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UROLOGICAL SURVEY

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STONE DISEASE

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Narrow-band imaging digital flexible ureteroscopy in detection of upper urinary tract transitional-cell carcinoma: initial experience

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Purpose: To characterize the appearance of normal and malignant upper urinary tract lesion appearance under narrow-band imaging (NBI) using the new URF-V digital flexible ureteroscope (DFU), and to determine if NBI, when used in conjunction with white light (WL), could improve detection of malignancy.
Patients and Methods: NBI and WL were performed in 27 patients at our university teaching hospital, 14 with known cases of upper urinary tract transitional-cell carcinoma (UUT-TCC) as follow-up (group A), and 13 patients with first-suspicion of cancer (group B). Full renal collecting system examination was performed first under WL and then under NBI by a single urologist. Biopsies were taken from all detected lesions using the biopsy forceps and sent for examination by a pathologist who was blinded to the gross description of the lesion. Pathology interpretations were then compared with the corresponding WL and NBI images. Holmium laser vaporization was performed for all apparent lesions.
Results: Subjectively, NBI significantly improved the endoscopic visualization of the tumors, providing a detailed description of their limits and vascular architecture. Objectively, five additional tumors (14.2%) in four patients, as well the extended limits of three tumors (8.5%) in three patients were detected by NBI when findings by WL imaging were considered normal.
Conclusion: This is one of the first reports regarding NBI for UUT-TCC. From this study, we recommend this technology as a valuable diagnostic method, because it considerably improves tumor detection rate by 22.7% compared with WL.

Editorial Comment

Narrow band imaging utilizes an optical image enhancement technology that enhances the contrast between capillaries and tissue surfaces. This study establishes superiority in the ability to identify lesions and define the limits of disease. Others have reported its value over standard cystoscopy for bladder tumor detection. A most important finding of this study was that in 3 patients - (11%) - traditional white light imaging would have detected NO cancer while narrow band imaging provided the true diagnosis. The impact of improved detection and definition of margins on recurrence and progression of disease warrants further long-term investigation.

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A prospective randomized comparison between early (<48 hours of onset of colicky pain) versus delayed shockwave lithotripsy for symptomatic upper ureteral calculi: a single center experience

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Background and Purpose: The role of early/emergency shockwave lithotripsy (SWL) in symptomatic upper ureteral calculi has still not been established. We have performed a randomized comparison between early (< 48 hours) vs. delayed (> 48 hours) SWL for symptomatic upper ureteral stones less than 1 cm to evaluate the feasibility, safety, and efficacy of early SWL in these patients.
Patients and Methods: One hundred and sixty consecutive patients with a single radiopaque upper ureteral stone < 1 cm, who presented with an episode of colicky pain and who were undergoing treatment between July 2008 and June 2009 in our department were included. The patients were hospitalized and randomized into two groups-group A: SWL was performed within 48 hours of onset of colicky pain (early SWL) using the electromagnetic lithotripter (Dornier Alpha Compact) along with analgesics and hydration therapy; group B: SWL was performed after 48 hours (delayed SWL) along with analgesics and hydration therapy. The statistical analysis was performed in two groups regarding the patient demographic profile, presence of hydronephrosis, time to stone clearance, success rates, number of sessions needed, auxiliary procedures, modified efficiency quotient (EQ), and complications.
Results: Eighty patients were enrolled in each group. The mean stone size was 7.3 mm in group A vs. 7.5 mm in group B (P = 0.52). The stone fragmentation rate was 88.75% in group A vs. 91.2% in group B (P = 0.35). The overall 3-month stone-free rate was 86.3% (69/80) for group A vs. 76.2% (61/80) for group B (P = 0.34). The mean time taken for stone clearance was significantly less in group A than in group B (10.2 days vs. 21.1 days; P = 0.01). The number of sessions needed in group A were significantly less than in group B (1.3 vs. 2.7; P = 0.01). The auxiliary procedure rate was also significantly lesser in group A than group B (16.3% vs. 32.5%; P = 0.001). The modified EQ (in %) was 67.2 in group A vs 59.4 in group B (P = 0.21). The steinstrasse formation and requirement for percutaneous nephrostomy (PCN) were significantly less in group A (P=0.02 and P=0.01 respectively).
Conclusions: Early SWL (within 48 hours of onset of colicky pain) is feasible, safe, and highly efficacious in the management of symptomatic proximal ureteral stones < 1 cm, resulting in a lesser requirement of number of SWL sessions, time taken for stone clearance, auxiliary procedure rate, and fewer complications in comparison with delayed SWL.

