detection of non-organ-confined prostate carcinoma.

Conclusions: The findings made in the current study suggest that the majority of patients with T1c prostate carcinoma have insignificant disease. Furthermore, it was found that the Epstein criteria for identifying insignificant prostate carcinoma remained a useful tool in the making of treatment-related decisions.

Editorial Comment

Considering the aggressive screening and more extensive biopsy sampling resulting in higher frequency of stage T1c, criteria predicting "minute" (minimal, insignificant) tumor in radical prostatectomy are of utmost importance.

The Epstein criteria for identifying insignificant prostate carcinoma remain a useful tool in the making of treatment related decisions. In this study prostate-specific antigen density < 0.15ng/mL was included in the criteria. In another study Epstein et al. (1) found a positive predictive value of 94.4% using a free/total PSA of 0.15 or greater and favorable needle biopsy findings (less than 3 cores involved, none of the cores with greater than 50% tumor involvement and Gleason score less than 7).

The involvement of the cores in percentage is controversial. Other authors consider that the extension of the tumor is a better way of evaluation. Noguchi et al. (2) consider that the combination of 1 positive core with cancer length less than 3 mm. that contains no Gleason grade 4 or 5 is probably the best predictor of prostate cancer less than 0.5 cc in men with nonpalpable tumors (stage T1c). These authors also found that PSA or PSA density in combination with needle biopsy findings did not enhance prediction of tumor significance.

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INVESTIGATIVE UROLOGY

Androgen receptor expression is inversely correlated with pathologic tumor stage in bladder cancer

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Urology. 2004; 64: 383-8

Objectives: To evaluate the expression of the androgen receptor (AR) in transitional cell carcinoma (TCC) of the bladder, and to assess whether its expression correlated with pathologic tumor stage. TCC of the bladder is three times more common in males than in females. The origin of this sex difference in incidence is unknown.

Methods: We evaluated tumor specimens from 49 consecutive patients treated for TCC of the bladder at our institution between July 2002 and June 2003. Immunohistochemistry was performed using a monoclonal mouse anti-AR antibody on paraffin-embedded tissue sections of tumors obtained from transurethral resection, radical cystectomy, or resection of metastases. Specimens were assessed for AR expression, and, in tumors that demonstrated AR staining, the percentage of nuclei that stained positive was recorded.

Results: Of the 49 tumors, 26 (53.1%) expressed the AR. The percentage of tumors that expressed the AR decreased with increasing pathologic stage, from 88.9% of pTa lesions to 0% of pT3 tumors. Overall, 75% of superficial tumors (pTa + pT1 + carcinoma in situ) expressed the AR compared with 21.4% of invasive tumors (pT2 + pT3; P = 0.002). In addition, among AR-expressing tumors, the mean percentage of nuclei that stained positive for the AR was significantly greater in pTa tumors (62.5%) than in pT1 (31%) or pT2 (20%) tumors (P = 0.005).

Conclusions: We found a decrease in AR protein expression in tumors with increased pathologic stage. Our data suggest that the loss of AR expression is associated with invasive bladder cancer.

Editorial Comment

A previous study that considered smoking and occupational risks showed that the sex-related risk of bladder cancer for men persists independently of other risks (1). Some experimental studies in rats showed that the bladder tumors development is significantly grater in males than in females (2,3), although studies in humans are still scarce. A functional role for the AR in human bladder cancer has been suggested by a recent study that demonstrated that androgen treatment inhibited bacille Calmette-Guérin-induced interleukin-6 expression in bladder cancer cell lines that expressed the AR. The study also demonstrated that pharmacologic androgen deprivation restored bacille Calmette-Guérin-induced interleukin-6 expression (4).

In this present important contribution, Boorjian et al., after evaluating 49 tumor specimens, found a decrease in androgen receptors correspondent to increased pathologic stage. The authors suggest that as a

potential therapeutic application, given the high percentage of superficial (particularly Ta) tumors that expressed the AR in the present study, together with the results of androgen deprivation therapy in animal studies, the potential exists to investigate the impact of androgen deprivation therapy in superficial bladder cancer.

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Dendritic cell immunotherapy for urological cancers using cryopreserved allogeneic tumour lysate-pulsed cells: a phase I/II study

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Objective: To assess the feasibility, toxicity and immunogenicity of dendritic cell (DC)-based immunotherapy in patients with advanced urological cancers.

