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UROLOGICAL SURVEY

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STONE DISEASE

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The effect of fat and nonfat components of the skin-to-stone distance on shockwave lithotripsy outcome

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Background: Few studies have addressed the effect of skin-to-stone distance (SSD) on the success of extracorporeal shockwave lithotripsy (SWL). Nevertheless, the effect of the two components of SSD, that is, the fat SSD (FSSD) and nonfat SSD (NFSSD) components, was not previously investigated.
Methods: In this prospective study, all patients (n = 113) who had single radio-opaque kidney stones and underwent SWL for the first time between January 2006 and June 2007 were recruited. SSD, FSSD, and NFSSD were measured by noncontrast CT scan at 0°, 45°, and 90° and the average was calculated. The outcome was defined as successful (completely stone free or residual fragments ≤ 3 mm) or unsuccessful (residual fragments > 3 mm or complete failure of fragmentation).
Results: Sixty-nine (61%) patients had successful treatment. On univariate analysis, SSD, FSSD, and NFSSD were significantly lower in the successful group compared with those with unsuccessful outcome (71.9 ± 13.3 vs. 86.2 ± 25.1 mm [p = 0.001], 27.2 ± 10.3 vs. 36.1 ± 17.3 mm [p = 0.011], and 44.7 ± 7.2 vs. 50.1 ± 13.9 mm [p = 0.02], respectively). The muscle component of the NFSSD was also lower in the successful group (21.5 ± 4.1 vs. 25.2 ± 10.0 mm [p = 0.01]). On multivariate analysis, factors that independently predicted treatment success were SSD, stone attenuation, and stone size but not the FSSD or NFSSD.
Conclusions: Although the total SSD appeared to be a significant predictor of SWL success, its fat and nonfat components did not independently predict the final outcome and only appeared to be important through their contribution to the total SSD.

Editorial Comment

It is important to note that the average skin-to-stone distance (SSD) of 7.8 cm and average BMI of 25 indicates that the study population was relatively healthy, and it may be worthwhile to extend this study to patients with morbid obesity to confirm that the relative contribution of fat vs. muscle to the SSD does not affect efficacy. The article has important implications. Despite the fact that disproportionate amounts of fat vs. non-fat in the retroperitoneum have been reported in child vs. adult, athlete vs. obese, Asian vs. Caucasian; for ESWL, differences in skin-to-stone distance are more important than the type of tissue between the shock and the stone; specifically the main issue is the distance traveled. The other major contribution of this article relates to their stringent evaluation of success with CT scans at 6 weeks and well defined endpoints. Specifically, with a mean stone size of about 12 mm, approximately 40% were stone-free, 20% had residual fragments < 3 mm, 30% had residual fragments > 3 mm and 10% had no fragmentation. It is feasible that as 92% of patients were treated with sedation, higher success rates might have been noted with general anesthesia as reported in other studies.

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Emergency ureteroscopic treatment for upper urinary tract calculi obstruction associated with acute renal failure: feasible or not?

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Purpose: To determine the efficacy and safety of emergency ureteroscopy (URS) and holmium:yttrium-aluminum-garnet (Ho:YAG) laser lithotripsy for ureteral calculi that are associated with acute renal failure (ARF).
Patients and Methods: We retrospectively evaluated a cohort of 49 patients who underwent URS from November 2005 to November 2008 for ARF that was caused by calculi obstruction of the upper urinary tract. The mean (maximal diameter) stone size was 1.48 cm. Acute renal failure was demonstrated by oliguria or anuria and marked increase in serum creatinine and blood urea nitrogen levels. All the patients were treated with URS and Ho:YAG laser lithotripsy emergently. Ureteral stent placement was performed in all cases after lithotripsy. A plain film of the kidneys, ureters, and bladder and abdominal ultrasonography were performed to evaluate efficacy of treatment on the first day postoperatively. Serum creatinine and blood urea nitrogen levels and urine volume were successively monitored until they returned to normal. All patients had postoperative imaging, including ultrasonography and excretory urography, to confirm stone clearance and exclude late obstructive complications 3 months after URS.
Results: URS and laser lithotripsy were successfully performed in all patients. There were no major intraoperative complications, and no procedure was converted to open surgery. The mean operative time was 35 minutes. The successful fragmentation rate was 95.5%. The overall stone-free rate was 91.8%. Normal renal function returned in 46 (93.8%) patients within 7 days. No postoperative ureteral stricture occurred after 3 months.
Conclusions: URS and Ho:YAG laser lithotripsy represent an effective and safe modality for treating patients with ARF that is caused by calculi obstruction of the upper urinary tract in strictly selected situations.

Editorial Comment

The authors report remarkable results (92% stone-free rates, ability to reach all proximal ureteral stones) despite using a relatively large semi-rigid ureteroscope and not utilizing a flexible ureteroscope for any cases. Indeed, they report treating stones larger than 3 cm in size in less than 1 hour. They utilized higher energy settings (1.8 J), which may facilitate more rapid fragmentation, but have been reported in "in vitro" studies to lead to larger stone fragments. It may be that the longer stenting times (4-12 weeks) helped facilitate stone passage without the development of recurrent obstruction. The authors provide important information concerning the safety of ureteroscopy in the face of acute renal failure, and the course of resolution of the renal failure with alleviation of the obstruction. Likely, the short operative time is critical in these patients to minimize the risks of peri-operative complication related to irrigant fluid absorption and length of anesthetic.

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ENDOUROLOGY & LAPAROSCOPY

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Quality of life after open or robotic prostatectomy, cryoablation or brachytherapy for localized prostate cancer

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Purpose: Health related quality of life concerns factor prominently in prostate cancer management. We describe health related quality of life impact and recovery profiles of 4 commonly used operative treatments for localized prostate cancer.