Editorial Comment

This intriguing study lends support to the theory that early management of obstructive ureteral calculi should be considered. Indeed, for a 7 mm proximal ureteral stone, that would have only a 30% chance of spontaneous stone passage, in situ SWL on an urgent basis is an excellent alternative. Ease of scheduling and insurer authorization would likely be a limiting factor for implementation of such a protocol. The impact on time to stone passage and development of steinstrasse is clear. What is less clear is the impact on re-treatment rates - the algorithm followed by the authors of re-image and retreat every 24 hours as an inpatient diverges from current practice in the US where outpatient therapy and re-imaging in 2 weeks might allow more patients the opportunity for stone passage. Similarly, the addition of an alpha-blocker after SWL to promote stone expulsion could change the findings of this study. Lastly treating at a slow rate (60/min.) may have resulted in smaller fragments and improved outcomes. Despite these limitations, the study provides food for thought

- that early intervention prior to the development of ureteral edema and mucosal hyperplasia - may improve outcomes.

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ENDOUROLOGY & LAPAROSCOPY

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Long-term results of a prospective, randomized trial comparing retroperitoneoscopic partial versus total adrenalectomy for aldosterone producing adenoma

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Purpose: The indication for laparoscopic total or partial adrenalectomy in patients with aldosterone producing adrenal adenoma remains controversial. We compared retroperitoneoscopic partial and total adrenalectomy for aldosterone producing adrenal adenoma in a prospective, randomized, multicenter trial.
Materials and Methods: Patients with aldosterone producing adrenal adenoma were randomized to retroperitoneoscopic partial or total adrenalectomy. Patient characteristics, surgical data, complications and postoperative clinical results were analyzed statistically.
Results: From July 2000 to March 2004, 212 patients were enrolled in this study, including 108 and 104 who underwent total and partial adrenalectomy, respectively. The 2 groups were comparable in patient age, gender, body mass index and tumor site. Mean follow-up was 96 months in each group. No conversion to open surgery was needed and no major complications developed. Partial adrenalectomy required a shorter operative time than total adrenalectomy but this did not attain statistical significance. Intraoperative blood loss in the partial adrenalectomy group was significant higher than in the total adrenalectomy group ($p < 0.05$) but no patient needed blood transfusion. All patients in each group showed improvement in hypertension, and in all plasma renin activity and aldosterone returned to normal after surgery. No patient required potassium supplements postoperatively. In the total and partial adrenalectomy groups 32 (29.6%) and 29 patients (27.9%), respectively, were prescribed a decreased dose of or fewer antihypertensive medicines at final follow-up.
Conclusions: Retroperitoneoscopic partial adrenalectomy is technically safe. It has therapeutic results similar to those of total adrenalectomy in patients with primary aldosteronism due to aldosteronoma.

