
UROLOGICAL SURVEY

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STONE DISEASE

Secondary signs of non-enhanced CT prior to laser ureterolithotripsy: is treatment outcome predictable?

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Purpose: To correlate the presence of secondary signs of non-enhanced computed tomography (NECT) in renal units harboring ureteral calculi with intraoperative findings and treatment outcome after holmium:yttrium-aluminum-garnet laser (Ho:YAG) ureterolithotripsy.

Subjects and Methods: Two-hundred patients were prospectively included after ureteral calculi were detected on NECT. All patients underwent Ho:YAG ureterolithotripsy at the Medical University of Vienna. All CT studies were reviewed by one specialized urologist blinded to pre- and postoperative parameters for secondary signs as renal enlargement, perinephric stranding, ureteral dilation, periureteral edema, and ureteral rim sign. The impact of secondary signs on intraoperatively-verified impaction and treatment outcome was evaluated. **Results:** Of the 200 patients 85 (42.5%) harbored proximal and 115 (57.5%) harbored distal ureteral calculi. The stone-free rates for proximal and distal calculi were 80% and 97%, respectively. Although proximal stone location and intraoperatively-verified impaction correlated significantly with stone-free rates ($P < 0.0001$, $P = 0.01$), the presence of secondary signs could not predict intraoperatively-verified stone impaction or stone-free rates (renal enlargement: $P = 0.2$, $P = 0.5$; perinephric stranding: $P = 0.7$, $P = 0.5$; ureteral dilation: $P = 0.7$, $P = 0.7$; periureteral edema: $P = 0.8$, $P = 0.06$; ureteral rim sign: $P = 0.8$, $P = 0.3$).

Conclusion: Preoperative secondary signs seen on NECT in patients harboring ureteral calculi do not correlate with intraoperative findings of impaction, and do not predict treatment outcome after Ho:YAG ureterolithotripsy.

Editorial Comment

Previous studies have demonstrated that patients with secondary signs of obstruction on CT scan imaging are more likely to require surgical intervention. It would be helpful if CT scan findings could predict the success rate with ureteroscopic lithotripsy. As such, the success rates are high and complication rates uncommon with Holmium laser lithotripsy, therefore the likelihood of identifying preoperative prognostic factors is low.

The low level of success with proximal ureteral stones could be related to the reliance on semi-rigid ureteroscopy in this study - the addition of flexible ureteroscopes and stone retrieval devices may have helped improve success rates. As such, the impact of proximal ureteral stone location and endoscopic evidence of impaction may warrant further evaluation using these two modalities.

The authors report that over one-third of patients had stone impaction at the time of ureteroscopy, as defined by adherence to the ureteral wall necessitating detachment with the Holmium laser. In our experience, the risk of impaction appears related to the duration of symptoms and obstructions. Indeed, it is surprising that such a high rate of impaction was detected as the median time to intervention was only 2 days after imaging.

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Quantitative assessment of citric acid in lemon juice, lime juice, and commercially-available fruit juice products

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Background and Purpose: Knowledge of the citric acid content of beverages may be useful in nutrition therapy for calcium urolithiasis, especially among patients with hypocitraturia. Citrate is a naturally-occurring inhibitor of urinary crystallization; achieving therapeutic urinary citrate concentration is one clinical target in the medical management of calcium urolithiasis. When provided as fluids, beverages containing citric acid add to the total volume of urine, reducing its saturation of calcium and other crystals, and may enhance urinary citrate excretion. Information on the citric acid content of fruit juices and commercially-available formulations is not widely known. We evaluated the citric acid concentration of various fruit juices.

Materials and Methods: The citric acid content of 21 commercially-available juices and juice concentrates and the juice of three types of fruits was analyzed using ion chromatography.

Results: Lemon juice and lime juice are rich sources of citric acid, containing 1.44 and 1.38 g/oz, respectively. Lemon and lime juice concentrates contain 1.10 and 1.06 g/oz, respectively. The citric acid content of commercially available lemonade and other juice products varies widely, ranging from 0.03 to 0.22 g/oz.

Conclusions: Lemon and lime juice, both from the fresh fruit and from juice concentrates, provide more citric acid per liter than ready-to-consume grapefruit juice, ready-to-consume orange juice, and orange juice squeezed from the fruit. Ready-to-consume lemonade formulations and those requiring mixing with water contain ≤ 6 times the citric acid, on an ounce-for-ounce basis, of lemon and lime juice.

Editorial Comment

Citrate is the most abundant urinary organic ion and a potent inhibitor of crystallization, nucleation and crystal growth and aggregation. It acts by binding free calcium, binding to the calcium oxalate crystal surface, and blocking crystal-epithelial cell interactions. It may also impact urinary pH. This evaluation of the citric acid concentration of various fruit juices answers important questions that will help with the dietary counseling of our patients with stone disease.

As with most good studies, it also provokes further questions worthy of investigation. How does the bioavailability of the dietary citrate sources differ, and how does each source impact urinary citrate and pH? Is there variability in citrate contents based on the climate or soil composition where the fruits were grown? Though citrate levels are lower for orange juice, potassium levels are higher - would the added alkali load with orange juice enhance urinary citrate excretion and offset its lower citrate level?

For now, it is important we emphasize for patients that fresh or concentrated lemon or lime appears to be their best shot at squeezing their risk of stone recurrence.

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ENDOUROLOGY & LAPAROSCOPY

3-year actuarial biochemical recurrence-free survival following laparoscopic radical prostatectomy: experience from a tertiary referral center in the United States

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Purpose: We performed a prospective analysis of pathological and oncological outcomes following laparoscopic radical prostatectomy at a medical center in the United States.