Materials and Methods: Beginning in February 2000 all patients treated with open radical prostatectomy, robot assisted laparoscopic prostatectomy, brachytherapy or cryotherapy were asked to complete the UCLA-PCI questionnaire before treatment, and at 3, 6, 12, 18, 24, 30 and 36 months after treatment. Outcomes were compared across treatment types with statistical analysis using univariate and multivariate models.

Results: A total of 785 patients treated between February 2000 and December 2008 were included in the analysis with a mean followup of 24 months. All health related quality of life domains were adversely affected by all treatments and recovery profiles varied significantly by treatment type. Overall urinary function and bother outcomes scored significantly higher after brachytherapy and cryotherapy compared to open radical prostatectomy and robotic assisted laparoscopic radical prostatectomy. Brachytherapy and cryotherapy had a 3-fold higher rate of return to baseline urinary function compared to open radical prostatectomy and robotic assisted laparoscopic radical prostatectomy. Sexual function and bother scores were highest after brachytherapy, with a 5-fold higher rate of return to baseline function compared to cryotherapy, open radical prostatectomy and robotic assisted laparoscopic radical prostatectomy. All 4 treatments were associated with relatively transient and less pronounced impact on bowel function and bother.

Conclusions: In a study of sequential health related quality of life assessments brachytherapy and cryotherapy were associated with higher urinary function and bother scores compared to open radical prostatectomy and da Vinci prostatectomy. Brachytherapy was associated with higher sexual function and bother scores compared to open radical prostatectomy, robotic assisted laparoscopic radical prostatectomy and cryotherapy.

Editorial Comment

The authors compared 4 commonly used operative treatments for localized prostate cancer: open radical prostatectomy (ORP), robot assisted laparoscopic prostatectomy (RALP), brachytherapy (BT) or cryotherapy.

A total of 785 patients were included in the analysis with a mean follow-up of 24 months.

BT and cryotherapy were associated with a 3-fold higher rate of return to baseline urinary function compared to ORP and RALP. Moreover, all treatments had a more adverse impact on sexual function and bother than on urinary and bowel domains.

Although the advent of RALP has improved visualization and surgeons' ergonomics it has not demonstrated a significant improvement of urinary continence or sexual function in this prospective, longitudinal study of health-related quality of life outcomes using validated self-reported questionnaires.

The authors have shown the 8 years clinical follow-up analyzing different treatment modalities for localized prostate cancer. I believe this assessment should be followed by health care providers managing patients with prostate cancer so we can better serve our patients.

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IMAGING

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Positive predictive value of CT urography in the evaluation of upper tract urothelial cancer

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AJR Am J Roentgenol. 2010; 195: W337-43

Objective: The purpose of this study was to determine the positive predictive value of CT urography in the diagnosis of upper tract urothelial malignancies.
Materials and Methods: Retrospective review of the records of patients who underwent 2,602 CT urographic examinations revealed that 81 (3%) examinations of 77 patients had findings suggesting upper tract urothelial cancer. Two radiologists in consensus categorized the findings as large masses (> 5 mm), small masses (≤ 5 mm), or urothelial thickening. The positive predictive value of CT urography was determined with the findings at pathologic examination (n = 42), followup imaging (n = 29), or clinical follow-up alone (n = 5). One patient with insufficient follow-up information was excluded. The effects of age, sex, indication for examination, imaging appearance, and urine cytology were analyzed with the Fisher's exact test or Student's t test. Multivariate logistic regression analysis was used to generate a model for predicting the probability of the presence of upper tract urothelial cancer in patients with positive CT urographic examinations.
Results: The positive predictive value of CT urography for upper tract urothelial cancer was 53% (40/76) overall, 83% (29/35) for large masses, 0% (0/17) for small masses, and 46% (11/24) for urothelial thickening. Imaging appearance, urine cytology, and age were significant univariate predictors ($p < 0.05$) of the presence of upper tract urothelial cancer in patients with positive CT urographic examinations. The independent variables most likely associated with upper tract urothelial cancer were urine cytology (odds ratio, 60.0; 95% CI, 5.5-653.7) and imaging appearance (odds ratio, 24.4; 95% CI, 3.0-201.9) after adjusting for age and clinical indication.
Conclusion: The positive predictive value of CT urography for upper tract urothelial cancer is moderate because benign findings mimic cancer. Positive findings on a CT urogram are more likely to indicate cancer in the setting of large masses or positive urine cytology.

Editorial Comment

Several studies have been shown that multidetector computerized tomography urography (CT urography) is more sensitive, specific and accurate than excretory urography in the diagnosis of upper urinary tract

transitional cell carcinoma in patients with hematuria and in patients with history of urothelial cancer. In this retrospective study the authors shows that positive predictive value (PPV) of abnormal findings suspicious for upper tract urothelial cancer on CT urography was only moderate, that is 53% (of 76 patients with either minimally or highly suspicious findings, only 40 had pathologically proved upper tract urothelial cancer). CT urography findings suspicious for urothelial carcinoma were classified in three main categories: large mass (lesions > 5 mm in maximum diameter), small mass (lesions 5 mm in maximum diameter), or urothelial thickening. For findings classified as large masses, the PPV was 83% and for small masses was 0%. We have to consider however, the large number and the variety of false-positive findings in this study. This was probably related to the retrospective analysis of reported findings. False positive findings were caused mainly by normal or hypertrophied papilla, blood clot and inflammation. Usually nonenhancing blood clots may be differentiated from enhancing urothelial tumor by comparing the findings between non-contrast phase and nephrographic phase. Presence of mild, homogeneously enhanced and thickened pelviocalyceal urothelium is relatively frequent feature of patients with symptomatic or asymptomatically urinary tract infection. Normal prominent renal papillae may occasionally invaginate deeply into the calices and thus simulate urothelial tumor. The awareness of such anatomic variation and the search for this finding in other papillae in the same patient, are helpful for the adequate diagnosis.