Patients and Methods: Patients with hormone-refractory prostate cancer (11) and metastatic renal cell carcinoma (five) received 1-3 x 10(6) intradermal allogeneic tumour lystate-pulsed DCs fortnightly for six vaccinations then monthly until disease progression. Intradermal keyhole limpet haemocyanin was injected near the DCs as the adjuvant. DC vaccine was prepared from buffy coats, then lysate-pulsed, cryopreserved in aliquots, and tested for phenotypic expression and activity in an allogeneic mixed lymphocyte reaction before clinical use.

Results: There was no evidence of significant toxicity from vaccine or adjuvant. Delayed-type hypersensitivity skin testing and biopsy revealed a cellular infiltrate to intradermal re-challenge to tumour lysate and adjuvant in almost all patients. In addition, there was increased expression of T helper type 1 cytokines, interferon-gamma-expressing T cell by ELISPOT analysis, but also interleukin-10 in a few patients. Vaccination resulted in a reduction in the level of prostate-specific antigen (PSA) in one patient, a reduction in PSA velocity in a further man and an increased PSA doubling time in six. Two of five patients with renal cell carcinoma had stabilization of disease.

Conclusion: The cryopreservation and repeated administration of DC vaccine was feasible and not toxic. There was evidence of induction of both humoral and cellular immunity to vaccine and adjuvant in most patients. The use of sequential aliquots of identical cryopreserved vaccine will ensure quality control and

greatly facilitate future clinical studies in terms of consistency of vaccine administered and the provision of primed DCs for in vitro assessment of response.

Editorial Comment

This is a very well done scientific research with immediate potential clinical implications. As the authors stated, one of the most significant limitation to current dendritic cell-based immunotherapy is the need to prepare fresh vaccine repeatedly. The ability to culture and cryopreserve numerous aliquots of identical dendritic cells from a single venesection would reduce hospital intervention for patients, and greatly facilitate clinical trials by allowing the manipulation of dendritic cells before or after freezing, and their subsequent use as sequential vaccines.

The authors demonstrated the feasibility of a potentially generic approach to cellular immunotherapy, and the preparation of identical aliquots of dendritic cell vaccine that were readily tested for safety and immunoreactivity before injecting into patients. Dendritic cell therapy resulted in significant in vitro immunological responses in patients even with very advanced disease. Also, in this study, dendritic cell vaccine showed to be safe and non-toxic

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RECONSTRUCTIVE UROLOGY

Vaginal and penile reconstruction

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Purpose of Review: Reconstructive surgery for patients with genital abnormalities or for patients who require reconstructive efforts is challenging. This review highlights those articles, which are outstanding among all those important papers, which have been published during the last year (2002-2003).

Recent Findings: A greater understanding of embryonal development improves the success of reconstructive surgery. Other factors, such as the patient's sex, influence the surgical technique used and the degree of invasiveness or complexity. In the adult the pressure to shorten hospital stays has played a big part in the continual modification and enhancement of surgical techniques. In addition to modified techniques, new off-the-shelf materials are introduced to the clinic, which seem to have the potential to improve the surgical outcome and shorten hospital stays.

Summary: With the continued successful basic anatomy and basic research, reconstructive surgery brings higher success rates. Long-term results are still required to validate the reliability of these new surgical techniques and materials.

Editorial Comment

This paper nicely outlines the current status of reconstruction of male and female genitalia for a successful reconstruction in genital abnormalities a greater understanding of the embryonal development is advantages. Flap technology and prefabrication are the currently preferred methods for surgical success in transsexual

patients. However, here again we are awaiting the clinical application of tissue-engineered segments for both the penile autologous prosthesis and vaginal cavity.

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Orthotopic bladder substitution in women: nontraditional applications

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J Urol. 2004; 171: 1585-8

Purpose: Orthotopic urinary diversion is a feasible and optimal technique for many women undergoing cystectomy. Although successful outcomes have been achieved, groups at most centers have strict selection criteria. We evaluated our experience with female orthotopic diversion in traditional and nontraditional candidates.

Materials and Methods: From September 1, 1995 to February 6, 2003 53 females with a mean age of 62 years underwent orthotopic bladder substitution. Median followup was 24 months. Clinicopathological parameters were evaluated in traditional and nontraditional patients. The nontraditional subset comprised 22 women older than 70 years (12) or had a history of pelvic radiation (2), neoadjuvant chemotherapy (6) or stress incontinence (2).