Materials and Methods: A total of 528 men underwent laparoscopic radical prostatectomy between April 2001 and August 2005. We excluded 4 open surgical conversions (0.8%) and 16 men (3.0%) without followup. The remaining 508 men had a mean preoperative prostate specific antigen of 6.0 ng/mL (range 0.3 to 27) and Gleason score of 6.3 (range 6 to 10). Stage was cT1b in 1 case (0.2%), cT1c in 350 (68.9%), cT2a in 135 (26.6%), cT2b in 21 (4.1%) and cT2c in 1 (0.2%). Of the patients 89% underwent cavernous nerve preservation. Biochemical recurrence was defined and timed at the first prostate specific antigen of 0.2 ng/mL or greater if at repeat testing it remained 0.2 ng/mL or greater.

Results: Mean followup was 13.2 months (median 12, range 2 to 52). Pathological stage was pT0N0/Nx in 2 men (0.4%), pT2N0/Nx in 414 (81.5%), pT3aN0/Nx in 72 (14.2%), pT3bN0/Nx in 17 (3.3%) and pT2-3N1 in 3 (0.6%). Positive margin rates increased with higher stage (8.2% in pT2 and 39.3% in pT3 cases, $p < 0.0001$). Three-year actuarial biochemical recurrence-free survival was 98.2% for pT2N0/Nx and 78.7% for pT3N0/Nx/N1 disease ($p < 0.0001$), and it was 94.5% overall. Multivariate analysis controlling for age, preoperative prostate specific antigen, postoperative Gleason score and stage, and margin status showed that only Gleason score (greater than vs. less than 7) and stage (pT3 or any N1 vs. pT2) predicted biochemical progression.

Conclusions: Laparoscopic radical prostatectomy can provide excellent cancer control outcomes for clinically localized prostate cancer with high actuarial biochemical recurrence-free survival rates at 3 years.

Editorial Comment

Since the first laparoscopic radical prostatectomy (LRP) was described by Schuessler et al. in 1997 and then by Guillonnet et al. in 1999 this surgical technique has evolved, as well, as the laparoscopic instruments and better understanding of the “laparoscopic” anatomy allowed several other investigators to demonstrate no difference of oncological outcomes between the open and laparoscopic approach in their reports. In a couple of years we will celebrate the 10th anniversary of LRP performed by high volume tertiary care centers. I foresee that the oncological outcomes will be similar as the open surgical technique. Furthermore, we do need reports from trials that can compare different surgical approaches for the treatment of Prostate Cancer. Moreover, the ideal prostate cancer marker should be identified in the near future to prevent overtreatment of the disease and also to decrease disease specific mortality.

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Comparison of laparoscopic and open partial nephrectomy for tumor in a solitary kidney

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Purpose: We compared the postoperative and renal functional outcomes of patients undergoing open or laparoscopic partial nephrectomy for tumor in a solitary functioning kidney.

Materials and Methods: Between 1999 and 2006, 169 open and 30 laparoscopic partial nephrectomies were performed for 7 cm or smaller tumors in a solitary functioning kidney. Data were collected in an institutional review board approved registry and median follow-up was 2.0 years. Preoperative and postoperative glomerular filtration rates were estimated with the abbreviated Modification of Diet in Renal Disease equation.

Results: By 3 months after open or laparoscopic partial nephrectomy, the glomerular filtration rate decreased by 21% or 28%, respectively ($p = 0.24$). Postoperative dialysis was required acutely after 1 open partial nephrectomy (0.6%) and 3 laparoscopic partial nephrectomies (10%, $p = 0.01$), and dialysis dependent end stage renal failure within 1 year occurred after 1 open partial nephrectomy (0.6%) and 2 laparoscopic partial nephrectomies (6.6%, $p = 0.06$). In multivariate analysis warm ischemia time was 9 minutes longer ($p < 0.0001$) and the chance of postoperative complications was 2.54-fold higher ($p < 0.05$) with laparoscopic partial nephrectomy. Longer warm ischemia time (more than 20 minutes) and preoperative glomerular filtration rate were associated with poorer postoperative glomerular filtration rate in multivariate analysis. Notwithstanding the association with warm ischemia time, the surgical approach itself was not an independent predictor of postoperative glomerular filtration rate ($p = 0.77$).

Conclusions: While laparoscopic partial nephrectomy is technically feasible for tumor in a solitary kidney, warm ischemia time was longer and complication rates higher compared with open partial nephrectomy. In addition, although average loss of renal function at 3 months is equivalent (after accounting for warm ischemia time), a greater proportion of patients required dialysis temporarily or permanently after laparoscopic partial nephrectomy in this initial series. Therefore, open partial nephrectomy may be the preferred nephron sparing approach at this time for these patients at high risk for chronic kidney disease.

Editorial Comment

The authors should be congratulated for this enlightening, instructive manuscript.

Laparoscopic partial nephrectomy is a complex procedure with a steep learning curve but it has been demonstrated by several investigators including the present authors that it is a technically feasible surgery for small tumors even in solitary kidneys.

The warm ischemia time (WIT) was longer and complication rates higher compared with open partial nephrectomy but the loss of renal function was equal in 3 months for both groups.

Nonetheless, this minimally invasive approach is another viable treatment option that can be reserved for patients that can tolerate a slightly longer WIT (9 min. longer than open surgery).

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IMAGING

Focal prostatic atrophy: mimicry of prostatic cancer on TRUS and 3D-MRSI studies

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Objective: It is well known that histologically focal prostatic atrophy (FPA) is one of the most frequent mimics of prostatic adenocarcinoma. The purpose of our study was to show that FPA may also simulate prostate cancer on transrectal ultrasound studies (TRUS) and on 3D-magnetic resonance spectroscopic imaging of the prostate (3D-MRSI).

Materials and Methods: From 2004 to 2006, 625 men suspected of prostate cancer, underwent TRUS guided biopsy (n = 513, group I) or TRUS-guided biopsy directed with 3D-MRSI of the prostate (n = 142, group II). The latter group was formed only by patients with elevated PSA levels and prior negative prostate biopsies. All sites showing FPA on histopathologic analysis were correlated with findings observed on gray scale and color Doppler-TRUS studies or on 3D-MRSI of the prostate.