The authors of this manuscript, however, offered important information regarding the value of urine cytology studies, which were available in 80% of patients. Urine cytology was very important for the adequate characterization of pelviocalyceal abnormalities, such as urothelial tumor. When urine cytology was suspicious or malignant and an upper tract urothelial abnormality was found at CT urography, the PPV for upper tract urothelial carcinoma was 92%.

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Urinary calculi composed of uric acid, cystine, and mineral salts: differentiation with dual-energy CT at a radiation dose comparable to that of intravenous pyelography

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Purpose: To retrospectively evaluate radiation dose, image quality, and the ability to differentiate urinary calculi of differing compositions by using low-dose dual-energy computed tomography (CT).
Materials and Methods: The institutional review board approved this retrospective study; informed consent was waived. A low-dose dual-energy CT protocol (tube voltage and reference effective tube current-time product, 140 kV and 23 mAs and 80 kV and 105 mAs; collimation, 64 × 0.6 mm; pitch, 0.7) for the detection of urinary calculi was implemented into routine clinical care. All patients (n = 112) who were examined with this protocol from July 2008 to August 2009 were included. The composition of urinary calculi was assessed by using

commercially available postprocessing software and was compared with results of the reference standard (ex vivo infrared spectroscopy) in 40 patients for whom the reference standard was available. Effective doses were calculated. Image quality was rated subjectively and objectively and was correlated with patient size expressed as body cross-sectional area at the level of acquisition by using Spearman correlation coefficients.
Results: One calcified concrement in the distal ureter of an obese patient was mistakenly interpreted as mixed calcified and uric acid. One struvite calculus was falsely interpreted as cystine. All other uric acid, cystine, and calcium-containing calculi were correctly identified by using dual-energy CT. The mean radiation dose was 2.7 mSv. The average image quality was rated as acceptable, with a decrease in image quality in larger patients.
Conclusion: Low-dose unenhanced dual-source dual-energy CT can help differentiate between calcified, uric acid, and cystine calculi at a radiation dose comparable to that of conventional intravenous pyelography. Because of decreased image quality in obese patients, only nonobese patients should be examined with this protocol.

Editorial Comment

Nowadays multi-detector computed tomography (MDCT) is used in attempt to determine the chemical composition of urinary tract stones. However, the attenuations values given in Hounsfield units of different types of calculi obtained with current technique overlap, making reliable distinction of chemical composition of urinary calculi very difficult. With the advent of new dual-source CT systems, CT scans are simultaneously and quickly obtained using two orthogonally positioned x-ray tubes and detector sets (double source at 80 and 140 kV); both helical acquisitions run simultaneously and are not limited by changes between the two scans in contrast enhancement or patient motion (1). Dual-energy CT may be used to distinguish pure uric acid, mixed uric acid, and calcified stones. However, dual-source CT imaging delivery a higher radiation dose to the patient than the currently recommended lower-dose MDCT protocols.

The authors of this manuscript offer a great contribution to this subject by developing a low-dose unenhanced dual-source dual-energy CT protocol that can help differentiate between calcified, uric acid, and cystine calculi at a radiation dose comparable to that of conventional intravenous pyelography (mean 2.7 mSv). This protocol however was useful only in nonobese patients. New variation in dual-source CT protocols, are still in progress in an attempt to further decrease the radiation dose to the patients while keeping the ability to differentiate chemical composition of urinary tract calculi (1).

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PATHOLOGY

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Application of the Epstein criteria for prediction of clinically insignificant prostate cancer in Korean men

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BJU Int. 2010; 105: 1526-30

Objective: To investigate the rate of pathologically confirmed unfavourable prostate cancers among Korean men who fulfilled the contemporary Epstein criteria for clinically insignificant prostate cancer.
Patients and Methods: This was a retrospective study of 131 Korean men who underwent radical prostatectomy (RP) for clinically insignificant prostate cancer as defined by contemporary Epstein criteria. We assessed the percentage of unfavourable prostate cancer (pathological Gleason sum > or = 7 and/or extraprostatic extension [EPE]) among these men and tried to identify useful predictors for such unfavourable tumour profiles using uni- and multivariate analyses.
Results: Among 131 men with clinically insignificant prostate cancer, 40 (30.5%) had pathological Gleason > or = 7 tumours after RP. Of these 40 men, four (3.1%) also had EPE on examination of RP specimen. All those who did not have Gleason score upgrading after RP had organ-confined disease from examination of RP specimen. Overall, 40 (30.5%) of the 131 men who fulfilled the contemporary Epstein criteria for clinically insignificant prostate cancer before RP had pathologically unfavourable disease. Among our patients, no significant preoperative predictor of pathologically unfavourable disease was identified using uni- and multivariate analyses.
Conclusion: Our results showed that a significant proportion of contemporary Korean patients who meet all the conditions of the contemporary Epstein criteria for prediction of clinically insignificant prostate cancer might actually harbour prostate cancer with unfavourable pathological features. Such findings should be considered when treatment options are contemplated based upon the Epstein criteria among Asian patients.

Editorial Comment

Watchful waiting (active surveillance) has gaining popularity as a management strategy for newly diagnosed low-grade, limited cancer on needle biopsy based on the large discrepancy between incidence and mortality rate of prostate cancer. Data from the European Randomized Study of Screening for Prostate Cancer Trial showed that PSA screening reduced the rate of death from prostate cancer by 20% but was associated with a high risk of overdiagnosis (1).