Results: The entire group had a mean operative time, blood loss and hospital stay of 6.2 hours, 1,135 ml and 8.2 days, respectively. Tumor was organ confined in 38 and extravesical in 14 patients with bladder cancer. Complications were detected in 20 patients, including 9 who were traditional (23%) and 11 who were nontraditional (50%). Daytime and nighttime continence was reported by 46 (87%) and 45 (85%) patients, respectively, of whom 11 (21%) required intermittent catheterization. Of the patients with cancer 42 were disease-free, 2 were alive with disease and 6 died of disease. The nontraditional subset was older ($p < 0.0003$) and had shorter followup ($p = 0.05$), a higher American Society of Anesthesiologists score ($p = 0.01$) and a shorter overall survival ($p = 0.001$) than the traditional group. Continence was seen in 19 of 22 nontraditional patients (86%) and 4 (18%) required intermittent catheterization.

Conclusions: Orthotopic neobladder diversion offers excellent clinical and functional results, and should be the diversion of choice in most women following cystectomy. A subset of less favorable candidates can also successfully undergo orthotopic substitution with a tolerable toxicity profile.

Editorial Comment

In this paper the authors confirm previous studies on a successful use of orthotopic neobladder in a wide range of female patients. Despite extravesical disease, an age older than 70 years, a history of pelvic radiation, neoadjuvant chemotherapy, or preoperative stress incontinence, these patients had a continence rate of 86% and an intermittent catheterization rate of 18%. None of the patients had a urethral recurrence after a median follow up of 24 months.

This study reinforces previous suggestions that an orthotopic bladder substitution in women undergoing radical cystectomy is not only feasible but also applicable to a majority with localized bladder tumors. Not everybody might agree with the technique of surgery by the authors, which might be the reason for a higher rate

of urinary retention compared to other reports, but undoubtedly this paper shows that unfavorable factors must be a contraindication for an orthotopic neobladder.

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UROLOGICAL ONCOLOGY

Primary T1G3 bladder cancer: organ preserving approach or immediate cystectomy?

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Purpose: In this retrospective nonrandomized study we compared the long-term outcome in patients with newly diagnosed stage T1G3 bladder cancer treated with transurethral resection and bacillus Calmette-Guerin or immediate cystectomy.

Materials and Methods: Of 121 patients with a median age of 67 years (range 36 to 88) diagnosed with primary T1G3 bladder cancer between 1976 and 1999, 92 were treated by transureteral resection with additional intravesical bacillus Calmette-Guerin and 29 were treated with immediate cystectomy.

Results: Of the 92 patients treated with an organ preserving approach 29 remained disease-free, local recurrence developed in 33 (36%) and progression developed in 30 (33%) at a median followup of 6.9 years (range 0.6 to 16.5). Of these 92 patients 27 (29%) underwent deferred cystectomy at a median of 12.9 months (range 4.8 to 136), of whom 10 (37%) with a median postoperative followup of 19 months (range 2 to 173) died of progressive disease with a median survival of 13 months (range 3 to 34) after cystectomy. The majority of patients who died of progressive disease refused cystectomy, were referred too late for cystectomy, were inoperable or had upper urinary tract disease. Six of the 29 patients (21%) undergoing immediate cystectomy had progression at a median of 13.2 months (range 5.5 to 37). Overall and tumor specific survival at 5 years in patients treated with an organ preserving approach was 69% and 80%, and in those treated with immediate cystectomy it was 54% and 69%, respectively.

Conclusions: The results of this analysis demonstrate that the concept of an organ preserving approach is acceptable and spares the bladder in approximately half of the patients with primary T1G3 bladder cancer. Of the patients 30% require deferred cystectomy, making meticulous, close followup mandatory.

Editorial Comment

This paper is an non-randomized observation of patients with high risk bladder cancer treated either with TUR-B and BCG or with immediate cystectomy.

The data suggest alltogether that T1G3 bladder carcinoma is a dangerous disease but can be treated effectively by TUR-B and BCG. Cystectomy may be prevented by this treatment, according to this conservative estimate, in approximately 50%.

Interestingly, if patients were looked upon closely, median time to progression, overall mortality, and all other outcome data were similar between two groups. In both groups around 15% showed positive lymph nodes at lymphadenectomy.

Tumor specific survival at 5 years was 80% and 69%, respectively (not significant). In the group of patients treated with immediate cystectomy 48% died. Even more interestingly, for tumor specific survival the difference was significant in favor of deferred cystectomy (p = 0.02).