Results: From a total of 513 patients biopsied and studied by gray scale and color Doppler-TRUS(Group I) , 48 patients (9.3%) presented histological diagnosis of FPA associated with sonographic abnormalities in the peripheral zone of the prostate. Thirty-two patients presented hypoechoic nodules with absent flow and 16 patients had hypoechoic nodules with increased flow. From a total of 142 patients submitted to TRUS-guided biopsy directed with 3D-MRSI (Group II), 16 (11.2%) presented histological diagnosis of FPA associated with abnormalities strongly suspicious for prostate cancer on conventional MRI and/or on 3D-MRSI. These abnormalities were: focal area of low signal intensity on T2-w image or clusters of voxels with choline + creatine/ citrate ratio above 3 SDs.

Conclusion: Similarly to the histopathologic findings focal prostatic atrophy may mimic cancer on gray-scale and color Doppler-TRUS studies and on 3D-MRSI studies. Radiologists should be aware of this entity which together with prostatitis, represent an important cause of false-positive result on prostatic biopsy directed with endorectal MRSI (11.2%).

Editorial Comment

Prostatic atrophy is one of the most frequent mimics of prostatic adenocarcinoma. There are still controversies regarding the causal linkage of FPA to the prostate cancer and to other pre-neoplastic lesions. On conventional and color Doppler transrectal ultrasound and on magnetic resonance spectroscopic imaging studies (MRSI), FPA may also simulate prostate cancer. The vast majority of our cases that simulate prostate cancer were related to sub-type hyperplastic prostatic atrophy. We might speculate why FPA manifests as false-positive MRSI findings: in the hyperplastic sub-type, the number of cellular membranes are increased. This could explain the elevation of choline level without modification of the polyamine level. It has been shown that there is a positive and significant association between extent of FPA in biopsies and serum total or free PSA elevation. For this reason, pathologists should include the presence of FPA in the pathology report of a prostatic biopsy, particularly in those patients with absence of cancer. When extensive FPA is the only finding in patients with several negative prostatic biopsies, this lesion may be the source for PSA elevation.

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The 20-core prostate biopsy protocol--a new gold standard?

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Purpose: We investigated the ability of a 20-core prostate biopsy protocol to enhance the prostate cancer diagnosis rate.

Materials and Methods: We compared the diagnosis rate of prostate biopsies in 2 groups of consecutive patients, including group 1-10 cores and group 2-20 cores. The prostate specific antigen range in the 2 groups was 3 to 30 ng/mL and biopsies were performed because of increased prostate specific antigen (more than 3 ng/mL) and/or abnormal digital rectal examination. To analyze the results we divided each group into 3 subgroups according to prostate specific antigen, including group 1-3 to less than 6 ng/mL, group 2-6 or greater to less than 10 ng/mL and group 3-10 or greater to up to 30 ng/mL. Multivariate analysis was performed to assess the difference in the diagnosis rate among the subgroups according to the number of cores taken.

Results: The percent of positive biopsies was 39.7% in group 1 and 51.7% in group 2. Multivariate analysis confirmed that the number of biopsies taken was a factor that independently and significantly correlated with the prostate cancer diagnosis. The 20-core biopsy protocol was more efficient than the 10-core protocol in the 3 subgroups with 47.2% vs. 28.1% of patients diagnosed in group 1 (OR 3.26, $p = 0.001$), 40.5% vs. 36.1% in group 2 (OR 2.37, $p = 0.009$) and 69.8% vs. 39.7% in group 3 (OR 2.01, $p = 0.015$).

Conclusions: The 20-core biopsy protocol was more efficient than the 10-core biopsy protocol, especially in patients with prostate specific antigen between 3 and 6 ng/mL. Nevertheless, it is mandatory to confirm whether detected tumors are clinically significant on pathological examination of the radical prostatectomy specimens.

Editorial Comment

The authors of this manuscript demonstrated that the 20-core biopsy scheme was more efficient for diagnosing prostate cancer than the 10-core biopsy scheme in 3 distinct subgroups of PSA levels. Unfortunately they did not evaluate these two different protocols according to the patient age and prostate volume. As we know, prostate volume is a relevant variable in the planning of the optimal number of cores in the first scheme of biopsy. In our experience, there is no magic number of cores to be taken that could be adequate for all patients. We think that the location from where these cores were taken is more important than the total number of cores. Several reports in the literature has been shown that for prostate less than 40 cc, a scheme with 12 cores is usually adequate. However, this scheme is usually inadequate for prostate larger than 80 cc. Another important issue to consider is whether additional cores are or are not routinely obtained from suspicious hypoechoic lesion or area with clear abnormal flow on color Doppler examination. In a review of 589 consecutive TRUS-guided biopsy, where we prospectively removed 12 cores from prostates < than 40 cc; 14 cores from prostates with 41-60 cc; 16 cores from prostates with 61-80 cc and 18 cores from prostates > than 80 cc), there was no proportional increase in the prostate cancer detection rate. The two best results were obtained with 12 cores/ < 40 cc (44.8%) and 16 cores/ 61-80 cc) = 36.5%. The detection rate obtained with the scheme with 18 cores/ > 80 cc was only 29%. Additional cores obtained in all patients from suspicious lesions on gray-scale and/or color-Doppler were not included in these results. The presence of suspicious hypoechoic was not statistically significant but the use of color Doppler increased the overall diagnosis rate in 8% of patients (isoechoic cancer). Color-Doppler ultrasound was particularly useful for the detection of cancer in patients with larger glands.

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UROGENITAL TRAUMA

Retrograde urethrocytography impairs computed tomography diagnosis of pelvic arterial hemorrhage in the presence of a lower urologic tract injury

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Background: There is controversy about the appropriate sequence of urologic investigation in patients with pelvic fracture. Use of retrograde urethrography or cystography may interfere with regular pelvic CT scanning for arterial extravasation.