Epstein proposed a set of criteria based on PSA and preoperative biopsy features that identify a high likelihood of organ-confined insignificant cancers at radical prostatectomy (2). Insignificant cancers are defined as cancers confined to the prostate (pT2), Gleason low-grade (score ≤ 6), and low-volume (≤ 0.5 cc). It is important to be aware that insignificant cancer is not synonymous of latent (indolent) carcinoma. So far, there is no single marker of biological behavior for prostate cancer.

The preoperative biopsy and clinical features of Epstein's criteria for insignificant cancer are: clinical stage T1c, preoperative PSA density < 0.15, no Gleason pattern 4 or 5, no more than 2 cores with cancer, and no more than 50% of involvement of cancer in a single core. According to Bastian at Johns Hopkins, the predictive value using the Epstein's criteria for organ-confined disease and insignificant cancer is 92% and 84%, respectively.

Several studies have applied Epstein's criteria for prediction of clinically insignificant prostate cancer with differing results. In all studies, the criteria are predictive of a high frequency of organ-confined disease

but differ for insignificant cancer. In the study from Korea, the frequency of organ-confined disease was 97% (vs. 92% from Johns Hopkins) but 69% for insignificant cancer (vs. 84% from Johns Hopkins).

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The Epstein criteria predict for organ-confined but not insignificant disease and a high likelihood of cure at radical prostatectomy

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Eur Urol. 2010; 58: 90-5

Background: Few reports attempt to validate the role of Epstein criteria in selecting patients for an active surveillance protocol.
Objective: To determine the performance of the Epstein biopsy criteria for predicting pathologic end points and biochemical relapse-free survival (bRFS) in men with early stage prostate cancer (PCa) treated by radical prostatectomy (RP).
Design, Setting and Participants: Between October 1999 and January 2007, 746 consecutive patients were biopsied, and then underwent RP at our tertiary care institution. Two hundred sixty-eight patients met the entry criteria of Gleason 6 disease only on initial biopsy with complete pathologic information.
Measurements: Primary end point was insignificant disease. Insignificant disease was defined using a classical (organ-confined, Gleason score < 6, and tumor volume < 0.5 cm(3)) and more liberal (organ-confined, Gleason < 6 tumor of any volume) formulation. Secondary end points included organ-confined disease and bRFS.
Results and Limitations: One hundred thirty-six men (51%) met the Epstein biopsy criteria, and 167 (62%) had organ-confined cancer. Insignificant disease by the classical and liberal definitions was present in 68 (25%) and 92 (34%) patients, respectively. Cases meeting Epstein biopsy criteria were more likely to have insignificant disease by either definition ($p < 0.001$) and more likely to have organ-confined tumors ($p < 0.001$). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) varied widely among the end points, with sensitivity (74%) and NPV (86%) best for the classical definition of insignificant disease and specificity (74%) and PPV (92%) best for organ-confined disease. The estimated 5-yr bRFS was 100% for those meeting Epstein biopsy criteria compared to 83% for those not meeting these criteria.
Conclusions: The Epstein biopsy criteria predict for a high likelihood of organ-confined disease and the absence of biochemical failure up to 5 years after RP. These criteria are insufficiently robust to predict the presence of biologically insignificant disease.

Editorial Comment

The conclusion of Lee's et al. study from Cleveland Clinic is that Epstein biopsy criteria predict for a high likelihood of organ-confined disease but are insufficiently robust to predict the presence of insignificant disease defined as organ-confined, Gleason low-grade, and minimal volume (≤ 0.5 cc).

The findings are supported by other studies (1-3). Epstein's criteria are highly predictive for organ-confined prostate cancer. The frequency varies from 91% to 97%. However, the predictive value for insignificant cancer varies from 37% to 84%. Jeldre's et al. concluded that Epstein's criteria might underestimate the true nature of prostate cancer in as many as 24% of European patients (1). Approximately 31% Korean patients who meet all the conditions of the contemporary Epstein's criteria for prediction of clinically insignificant prostate cancer may actually harbor prostate cancer with unfavorable pathological features (2). In the Middle East (Egypt), 46% of patients may present unfavorable cancer (3).

There are several causes for the discrepancies. Prostate cancers diagnosed in Asian, American, and European men may have innate differences associated with racial and/or environmental factors. However, methodological factors seem to be more important: among others, number of patients studied, number of cores of the biopsy, and criteria for volume evaluation. The last one was considered by Lee's et al. study from the Cleveland Clinic.

According to volume, the authors defined prostate cancer by two ways: classical and liberal. The classical definition considered a tumor volume < 0.5 cc; and the liberal definition any grade of volume. Using the liberal definition, the predictive value of Epstein's criteria for insignificant cancer was 58%; using the classical definition was 37%. In a similar study at our Institution (data not published), the frequency was 55% and 46%, respectively.