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FEMALE UROLOGY

Mechanical properties of urogynecologic implant materials

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Int Urogynecol J Pelvic Floor Dysfunct. 2003; 14: 239-43

Synthetic suburethral slings have recently become popular despite the risk of erosion commonly associated with synthetic implants. Some of these materials seem to have unexpectedly low erosion rates. Based on the hypothesis that erosion is due, in part, to biomechanical properties, we undertook an in vitro study. The biomechanical properties of eight non-reabsorbable synthetic implant materials, stiffness (slope, N/mm) and peak load (N) were determined from load vs. displacement curves. Open-weave Prolene mesh showed unique biomechanical properties compared to other tested materials. The tension- free vaginal tape had the lowest initial stiffness (0.23 N/mm), i.e. low resistance to deformation at forces below the elastic limit, whereas the stiffest implant tested, a nylon tape, reached 6.83 N/mm. We concluded that the TVT and other wide-weave Prolene tapes have unique biomechanical characteristics. These properties may be at least partly responsible for the apparent clinical success of the implants

Editorial Comment

The authors review the biomechanical properties of currently popular implant materials used in the treatment of female stress urinary incontinence and pelvic reconstruction. Materials reviewed included polypropylene as well as polyethylene terephthalate (mersilene), expanded polytetrafluoroethylene (Gortex) and nylon. Parameters quantified included initial stiffness (load needed before the material begins irreversible deformation) and the mean peak load at which time the material will rupture. Testing indicated that the tension free vaginal tape was the least stiff of the materials tested.

The authors utilized a testing system, which is valuable to review for future researchers in this area. It would have been of great value to the reader if the authors had been able to also test the reviewed materials at identical widths; they noted in the report that some specimens were of smaller width than others secondary to their commercial production. The discussion section raises some valuable points regarding the interaction of the graft material on the native tissues and the effect of a biomechanical difference between the two. Though this paper does not comment on the manner of weave and mesh pore size it makes for excellent reading for those interested in the physical properties of these popular synthetic graft materials.

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A prospective multicenter randomized trial of tension-free vaginal tape and colposuspension for primary urodynamic stress incontinence: two-year follow-up

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Am J Obstet Gynecol. 2004; 190: 324-31

Objective: This study was undertaken to compare tension-free vaginal tape (TVT) with colposuspension as the primary treatment for stress incontinence.

Study Design: The trial was conducted in gynecology or urology departments in 14 centers in the United Kingdom and Ireland. Three hundred forty-four women with urodynamic stress incontinence were randomly assigned to groups: 175 to TVT and 169 to colposuspension. Patients were assessed using the Short Form-36 health status questionnaire, the Bristol Female Lower Urinary Tract Symptoms questionnaire, clinical examination, and a 1-hour perineal pad test. Unpaired and paired data were analyzed with the Wilcoxon rank sum and matched pairs tests, respectively, and proportions were compared with the Fisher exact test.

Results: When data were analyzed on an intention-to-treat basis, assuming patients with missing data to be treatment failures, 63% of the TVT group and 51% of the colposuspension group were objectively cured at 2 years (odds ratio 1.67, 95% CI 1.09-2.58).

Conclusion: The TVT procedure appears to be as effective as colposuspension for the treatment of urodynamic stress incontinence at 2 years.

Editorial Comment

The authors publish a follow up article to their six-month outcomes report between tension-free vaginal tape (TVT) and colposuspension (1). This is an excellent paper, which addresses surgical outcomes in patients who were randomized to one of the two anti-incontinence procedures. The paper's strength lies in its strict measurement tools including validated questionnaires, clinical examinations and pad tests. The comments section holds an interesting discussion regarding the possible patient desire for minimally invasive surgery to explain the differentially higher withdrawal rate after randomization but before surgery in the colposuspension group as opposed to the TVT group. This preference has been previously noted (2).

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PEDIATRIC UROLOGY

Paternity after adolescent varicocele repair

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Pediatrics. 2004; 114: 1631-3

Objective: Varicocelectomy has long been a therapeutic modality used in the treatment of male infertility. In the past decade, adolescent varicocelectomy has become a frequent procedure to preserve testicular growth and to help prevent future infertility. Because our clinical population includes a large portion of orthodox Jews who traditionally marry early and are forbidden to use birth control by religious law, we thought that by studying our patients, we might be able to accelerate our follow-up regarding paternity. In addition, we wanted to learn whether adolescent varicocelectomy might have any negative impact.

Methods: Questionnaires inquiring as to the marital and paternity status, postoperative course, and complications were sent to 50 patients who had undergone a unilateral or bilateral varicocele repair during adolescence and who were at least 21 years old at the time of this review. In addition, a careful chart review was performed to examine the perioperative and postoperative parameters of each respondent.