Study design: We performed a retrospective study at a regional trauma center in Toronto, Canada. Included were adult blunt trauma patients with pelvic fractures and concomitant bladder or urethral disruption who underwent initial pelvic CT before operation or hospital admission. Exposure of interest was whether retrograde urethrography (RUG) and cystography were performed before pelvic CT scanning. Main outcomes measures were indeterminate or false negative initial CT examinations for pelvic arterial extravasation.

Results: Sixty blunt trauma patients had a pelvic fracture and either a urethral or bladder rupture. Forty-nine of these patients underwent initial CT scanning. Of these 49 patients, 23 had RUG or conventional cystography performed before pelvic CT scanning; 26 had cystography after regular CT examination. Performing cystography before CT was associated with considerably more indeterminate scans (9 patients) and false negatives (2 patients) for pelvic arterial extravasation (11 of 23 versus 0 of 26, $p < 0.001$) compared with performing urologic investigation after CT. In the presence of pelvic arterial hemorrhage, indeterminate or false negative CT scans for arterial extravasation were associated with a trend toward longer mean times to embolization compared with positive scans ($p = 0.1$).

Conclusions: Extravasating contrast from lower urologic injuries can interfere with the CT assessment for pelvic arterial extravasation, delaying angiographic embolization.

Editorial Comment

This article brings up important points about the proper technique for performing retrograde urethrography for suspected traumatic urethral disruption injuries and for cystography for suspected bladder injuries. In this day and age, we only perform CT cystograms (instead of conventional cystography) to evaluate the patient with a pelvic fracture and gross hematuria. It was not clear from the article their criteria for deciding on bladder imaging, yet in our experience, the yield is small unless there is gross hematuria and a pelvic fracture.

The other point that this article raises, is that patients die after blunt trauma because of the “fatal triad”, namely being cold, coagulopathic and acidotic. In the initial time period after injury, adequate resuscitation and control of bleeding is key, to prevent the patient from spiraling downward. A bladder and/or urethral injury will not harm the patient or push him over the edge in the first few hours after a trauma. There is strong support for damage control of urologic injuries. It is reasonable that in a patient with a pelvic fracture who is hemodynamically unstable, the bleeding takes precedence and evaluating the urethra and bladder can wait.

As to pelvic fractures in general, the keys are to decrease the volume of the pelvis and so decrease the potential space for blood to collect. A small increase in radius increases volume by a great amount. By placing an external fixator a pelvic ring disruption, the true pelvis is reduced and cancellous bone re-approximated and in so doing allows venous bleeding to tamponade. Significant arterial bleeding, however will not stop with just true pelvis volume reduction. Arterial bleeding requires angiography and embolization. The most common arteries injured with pelvic fracture are the superior gluteal and the pudendals. Clearly, having significant

contrast extravasated from the bladder evaluation can potentially interfere with visualization of small pelvic arterial bleeders on subsequent angiography -however, the article is somewhat deceptive in that there was no statistical difference in the time to embolization in their two study populations. Perhaps, the study did not have the power to prove such- or the contrary, it may make no difference clinically.

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Three-dimensional analysis of pelvic volume in an unstable pelvic fracture

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Background: A model was developed to predict changes in pelvic volume associated with increasing pubic diastasis in unstable pelvic fractures.

Methods: Intact and postfracture pelvic volumes were calculated in 10 cadavers using computerized axial tomography (CT). The true pelvis was assumed to be either a sphere, a cylinder, or a hemi-elliptical sphere. Using the appropriate equations for calculating the volume of each of these shapes, pelvic volume was predicted and then compared with the measured values.

Results: The observed volume changes associated with increasing pubic diastasis were much smaller than previously reported. The mean difference between the measured and predicted volume was 20.0 +/- 9.9% for the sphere, 10.7 +/- 6.5% for the cylinder, and 4.5 +/- 5.9% for the hemi-elliptical sphere. The differences between these means were statistically significant ($p < 0.001$).

Conclusions: This data suggests that the hemi-elliptical sphere best describes the geometric shape of the true pelvis and better predicts quantitative changes in pelvic volume relative to an increasing pubic diastasis as the radius has little effect on the change in volume. Due to the small changes in volume observed with increasing diastasis, factors other than the absolute change in volume must account for the clinically observed effects of emergent pelvic stabilization.

Editorial Comment

This article is a complement to the above article on pelvic fracture. Reducing the absolute pelvic volume by pelvic reduction and stabilization is critical to helping venous bleeders to tamponade. Traditionally, the true pelvis is thought to be a sphere in shape, where an increase in pubis diastasis results in a marked volume increase, proportional to the radius cubed. They contend from their cadaveric experiments that the true pelvis is actually a hemi-elliptical sphere. Therefore, pelvic ring disruptions only increase the volume by the radius squared. This study suggests that reduction and stabilization of the pelvic ring disruption is more important than the reduction in volume.

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PATHOLOGY

The Impact of ISUP 2005 Consensus on Gleason Grading in Contemporary Practice

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Background: International Society of Urological Pathology (ISUP) in 2005 attempted to achieve a consensus in the application of Gleason grading system in contemporary practice. We investigated how the ISUP consensus impacted the Gleason grading in a center with a large urological pathology practice.

Design: We compared the Gleason score (GS) distribution and the GS concordance on biopsy and radical prostatectomy (RP) in two patient cohorts (before and after the ISUP consensus) in our institution. Both cohorts had similar demographic, preoperative clinical, and RP characteristics. The first cohort consisted of 908 consecutive patients with matched biopsies and RP, performed from 07/2000 to 06/2004 in our institution, prior to the ISUP consensus. The second cohort consisted of 423 patients with matched biopsies and RPs, performed from 10/2005 to 06/2007, after the ISUP consensus. All biopsies and RPs were reported by one group of pathologists.