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RECONSTRUCTIVE UROLOGY

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The use of penile skin graft versus penile skin flap in the repair of long bulbo-penile urethral stricture: a prospective randomized study

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Objectives: To evaluate the use of penile circular skin graft versus flap as a ventral onlay for bulbo-penile stricture urethra.
Material and Methods: Between 2003 and 2009, 37 patients with bulbo-penile stricture were randomized to penile methods circular skin graft (PCG = 18) or flap (PCF = 19). Inclusion criteria included postinstrumentation or idiopathic stricture. Exclusion criteria were unhealthy skin and previous urethrotomy/urethroplasty. Patients had urethrogram at three weeks, three months, one year, and urethroscopy when needed. Any subsequent urethrotomy/urethroplasty was considered a failure. Chi-square and Student's t test were used for analysis.
Results: Patients' ages were 45.3 (range: 30-65) and 45.5 (35-60) yr in PCG&PCF respectively. Stricture length was 15.2 (10-22) &14.1 (9-21) cm in PCG&PCF respectively. The stricture was postinstrumentation in 9 and 11 and idiopathic in 9 and 8 patients in PCG&PCF respectively. Mean follow up was 36.2 (12-60) and 37.1 (range: 13-24) months in PCG and PCF respectively. Operative time was significantly shorter in PCG than in PCF (203.3 and 281.6 min, respectively; P = .000). Early postoperative complications were similar in both groups. Superficial skin necrosis occurred only in the PCF group (3 cases). Late complications of mild postvoid dribbling occurred similarly in both groups. One patient in PCF had a urethro-cutaneaous fistula at the level of fossa navicularis that was repaired later. Stricture recurred in 5 (27.7%) and 4(21%) patients in PCG and PCF, respectively (P = .249). Four patients had visual internal urethrotomy (2, 2), four needed anastmotic urethroplasty (2, 2) in PCG and PCF, respectively, and one needed buccal mucosal graft in the PCG group.
Conclusions: At intermediate follow-up, both penile circular graft and flap had similar and high success as a ventral onlay for repair of long bulbo-penile stricture with a low rate of complications.

Editorial Comment

Hussein et al. raise the bar in reconstructive urology research by completing a randomized clinical trial of distal penile fasciocutaneous skin flap urethroplasty vs. distal penile skin graft urethroplasty for non- lichen sclerosus strictures of the bulbo-penile urethra. They chose to compare two surgical techniques, which were similar in many ways but distinct in one important way. Similarities included the circumcising incision, the distal penile skin and the ventral onlay approach. The difference was in whether a graft or flap was used. The similarities in technique were likely helpful in recruiting patients. The similarities were also important in helping isolate the treatment effect of interest – flap vs. graft. Indeed, they did not detect a difference between the two groups in their primary outcome – a subsequent procedure to treat a stricture recurrence (21% for flap vs. 28% for graft). Here is where some additional planning could have strengthened the study. In order to detect a 10% difference at a significance level of p = 0.05 at a power of 0.8 they would have needed to randomize 353 patients to each arm of the study, rather than 19 patients as done here. Indeed, with only 19 patients in each arm they would have only been able to detect a massive difference between the recurrence rates. Additionally, the primary outcome of interest – need for additional procedures – introduces significant subjectivity into the success rates. A more objective outcome measure would have been preferable. Still, this study represents a great advance for the field of reconstructive urology and hope it will stimulate others to contribute randomized studies to the literature.

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Halofuginone-coated urethral catheters prevent periurethral spongiofibrosis in a rat model of urethral injury

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Background and Purpose: Urethral strictures are from periurethral spongiofibrosis that develops as a result of urethral trauma, disease, or iatrogenic injury. The spongy tissue that surrounds the strictured urethra has an altered ratio of collagen, with increased collagen type I relative to type III. We evaluated the ability of a urethral catheter that was coated with halofuginone (HF), a potent type I collagen inhibitor, to prevent spongiofibrosis formation in a rat model.
Materials and Methods: HF was coated on silicone catheters and release kinetics were measured. Success of impregnation was evaluated with scanning electron microscopy, serial weights, and drug elution data. Urethral strictures were induced in rats using electrocautery. Half the animals had placement of an HF-coated catheter while the others had uncoated silicone controls. Animals were sacrificed at predetermined time points, and urethral tissue was either processed for staining with Masson trichrome and anti-alpha-1 collagen or digested to determine HF concentration. Serum drug levels were also determined in treated animals. Slides were graded by a pathologist who was blinded to treatment to determine collagen deposition.
Results: HF was coated successfully on silicone catheters. Local urethral concentration of HF was tenfold higher than serum concentration in treated rats. Animals with HF-coated catheters had no new type I collagen deposition after urethral injury. Control animals had increased periurethral collagen type I deposition, typical of urethral stricture formation.
Conclusions: HF can be coated successfully on silicone catheters. HF successfully inhibits periurethral type I collagen deposition after urethral injury. This may become an important therapy to prevent urethral stricture formation or recurrence after endoscopic therapy.

Editorial Comment

The authors present preliminary work in an animal model of urethral injury in which an extract of a Chinese herb is impregnated onto a urethral catheter to prevent build-up of Type 1 collagen. Urethral stricture is known to be associated with accumulation of Type 1 rather than Type 3 collagen in the corpus spongiosum. Halofuginone has been shown to prevent collagen accumulation in other urologic models; however, this is the first study to deliver the compound locally rather than systemically. Indeed, urethral stricture is an attractive field for such a delivery system, in that a urethral catheter provides convenient delivery device. We look forward to future developments in this area.

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UROLOGICAL ONCOLOGY

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Do patients benefit from routine follow-up to detect recurrences after radical cystectomy and ileal orthotopic bladder substitution?