Results: Of the 43 responses (86% response rate), 18 of 18 patients who had attempted to father a child were successful. The remaining 25 were not married or had never attempted to father a child. In the paternity group, 10 of the fathers had undergone an Ivanissevich repair; the remaining 8 had a Palomo repair. Sixteen of the 18 had unilateral varicocelectomies, and 2 underwent bilateral repairs. Of those with a unilateral varicocele, the indication for surgery in 10 was a grade 2 to 3 varicocele associated with a > 20% volume difference when compared with the right testicle. Three had 10% to 20% volume loss, whereas the remaining three had unusually large grade 3 varicoceles without concurrent volume difference.

Conclusions: Varicocelectomy in the adolescent population has been proposed as a therapeutic intervention to preserve both fertility and testicular growth. Although not showing a cause-and-effect relationship, it is our contention that varicocelectomy in adolescence at worst does no harm and at best preserves fertility.

Editorial Comment

The authors report on the follow-up of 50 patients who had undergone varicocele surgery and were at least 21 years old. 43 (86%) responded and of those, 18/18 who had attempted paternity had fathered a child. They conclude that "varicocelectomy in adolescence at worst does no harm and at best preserves fertility."

This is a fascinating report by an excellent group. However, it is still best to remain skeptical about their conclusion. First, regarding the presumption that the surgery did not harm, there are several issues. 1) 7 patients did not respond. Can we presume that their results are the same as the responders? Probably not. 2) Three of the 18 had a recurrent varicocele and one of these required a second operation. 3) Similarly, three of the patients developed hydroceles (and again one required operative repair).

Regarding the suggestion that the patients benefited from the repair, there are also some issues. 1) Again, the non-responders may not have the same paternity as those that did respond. 2) There are no controls. We do not know the paternity rate of patients with the same varicoceles who are untreated. Indeed, we have no idea of the natural history of a varicocele in this population. 3) Eighteen of 18 is clearly a high rate of paternity (assuming the self-report is truly accurate), but this is a very small group. If there were a statistical comparison to a control group, a high rate of failed paternity would be needed to show a statistical difference. 4) Fifty patients were operated on, but we do not know how many adolescents with varicocele were seen. Presumably

these were the worst cases, but there are not data on presented. How many teens with normal fertility underwent unnecessary surgery?

Although we would all like to think that repair of adolescent varicoceles is beneficial in selected cases. However, a randomized prospective trial designed to prove its efficacy would be welcome.

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The outcome of prenatally diagnosed renal tumors

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J Urol. 2005; 173: 186-9

Purpose: We assessed the incidence of perinatal morbidity and evaluated the outcome in children with prenatally diagnosed renal tumors in a retrospective multicenter study.

Materials and Methods: A review of the records of patients from 20 institutions identified 28 children with prenatally diagnosed renal tumors. Prenatal findings, clinical charts, and radiological, surgical and pathological reports were reviewed in this study.

Results: There were 26 congenital mesoblastic nephromas and 2 Wilms tumors. One or more complications were identified in 20 of the 28 cases (71%) during the perinatal period. Polyhydramnios was observed in 11 fetuses (39%), 2 presented with hydrops fetalis and 7 presented in acute fetal distress requiring emergency cesarean section, of which 1 died in utero before delivery. Median gestational age of the 27 neonates born alive was 35 weeks (range 29 to 39), including 13 (46%) who were pre-term (less than 34 weeks of gestation). Complications at birth included hemodynamic instability in 3 newborns, of whom 2 underwent emergency surgery, respiratory distress syndrome in 8 (30%) and hypertension in 6 (22%). Surgical complications occurred in 7 patients (26%), including tumor rupture in 1 and intraoperative bleeding with postoperative death in 1. At a median follow-up of 42 months (range 2 to 105) 26 of the 27 children were in complete remission.

Conclusions: Fetal renal tumors have an excellent oncological outcome but a high risk of perinatal complications. Prenatal diagnosis should allow planning the delivery at a pediatric tertiary care center to avoid a potentially life threatening condition in neonates in the first hours of life.

Editorial Comment

Although neonatal renal tumors are rare, the authors report the outcome of 28 cases diagnosed prenatally. These tumors are thought to be benign based on the limited post-natal experience. However, the authors note a strikingly high complication rate, especially prenatally. Forty-six percent were born premature and a large number had hemodynamic instability, hypertension or respiratory distress. There were 7 major surgical complications. Although 26 of the 28 are doing very well at a mean follow-up of 42 months, the authors emphasize that when diagnosed in fetal life, the course of these patients is anything but benign.

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