Results: The ratio of GS 3+4 vs. 4+3 for GS7 on biopsy and RP was similar in both cohorts. Biopsy GS 7 (3+4 vs. 4+3): 24% vs. 6% (2001-2004) and 35% vs. 8% (2005-2007). RP GS 7 (3+4 vs. 4+3): 39% vs. 9% (2001-2004) and 48% vs. 12% (2005-2007). Biopsy GS compared to RP GS were upgraded in 8% and 5% and downgraded in 29% and 30% in cohorts 2001-2004 and 2005-2007, respectively. The most common change from biopsy to RP in both patient cohorts occurred due to biopsy GS 6 upgrade to RP GS 7 (change in secondary grade from 3 to 4).

Conclusions: We document a trend for upgrading GS on both biopsy and RP in our practice after the ISUP consensus. The significance of this change for patient management and prognosis is uncertain. Although the overall GS concordance on biopsy and RP have not been significantly impacted by the ISUP consensus, the complete agreement for GS7 has improved after the ISUP consensus.

Editorial Comment

The Gleason grading system is the most commonly used grading system for prostate carcinoma in the United States. Due to its unique aspects is gaining worldwide acceptance. The Gleason grading system is solely based on the architectural pattern, cytologic features are not factored in, the overall grade is not based on the highest grade within the tumor, and the prognosis of prostate cancer is intermediate between that of the most predominant pattern of cancer and that of the second most predominant pattern (1-4).

At the International Society of Urological Pathology (ISUP) consensus conference in 2005, the Gleason grading system underwent its first major revision (5). Several important reasons were considered for the need of a revision of the system: 1). In the 1960s, there was no screening for prostate cancer other than by digital rectal examination, as serum PSA had not yet been discovered. In Gleason's 1974 study (1), most (86%) of the men had advanced disease with either local extension out of the prostate on clinical examination or distant metastases. Only 6% of patients had nonpalpable tumor diagnosed by transurethral resection and 8% of patients were diagnosed with a localized nodule on rectal examination; 2). The method of obtaining prostate tissue was also very different from today's practice. Typically, only a couple of thick-gauge needle biopsies were directed into an area of palpable abnormality. The use of 18-gauge thin biopsy needles and the concept of sextant needle biopsies to more extensively sample the prostate were not developed until the 1980s. Consequently, the grading of prostate cancer in thin cores and in multiple cores from different sites of the prostate were not issues in Gleason's era; 3). In the 1960s, radical prostatectomy was relatively uncommon, prostates were not as often removed intact, and glands were not processed in their entirety or as extensively and systematically to the degree currently seen. Further issues relating to radical prostatectomy specimens such as the grading

of multiple nodules within the same prostate or dealing with tertiary patterns were not addressed within the original Gleason system; 4). The Gleason system also predated the use of immunohistochemistry. It is likely that with immunostaining for basal cells many of Gleason's original $1 + 1 = 2$ adenocarcinomas of the prostate would today be regarded as adenosis (atypical adenomatous hyperplasia). Similarly, many of the cases in 1967 diagnosed as cribriform Gleason pattern 3 carcinoma would probably be currently referred to as cribriform high-grade prostatic intraepithelial neoplasia, if labeled with basal cell markers.

Stratifying the Gleason score into prognostic groups 2-4, 5-6, 7, and 8-10, using the modified Gleason grading there is a tendency for a change toward a higher prognostic group in approximately 25% of the biopsies (6). This occurs due to some new pathology criteria used in the revised ISUP grading: a) inclusion of most cribriform patterns in grade (pattern) 4; b) considering ill-defined glands with poorly formed glandular lumina as pattern 4; c) ignoring in high-grade cancer lower grade patterns if they occupy less than 5% of the area of the tumor; d) including high-grade tumor of any quantity within the Gleason score; and, e) for tertiary Gleason patterns, both the primary pattern and the highest grade are recorded.

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A contemporary study correlating prostate needle biopsy and radical prostatectomy Gleason score

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Purpose: We determined whether contemporary practice patterns of Gleason grading for prostate needle biopsy and radical prostatectomy have evolved.

Materials and Methods: We correlated needle biopsy (assigned at Johns Hopkins Hospital and other institutions) and radical prostatectomy Gleason score for 1,455 men who underwent radical prostatectomy at Johns Hopkins Hospital from 2002 to 2003, and compared the results with those of a 1994 study of similar design.

Results: Outside institutions diagnosed Gleason score 2-4 in 1.6% (23 of 1,455) of needle biopsies vs. 22.3% (87 of 390) in 1994. Of needle biopsies labeled Gleason score 2-4, 30.4% revealed radical prostatectomy Gleason score 7-10. In 2002 to 2003 no Johns Hopkins Hospital needle biopsy was assigned Gleason score 2-4. Needle biopsies designated Gleason score 6 or less had 80.0% accuracy with regard to radical prostatectomy Gleason score vs. 63% accuracy in older data. For needle biopsy Gleason score 7 or greater, 35.5% (outside institution) and 24.8% (Johns Hopkins Hospital) of radical prostatectomies displayed Gleason score less than 7. Overall, outside and Johns Hopkins Hospital needle biopsy diagnoses showed 69.7% and 75.9% agreement with radical prostatectomy Gleason score, respectively. Direct comparison of Johns Hopkins Hospital and needle biopsy Gleason scores elsewhere revealed 81.8% agreement, with 87.1% for Gleason score 5-6, 68.1% for Gleason score 7 and 35.1% for Gleason score 8-10. For 59.4% of outside needle biopsies with Gleason score 8-10, Johns Hopkins Hospital Gleason score was 7 or less. Conversely, for 64.9% of Johns Hopkins Hospital needle biopsies with Gleason score 8-10, outside Gleason score was 7 or less. For needle biopsies with Gleason score 5-6, 7 and 8-10, the incidence of nonorgan confined disease at radical prostatectomy was 17.7%, 47.8% and 50.0%, respectively, for Johns Hopkins Hospital vs. 18.2%, 44.6% and 37.5% for outside institutions.