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Eur Urol. 2010; 58: 486-94

Background: The need for and intensity of follow-up to detect disease recurrence after radical cystectomy (RC) for transitional cell carcinoma (TCC) remains a matter for debate.
Objective: To determine whether diagnosis of asymptomatic recurrence after RC by routine follow-up investigations confers a survival benefit versus symptomatic recurrence.
Design, Setting, and Participants: Retrospective analysis of 479 patients with nonmetastatic bladder TCC receiving no neoadjuvant chemotherapy/radiation therapy and prospectively followed with a standardised protocol for a median 4.3 yr (range: 0.3-20.9) after RC at an academic tertiary referral centre.
Intervention: RC and extended pelvic lymph node dissection with ileal orthotopic bladder substitution.
Measurements: Cancer-specific survival (CSS) and overall survival (OS) probability for asymptomatic and symptomatic recurrent patients were estimated using the Kaplan-Meier method. The effects of age, nerve-sparing surgery, pathologic tumour stage, lymph node status, adjuvant chemotherapy, mode of recurrence diagnosis, and recurrence site on survival were assessed with multivariable Cox regression models.
Results and Limitations: Of the 174 of 479 patients (36.3%) with tumour recurrence, 87 were diagnosed by routine follow-up investigations and 87 by symptoms. Routine follow-up mostly detected lung metastases and urethral recurrences, while symptoms were predominantly the result of bone metastases and concomitant pelvic/distant recurrences. Of 24 patients with urethral recurrences, 13 had carcinoma in situ (CIS). Of these, 12 were successfully managed with urethra-sparing treatment, and 6 are still alive with no evidence of disease. Most other recurrent long-term survivors had lung and extrapelvic lymph node metastases. Cumulative 5-yr survival rates of the entire cohort were 69.8% (95% confidence interval [CI], 65.5-74.3%) for CSS and 61.9% (95% CI, 57.4-66.7%) for OS. In multivariable analysis, mode of recurrence diagnosis and site of initial recurrence were the only independent predictors of CSS and OS. Patients with recurrences detected by routine follow-up investigations and with secondary urothelial tumours as site of recurrence had a slightly but significantly higher survival probability.
Conclusions: Patients diagnosed with asymptomatic recurrences during our routine follow-up after RC had a slightly higher survival than patients with symptomatic recurrences. Routine follow-up appears particularly effective in early detection of urethral CIS, which can be treated conservatively. In addition, the predominance of lung and extrapelvic lymph node metastases in survivors may justify the use of routine cross-sectional imaging.

Editorial Comment

Why do patients need follow-up after cystectomy? This retrospective analysis on 174 patients with cystectomy and orthotopic neobladders shows the evidence behind current recommendations of routine follow-up procedures.

Interestingly, only about 7% of patients had isolated pelvic recurrences whereas about 61% had distant recurrences only. Ten percent of patients had concomitant local and distant recurrences. Roughly, half of patients were detected without symptoms by routine follow-up procedures. Especially urethral recurrences, which are easily detected by cytology/biopsy, had the potential of cure.

Thus, routine follow-up including urethral barbotage cytology and routine x-ray analyses are advocated in patients with orthotopic neobladders.

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Multicentric oncologic outcomes of high-intensity focused ultrasound for localized prostate cancer in 803 patients

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Background: High-intensity focused ultrasound (HIFU) is an emerging treatment for select patients with localized prostate cancer (PCa).
Objectives: To report the oncologic outcome of HIFU as a primary care option for localized prostate cancer from a multicenter database.
Design, Setting, and Participants: Patients with localized PCa treated with curative intent and presenting at least a 2-yr follow-up from February 1993 were considered in this study. Previously irradiated patients were excluded from this analysis. In case of any residual or recurrent PCa, patients were systematically offered a second session. Kaplan-Meier analysis was performed to determine disease-free survival rates (DFSR).
Measurements: Prostate-specific antigen (PSA), clinical stage, and pathologic results were measured pre- and post-HIFU.
Results and Limitations: A total of 803 patients from six urologic departments met the inclusion criteria. Stratification according to d'Amico's risk group was low, intermediate, and high in 40.2%, 46.3%, and 13.5% of patients, respectively. Mean follow-up was 42+/-33 mo. Mean PSA nadir was 1.0+/-2.8 ng/ml with 54.3% reaching a nadir of < or =0.3 ng/ml. Control biopsies were negative in 85% of cases. The overall and cancer-specific survival rates at 8 yr were 89% and 99%, respectively. The metastasis-free survival rate at 8 yr was 97%. Initial PSA value and Gleason score value significantly influence the DFSR. The 5- and 7-yr biochemical-free survival rates (Phoenix criteria) were 83-75%, 72-63%, and 68-62% (p=0.03) and the additional treatment-free survival rates were 84-79%, 68-61%, and 52-54% (p<0.001) for low-, intermediate-, and high-risk patients, respectively. PSA nadir was a major predictive factor for HIFU success: negative biopsies, stable PSA, and no additional therapy.
Conclusions: Local control and DFSR achieved with HIFU were similar to those expected with conformal external-beam radiation therapy (EBRT). The excellent cancer-specific survival rate is also explained by the possibility to repeat HIFU and use salvage EBRT.

Editorial Comment

High-intensity focused ultrasound (HIFU) is not regarded an established treatment in prostate cancer patients as radical prostatectomy and radiation therapy are. Therefore, reports on the long-term outcomes of

patients treated with HIFU are very interesting and should be analyzed carefully. Here, the authors report on 803 patients treated with HIFU against localized primary prostate cancer. Forty percent, 46% and 14% were of low, intermediate and high-risk group according to Amico, respectively. If only the outcomes of the most recently treated patients is regarded, only 57% had a nadir PSA < 0.3, 19% had a nadir PSA between 0.3 and 1, and 19% had a nadir PSA of > 1. The biochemical-free survival rates of these groups are important for the assessment of the curative efficacy. After 7 years of follow-up roughly 90% of patients with a PSA nadir of < 0.3 remained biochemically recurrence-free, whereas these figures were much lower for patients with a PSA nadir of 0.3-1 (~ 50% recurrence-free) and with a PSA nadir of > 1 (~ 40% recurrence-free).

These and other figures show that the cure rate of patients with localized prostate cancer after HIFU treatment to my opinion is not yet comparable to the outcome after radical prostatectomy or modern radiation therapy.