Conclusions: The last decade has seen the near elimination of once prevalent under grading of needle biopsy. All cases still assigned Gleason score 2-4 show Gleason score 5 or greater at radical prostatectomy and nearly a third reveal Gleason score 7-10, reaffirming that Gleason score 2-4 is a needle biopsy diagnosis that should not be made. As evidenced by variable over grading and under grading, as well as poor correlation with pathological stage, difficulties in the assignment of Gleason pattern 4 and overall Gleason score of 8-10 on needle biopsy remain an important issue.

Editorial Comment

This study underlines the issue related to the Gleason score 2-4 in biopsies. In an Editorial published in 2000 (1), Epstein favors that Gleason score 2-4 adenocarcinoma of the prostate on needle biopsy is a diagnosis that should not be made. His arguments are based on the following facts: 1) the vast majority of tumors graded as Gleason score 2-4 on needle biopsy, when reviewed by experts in urologic pathology, are graded as Gleason scores 5-6 or higher; 2) Gleason score has a poor reproducibility in its diagnosis even among urologic pathologists; 3) assigning a Gleason score 2-4 to adenocarcinoma on needle biopsies can adversely impact patient care, because clinicians may assume that low-grade cancers on needle biopsy do not need definitive therapy. Not assigning a Gleason score 2-4 to adenocarcinoma on needle biopsy it does not mean that low-grade prostate does not exist. Gleason score 2-4 adenocarcinomas are typically seen on TURP. Low-grade cancers are rarely seen on needle biopsy because they are predominantly located anteriorly in the prostate within the transition zone and they tend to be small. In a series of 2285 biopsies in consultation, Epstein assigned a Gleason score of 2-4 in only 26/2285 (1.1%) consult biopsies demonstrating cancer.

The 2005 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma recommended that, rather than stating categorically that a Gleason score 4 on needle biopsy should “never” be made, this diagnosis should be made “rarely, if ever”. While recommending that the diagnosis of Gleason score 4 on needle biopsy should be made “rarely, if ever” is similar to “never”, it does allow for the exceedingly rare case where low grade cancer has been sampled on needle biopsy. The consensus conference cautioned that although the potential exists for rendering a diagnosis of Gleason score 4 on needle biopsy, it is a diagnosis that general pathologists should almost never make without consultation to an experienced urologic pathologist.

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UROLOGICAL ONCOLOGY

Dihydrotestosterone levels and survival in screening-detected prostate cancer: a 15-yr follow-up study

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Objectives: It has been hypothesized that dihydrotestosterone (DHT), the main intracellular androgen in the prostate, affects prostatic tumour progression. In this study, we evaluated serum DHT levels at the time of prostate-cancer diagnosis in relation to survival.

Methods: Sixty-five screening-detected patients diagnosed in 1988-1989 were followed for 15 yr. DHT levels at the time of diagnosis were determined through radio-immuno assay. Subjects were followed up through the nationwide tax register. Medical records of all dead subjects were reviewed, and cause of death was established by an endpoint committee. Data were analyzed through Kaplan-Meier estimation and Cox proportional-hazards regression.

Results: Seventeen of 41 deaths in the cohort during follow-up were attributed to prostate cancer. Patients with DHT above the median had a significant better prostate-cancer-specific survival than those with DHT below the median (log rank $p = 0.0075$). In the univariate analyses, one unit increase in DHT was associated with a hazard ratio (HR) of 0.14 (95% CI=0.02-0.93). In the multivariate model, including prostate-specific antigen level, the association between DHT and prostate-cancer-specific survival was not significant (HR=0.18; 95% CI=0.02-1.6). DHT level below the median remained significantly associated with decreased survival in the multivariate model (HR=0.23; 95% CI=0.06-0.90). No association was found between DHT level and hazard of dying from causes other than prostate cancer.

Conclusions: Although the prognostic value of DHT levels at diagnosis remains unclear, these results provides evidence of an association between low DHT and decreased survival in prostate cancer patients.

Editorial Comment

The association of androgens and prostate cancer is still debated. This trial analyzes the relation of dihydrotestosterone (DHT) levels and survival in prostate cancer patients. Testosterone is the principal androgen and the main intracellular androgen in the prostate is DHT. DHT arises from intracellular conversion of testosterone and binds to the intracellular androgen receptor with an affinity seven-fold higher than testosterone.

The authors found a correlation of decreased survival and low DHT serum levels in their cohort of 65 patients. Although this study is hampered by several flaws such as small patient numbers, this is still a very

interesting manuscript, and to my knowledge, the first to look into DHT serum levels and prostate cancer survival. Further studies should focus into this topic.

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The template of the primary lymphatic landing sites of the prostate should be revisited: results of a multimodality mapping study

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Eur Urol. 2008; 53: 118-25

Objectives: To map the primary prostatic lymphatic landing sites using a multimodality technique.

Methods: Thirty-four patients with organ-confined prostate cancer (cT1-cT2; cN0) underwent single-photon emission computed tomography fused with data from computed tomography (SPECT/CT) (n = 33) or magnetic resonance imaging (SPECT/MRI) (n = 1) 1h after ultrasound-guided intraprostatic injection of technecium (Tc-99m) nanocolloid. The presence of lymph nodes (LNs) containing Tc-99m was confirmed intraoperatively with a gamma probe. A backup extended pelvic lymphadenectomy (PLND) was performed to preclude missed primary lymphatic landing sites. The SPECT/CT/MRI data sets were used to generate a three-dimensional projection of each LN site.

Results: A total of 317 LNs (median, 10 per patient; range, 3-19) were detected by SPECT/CT/MRI, 314 of which were confirmed by gamma probe. With an "extended" PLND, two thirds of all primary prostatic lymphatic landing sites are resected compared with only one third with a "limited" PLND.

Conclusions: The multimodality technique presented here enables precise mapping of the primary prostatic lymphatic landing sites. PLND for prostate cancer should include not only the external and obturator regions as well as the portions medial and lateral to the internal iliac vessels, but also the common iliac LNs at least up to the ureteric crossing, thus removing approximately 75% of all nodes potentially harbouring metastasis.

Editorial Comment

This report from Berne, Switzerland focuses on the extend of retroperitoneal lymph node dissection in prostate cancer. The authors used Spect/CT and MRI data to localize the lymph nodes in prostate cancer and tried to remove these during radical prostatectomy. They found primary landing site lymph nodes up to the mesenteric vein and para-aorta. The authors conclude that upon classical lymph-node dissection (LND) only 38% of the relevant lymph nodes are removed. On the other hand, pararectal, pre-sacral and para-aortal LND would add to morbidity and would compromise the results of nerve-sparing RPE. Therefore, an extended LND is seen as a compromise in patients with risk of nodal disease, where the template of classical extended LND is encompassed by a template including the common iliac arteries up to where the ureters cross. By this extended template up to 75% of the relevant lymph nodes would be removed.

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NEUROUROLOGY & FEMALE UROLOGY

Dyspareunia response in patients with interstitial cystitis treated with intravesical lidocaine, bicarbonate, and heparin

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Objectives: To test the dyspareunia response of patients with interstitial cystitis/painful bladder syndrome treated with an intravesical therapeutic solution of lidocaine, heparin, and sodium bicarbonate.

Methods: We studied consecutive patients with interstitial cystitis/painful bladder syndrome who were sexually active and were treated with an intravesical therapeutic solution. All patients provided their medical history, underwent a physical examination, and completed the Pelvic Pain Urgency Frequency symptom scale, voiding diary, and the pain domain (questions 17 to 19) of the Female Sexual Function Index before and after therapy. The patients were treated with intravesical instillations three times weekly for 3 weeks. The patients returned for follow-up 3 weeks later. The patients rated their response using a Patient Objective Rating of Improvement of Symptom scale.

Results: A total of 23 patients (mean age 38 years) were included in this study. Of the 23 patients, 15 (65%) reported improvements of greater than 50% on the Patient Objective Rating of Improvement of Symptom scale. Before and after instillation, nocturia was 4 +/- 2 versus 2 +/- 1 ($P < 0.001$), the voided volume was 98 +/- 59 mL versus 169 +/- 80 mL ($P < 0.001$), the Pelvic Pain Urgency Frequency score was 21 +/- 6 versus 15 +/- 6 ($P < 0.001$), and the Female Sexual Function Index pain domain score was 1.9 +/- 0.9 versus 3.7 +/- 1.6 ($P < 0.001$), respectively. Of the 23 patients, 13 (57%) reported resolution of dyspareunia. Of the 13 patients with bladder tenderness only versus the 7 with multiple tender locations on the vaginal examination, 11 (85%) versus 2 (29%) had resolution of dyspareunia ($P < 0.01$) and 12 (92%) versus 2 (29%) had successful overall outcomes ($P < 0.01$).

Conclusions: The results of this study have demonstrated that an intravesical therapeutic solution provides relief of voiding symptoms, pain, and dyspareunia in patients with interstitial cystitis/painful bladder syndrome. A randomized, prospective trial is warranted.

Editorial Comment

The authors analyzed the rate of dyspareunia in a female patient population diagnosed with interstitial cystitis and subsequently treated with intravesical instillations of a lidocaine/sodium bicarbonate/heparin solution three times a week for three weeks in a row. The therapy seemed to have a certain level of durability in that a definite percentage of patients were asymptomatic for three weeks. The authors noted that patients had a much higher response rate if prior to treatment they were plagued with bladder tenderness only on physical examination as opposed to a diffusely painful vagina on digital palpation.

This interesting paper highlights the association of sexual problems in patients with interstitial cystitis. It is heartening that those patients who had basically only bladder tenderness on vaginal palpation experienced an 85% resolution of their dyspareunia with this instillation therapy. The authors note that alkalinizing the lidocaine will allow it to have a greater penetration of bladder epithelium. Alkalinization of lidocaine has also been reported to diminish pain during interdermal injections with local infiltrated anesthesia. I found it noteworthy that the total solution instilled in the bladder was only 14 cc while the lidocaine gel instilled in the urethra to anesthetize prior to catheterization was 10 cc in itself. The logistical efficacy of intravesical therapies for patients in the office cannot be understated. Those with an interest in this specific population and therapy should definitely review the article upon which this report is based (1).

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The expectations of patients who undergo surgery for stress incontinence

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Objective: The purpose of this study was to assess patient expectations of surgical outcome after preoperative counseling of surgical procedures in a randomized trial of 655 women in a comparison of the rectus fascial sling and Burch colposuspension.

Study Design: Women who selected surgery for treating stress incontinence and who consented to this randomized, surgical trial completed a preoperative questionnaire to assess expectations for the postsurgical effects of surgery on urinary incontinence-related symptoms, limitations, and emotions. Associations of expectations with a range of preoperative urinary incontinence measures were explored.

Results: The most frequent preoperative symptoms were urine leakage (98%), embarrassment (88%), frequency (74%), physical activity (72%), and urgency (70%). Sexual and social limitations were less frequent (< or = 44%). Treatment expectations were higher for women who reported more symptom bother. As expected, most women (98%) had an expectation that urine leakage would be completely or almost completely eliminated. However, most women (92%) who reported urgency or frequency (83%) expected significant improvement of these symptoms after surgery.

Conclusion: Patients who undergo stress incontinence surgery have high expectations regarding the outcome of incontinence surgery, which include the resolution of urgency and frequency.