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NEUROLOGY & FEMALE UROLOGY

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Salvage spiral sling techniques: alternatives to manage disabling recurrent urinary incontinence in females

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J Urol. 2010; 184: 2429-33

Purpose: Females with recurrent stress urinary incontinence after anti-incontinence surgery represent a therapeutic challenge. In our experience and that of others standard sling procedures have occasionally failed to correct these problems. We determined the effectiveness of various spiral sling techniques used in these cases to manage pipe stem urethras in which conventional slings had failed.
Materials And Methods: Between January 2007 and July 2008 we evaluated 30 female patients with persistent stress urinary incontinence after multiple failed anti-incontinence procedures. Preoperative and postoperative evaluation consisted of history, physical examination, number of pads, Stamey score and quality of life questionnaires.
Results: We followed 28 patients a minimum of 15 months (range 15 to 18). Mean patient age was 60 years (range 36 to 84). At presentation patients had undergone a mean of 3.5 prior vaginal procedures (range 1 to 6) and used a mean of 7 pads daily (range 3 to 12). Of the patients 21 received a synthetic spiral sling, 5 received an autologous spiral sling (rectus fascia in 3 and fascia lata in 2) and 3 received a lateral spiral sling. Mean pad use decreased to 0.9 daily (range 0 to 2, $p<0.05$). Postoperative mean Stamey score decreased from 2.6 to 0.3 ($p<0.05$). Complications included unilateral vesical perforation in 3 patients with a contralateral lateral spiral sling. The overall success rate was 72%.

Conclusions: Salvage spiral sling techniques are a satisfactory alternative treatment for refractory stress urinary incontinence. When synthetic material cannot be used, autologous tissue can provide similar results. When the bladder is perforated unilaterally, a lateral spiral sling can be used on the contralateral side.

Editorial Comment

This paper discusses the use of a salvage spiral urethral sling in a very difficult to treat patient population, that is, females who have failed multiple vaginal operations for urinary incontinence. The authors provide an excellent technical analysis and state that when using this technique they are able to salvage approximately three out of four. Of interest is that they describe the use of both autologous fascia as well as synthetic graft. Operative tactics are described in the event of a bladder injury at the time of dissection (laterally placed spiral sling); this is very valuable in view of the potential for injury during the periurethral dissection in this patient population with a history of multiple surgeries. In addition, the authors discuss the use of this operation as opposed to the use of artificial urinary sphincter. Given the success rate of this operation mirrors that reported for artificial urinary sphincter in female patients, it has a potential to achieve a great deal of popularity in this very difficult to treat population (1).

Reference

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Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder

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J Urol. 2010; 183: 234-40

Purpose: The Overactive Bladder Innovative Therapy Trial during phase 1 was a randomized trial demonstrating comparable effectiveness of percutaneous tibial nerve stimulation and extended-release tolterodine during 12 weeks of therapy for frequency, nocturia, urgency, voided volume and urge incontinence episodes. In this second phase of the Overactive Bladder Innovative Therapy Trial we assessed the sustained therapeutic efficacy of percutaneous tibial nerve stimulation in subjects with overactive bladder during 1 year.
Materials and Methods: After 12 weeks subjects randomized to weekly percutaneous tibial nerve stimulation with Urgent((R)) PC were offered an additional 9 months of treatment with assessments at 6 and 12 months from baseline. Outcome measures included voiding diary data, overactive bladder questionnaires, global response assessments and safety assessments.

Results: A total of 33 percutaneous tibial nerve stimulation responders continued therapy with 32 and 25 subjects completing 6 and 12 months of therapy, respectively. Subjects received a mean of 12.1 treatments during an average of 263 days, with a mean of 21 days (median 17) between treatments. Subject global response assessments showed sustained improvement from 12 weeks at 6 and 12 months, with 94% and 96% of responders, respectively. At 12 months mean improvements from baseline included a frequency of 2.8 voids daily ($p < 0.001$), urge incontinence of 1.6 episodes daily ($p < 0.001$), nocturia with 0.8 voids ($p < 0.05$) and a voided volume of 39 cc ($p < 0.05$). Overactive bladder questionnaire symptom severity was significantly improved from 12 weeks to 12 months ($p < 0.01$) as well as from 6 to 12 months ($p < 0.01$). No serious adverse events occurred.
Conclusions: Statistically significant overactive bladder symptom improvement achieved with 12 weekly percutaneous tibial nerve stimulation treatments demonstrates excellent durability through 12 months. The durability of response demonstrates the effectiveness of percutaneous tibial nerve stimulation as a viable, long-term therapy for overactive bladder.

Editorial Comment

In this study, the authors reviewed the response of patients to percutaneous tibial nerve stimulation (TTNS) over a one year time period. Of the 44 subjects enrolled in the trial, 35 responded to the therapy and of those 35 patients, 33 chose to continue on with the treatment. As noted by the authors, this trial identified that the symptom improvements obtained after the initial 12 treatments were able to be continued with routine ongoing therapy. The authors identified that a longitudinal 30 minutes session every 3 weeks would help keep the symptomatic response durable.

This is an important paper to review especially in view of the increasing popularity of this technology for the treatment of the overactive bladder. Its efficacy, when used with patients who are refractory to medication, raises the consideration for use as a first line therapy. The fact that after the initial 12 weeks sessions, a treatment every three weeks sustains the symptoms makes it an attractive alternative to daily anti-cholinergic therapy. The economic comparisons of the two long term results will be very interesting. Also exciting is the potential use for patients in the institutional setting in which the side effects of anti-cholinergics such as cognitive disorder, xerostomia, and constipation could be avoided by an every 3 week bedside treatment.