Editorial Comment

The authors reviewed the expectations of patients with regards to the anticipated results of their upcoming anti-incontinence operation (be it a Burch urethropexy or a autologous fascial suburethral sling). The patients had a consultation with their surgeon as well as viewing a standardized video presentation on the future surgery. The discussion of expectations and explanation of risks and benefits of surgery was standardized among the 22 surgeons at all the participating study sites. Even after both a video presentation and verbal discussion, 92% of the patients still expected that their urgency symptoms would resolve and 74% that their urinary frequency would improve with an anti-incontinence operation. Expectations were not related to preoperative health, age, physical examination or history of previous surgery.

An interesting article that formalizes the anecdotal experience of urologic surgeons: no matter how intensive the preoperative counseling and explanation of risks and benefits, patients expect an anti-incontinence

operation will address all aspects of their voiding dysfunction. It has been noted in the past that a certain percent of patients will have their urgency addressed with an anti-stress incontinence operation (1). The segment in whom the urgency persists will definitely report a lower satisfaction with their surgery even with a technically perfect procedure (2).

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PEDIATRIC UROLOGY

Outcome analysis of severe chordee correction using tunica vaginalis as a flap in boys with proximal hypospadias

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Purpose: There is ongoing controversy regarding optimal treatment for severe ventral curvature. It has been suggested that ventral corporeal lengthening may be associated with recurrent curvature and erectile dysfunction. To further assess these issues we reviewed our experience with ventral penile lengthening for correcting the severe ventral curvature associated with proximal hypospadias.

Materials and Methods: We reviewed the records of 38 boys with severe hypospadias and congenital ventral curvature greater than 45 degrees who were treated at our institution from 1995 to 2004 with placement of a flap or graft in the corporeal bodies to straighten the phallus. Of the patients 21 had perineal and 17 had penoscrotal hypospadias, including 22 with associated penoscrotal transposition and/or bifid scrotum and 6 with ambiguous genitalia. Testosterone stimulation before surgery was given in 11 children at surgeon discretion.

Results: Median age at surgery was 15 months. The urethral plate was divided in 94.7% of patients. A tunica vaginalis flap was used alone in 23 cases and associated with dura, pericardium or small intestinal submucosa in 8, 2 and 1, respectively. The remaining 4 patients underwent ventral grafting alone, including lyophilized dura in 1, pericardium in 1 and dermis in 1. Urethral reconstruction was achieved by the transverse island flap technique or 1 of its modifications in 34 children. Four boys underwent a 2-stage procedure. Followup available on 35 of 38 patients was 1 to 11 years (median 5.3). Recurrent ventral curvature in 5 of 35 patients was mild in 1 and clinically significant, requiring re-intervention, in 4. Four of 9 patients (44.4%) who underwent corporeal grafting with lyophilized dura had recurrent ventral curvature vs. 1 of 23 (4.3%) who had a tunica vaginalis

flap (chi-square 5.14, $p = 0.02$). At last followup straight erections were documented by patients and/or parents in 30 of 35 children (85.7%). Conclusions: The short-term outcome of ventral penile lengthening using tunica vaginalis flap alone for correcting severe chordee is favorable with a 95% success rate. Dural grafts were associated with a higher risk of recurrent ventral curvature compared to tunica vaginalis flaps. Although most of our patients were not yet adults, when chordee and erectile dysfunction may become apparent, we believe that tunica vaginalis flap repair is a good option for correcting severe ventral curvature.

Editorial Comment

Important points made in the manuscript include that if grafting is the surgeon's choice, that the grafts should be 20-30% larger than the defect. The tunica vaginalis flap was easy to harvest and these authors had excellent success. Being a flap rather than a graft, it can be cut to the appropriate size. The blood supply has been shown to be reliable and the complications noted doing a one-stage repair are in line with what one would expect from one-stage repairs without the severe curvature correction. I find most mild chordee can be corrected dorsally but I agree with these authors that the tunica vaginalis flap is their procedure of choice to correct severe chordee on the ventral aspect of the penis.

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Long-term tolerability of tolterodine extended release in children 5-11 years of age: results from a 12-month, open-label study

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Objective: To evaluate the long-term tolerability of tolterodine extended release (ER) in children (aged 5-11 yr) with urgency urinary incontinence (UUI).

Methods: This was a multicenter, open-label extension of a 12-wk, double-blind, placebo-controlled study of tolterodine ER. Patients had UUI suggestive of detrusor overactivity (≥ 1 diurnal incontinence episode per 24h for ≥ 5 of 7 d) and ≥ 6 voids per 24h at baseline and had completed the 12-wk double-blind study. Patients received tolterodine ER (2mg once daily) for 12 mo. The primary end points were the incidence and severity of adverse events (AEs) and the incidence and reasons for withdrawals. Visits were scheduled at 3, 6, 9, and 12 mo, and investigators were instructed to report all AEs. At 6 and 12 mo, vital signs were recorded and a physical examination was performed.

Results: A total of 318 patients were enrolled (double-blind tolterodine ER, $n = 221$; placebo, $n = 97$). The majority of patients were white (90%), mean \pm SD age was 7.6 ± 1.5 yr, and 54% were boys. Forty-nine percent of patients reported ≥ 1 AE during the study, similar to that observed in the preceding 12-wk study (42%). The most frequent AEs were urinary tract infection (7%), nasopharyngitis (5%), headache (5%), and abdominal pain (4%); 111 (35%) patients withdrew. The most common reasons for withdrawal were lack of efficacy (12%), symptom improvement (8%), and withdrawn consent (6%). Ten patients (3%) withdrew because of AEs.

Conclusion: Long-term treatment with tolterodine ER was well tolerated in children with UUI.

Editorial Comment

This is the first large-scale prospective study for long-term safety and tolerability of tolterodine extended release, showing mostly mild side effects and 65% of the patients completing the entire 12 month treatment period. Few long-term drug studies are performed in children, which makes this study more significant. My regret for the study is that they did not include an efficacy arm so that a practitioner could have all the information necessary to make wise treatment choices for their patients that may need long-term care.

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