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PEDIATRIC UROLOGY

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A multicenter, randomized, controlled trial of transureteral and shock wave lithotripsy -- which is the best minimally invasive modality to treat distal ureteral calculi in children?

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J Urol. 2010; 184: 1106-9

Purpose: Since there is insufficient evidence to determine the best treatment modality in children with distal ureteral calculi, we designed a multicenter, randomized, controlled trial to evaluate the efficacy and complications of transureteral and shock wave lithotripsy in these patients.
Materials and Methods: A total of 100 children with distal ureteral calculi were included in the study. Of the patients 50 were randomized consecutively to undergo shock wave lithotripsy using a Compact Delta II lithotriptor (Dornier MedTech, Kennesaw, Georgia), and 50 were randomized to undergo transureteral lithotripsy with holmium laser and pneumatic lithotriptor between February 2007 and October 2009. Stone-free, complication and efficiency quotient rates were assessed in each group.
Results: Mean +/- SD patient age was 6.5 +/- 3.7 years (range 1 to 13). Mean stone surface was 35 mm(2) in the transureteral group and 37 mm(2) in the shock wave lithotripsy group. Stone-free rates at 2 weeks after transureteral lithotripsy and single session shock wave lithotripsy differed significantly, at 78% and 56%, respectively ($p = 0.004$). With 2 sessions of shock wave lithotripsy the stone-free rate increased to 72%. Efficiency quotient was significantly higher for transureteral vs shock wave lithotripsy (81% vs. 62%, $p = 0.001$). Minor complications were comparable and negligible between the groups. Two patients (4%) who underwent transureteral lithotripsy sustained a ureteral perforation.
Conclusions: In the short term it seems that transureteral and shock wave lithotripsy are acceptable modalities for the treatment of distal ureteral calculi in children. However, transureteral lithotripsy has a higher efficacy rate when performed meticulously by experienced hands using appropriate instruments.

Editorial Comment

Citing a lack of well-designed randomized controlled trials for the treatment of distal ureteral stones, the authors of this study created a multicenter, randomized, controlled trial, which compared ureteroscopy with extracorporeal shock wave lithotripsy. They enrolled 100 children and randomized 50 of them to ureteroscopy with lithotripsy using primarily a pneumatic lithotripter. The other 50 children underwent shock wave lithotripsy. Success rates were significantly better for the patients who underwent ureteroscopy both at two weeks and at three months. The authors did have two cases of ureteral perforation in the ureteroscopy group, one of which required open surgery to correct. They cited some equipment problems as contributing to these two major complications and one also has to wonder if using a pneumatic lithotripter as opposed to Holmium laser in these patients may have also been a contributing factor. In terms of differences in minor complications, 30 of the patients in the lithotripsy group had some skin bruising and three patients developed “steinstrasse”. There was some mucosal tearing noted in two patients in the ureteroscopy group, which required temporary stent placement.

Although surgical experience is not accounted for in this study, certainly this is a factor that will have an impact on success rates and complications for these modalities. The results of this randomized controlled trial favor a ureteroscopic approach to distal stones despite the fact that it is a more invasive procedure by nature. Improved instrumentation for pediatric patients as well as routine use of Holmium laser lithotripsy over a pneumatic lithotripter will likely continue to make this modality a safe and more effective option for distal ureteral stone management in the pediatric population.

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Impact of epispadias repair on bladder growth in boys with classic bladder exstrophy

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Objective: Growth of the bladder in children with bladder exstrophy is primarily responsible for later ability to void continently. Improvement in bladder capacity has been noted in some boys following epispadias repair. Does the timing of epispadias repair influence the ability of the bladder to grow?
Methods: Data were collected regarding bladder volume measurements, obtained under anesthesia using a standard technique, during yearly follow-up of boys with classic bladder exstrophy. Volume prior to epispadias repair was compared to the next volume measure following repair. Timing of epispadias repair was compared to changes in bladder capacity in 30 boys. Monthly increases in bladder capacity were calculated in boys repaired at < 12 (4), 13-24 (12) and 25-48 (14) months.
Results: Patients who had surgery prior to 12 months of age had the highest rate of monthly increase in bladder capacity (2.40 cc/month). Monthly growth rates were 1.91 cc/month for patients repaired at 13-24 months and 1.18 cc/month for those repaired at 25-48 months.
Conclusions: Epispadias repair does lead to early increase in bladder capacity in boys with classic bladder exstrophy. The monthly increases in bladder capacity are greater in boys < 12 months. Improvement in bladder volume is less likely when epispadias is repaired after age 29 months.

Editorial Comment

This study evaluated the timing of epispadias repair in exstrophy patients with its impact on bladder capacity. The authors retrospectively reviewed all boys undergoing reconstruction, where adequate data were available. The infants underwent routine cystographic evaluation to measure changes in bladder capacity following the initial closure and again 8-16 months following epispadias repair. The authors divided their cohort into three groups: those who underwent epispadias repair prior to 12 months of age; those who were repaired between 13-24 months; and those having reconstruction at 25-48 months of age. They found the greatest increase in capacity over time in those who underwent epispadias repair prior to 12 months of age. Unfortunately, there were only four patients in this cohort. They had larger numbers in the other two groups and both of these showed a trend towards improved bladder capacity with epispadias repair at a younger age.

Although the small number of patients in this study does not lend itself to achieving statistical significance, the data would certainly argue in favor of performing epispadias repair at a younger age. Increasing bladder outlet resistance should improve bladder cycling and allow for improved capacity as the child gets older which will in turn give them the best chance for continence following bladder neck reconstruction. This is the same line of reasoning given by those who favor a complete primary repair at the time of bladder closure.

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