Editorial Comment

The authors compared retroperitoneoscopic partial and total adrenalectomy for aldosterone producing adrenal adenoma in a prospective, randomized, multicenter trial. Primary aldosteronism often has a higher rate

of cardiovascular complications, target organ damage and metabolic syndrome than essential hypertension. The laparoscopic removal of the adenoma has shown preferable and more beneficial than medical treatment or open surgery to manage functioning adrenal tumors. The authors ask an important and controversial question of organ-sparing adrenalectomy in patients with primary aldosteronism due to aldosteronoma. Moreover, they questioned the role of adrenal vein sampling as the gold standard diagnostic test to identify the side of aldosterone secretion versus high-resolution computerized axial tomography. The data revealed a total of 212 patients enrolled in this study, including 108 that underwent total adrenalectomy and 104 patients in the partial adrenalectomy group. No open conversion or blood transfusions were needed. No major intraoperative complications occurred and no tumor recurrence was noted during the mean 96-month follow-up. All patients in each group showed improvement in hypertension and in all plasma renin activity and plasma aldosterone recovered to normal after surgery. However, 32 of 108 patients (29.6%) with total adrenalectomy remained hypertensive with normal plasma aldosterone after surgery. Blood pressure was managed with 20 or 40 mg nifedipine retard daily. Patients with partial adrenalectomy no longer required antihypertensive medication after surgery and 29 patients (27.9%) were prescribed a decreased dose or fewer antihypertensive medications. The authors concluded that partial adrenalectomy for unilateral aldosterone producing adrenal adenoma is beneficial and may preserve adrenal function avoiding possible steroid replacement. Moreover, retroperitoneoscopic partial adrenalectomy is technically feasible with similar outcomes as total adrenalectomy in patients with primary aldosteronism due to aldosteronoma.

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Prostate size is not associated with recovery of sexual function after minimally invasive radical prostatectomy

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Urology. 2011; 77: 952-6

Objectives: To investigate the association of prostate weight with recovery of sexual function after minimally invasive radical prostatectomy.
Methods: Between April 2001 and September 2007, two surgeons performed 856 consecutive laparoscopic radical prostatectomies for clinically localized prostate cancer. Patients were stratified into three groups by prostate weight: < 35 g, 35-70 g, and > 70 g. Sexual and urinary outcomes were assessed prospectively using the Expanded Prostate Cancer Index Composite (EPIC) questionnaire. Patients who underwent nerve sparing (unilateral or bilateral) with complete preoperative EPIC data, a minimum preoperative Sexual Health Inventory for Men score ≥ 21, and a minimum of 3 months of complete postoperative EPIC data were included in the analysis.
Results: Of the cohort of 856 men, 324 (38%) had complete, evaluable data and met the inclusion criteria for this study. Preoperatively, there were no significant differences by prostate weight in the EPIC sexual function

or bother subscale scores or the proportion of patients participating in sexual intercourse. Postoperatively, we observed statistically similar returns to baseline EPIC sexual function and bother subscale scores and participation in sexual intercourse across all gland weight groups at all time points. EPIC sexual domain scores and the proportions of patients participating in sexual intercourse continued to increase up to 24 months postoperatively, but no group returned to preoperative function at any sampling point.
Conclusions: Prostate size is not associated with postoperative recovery of sexual function in men undergoing minimally invasive radical prostatectomy.

Editorial Comment

The authors investigated the association of prostate weight with recovery of sexual function after minimally invasive radical prostatectomy. Two surgeons performed 856 consecutive laparoscopic radical prostatectomies for clinically localized prostate cancer. Patients were stratified patients according on prostate size. Sexual and urinary outcomes were assessed prospectively using the Expanded Prostate Cancer Index Composite (EPIC) questionnaire. Patients who underwent nerve sparing (unilateral or bilateral) with complete preoperative EPIC data.

Possibly, higher prostate weight may present more technical challenges and adversely affect short- or long-term validated sexual HRQoL outcomes after laparoscopic prostatectomy. However, the study demonstrated all patients had similar patterns in recovery of sexual HRQoL scores regardless of prostate size after surgery, and an immediate decrease in sexual function and an increase in sexual bother followed by gradual recovery toward individual baseline score. Although, all patients exhibited an immediate decline in participation in sexual intercourse followed by a gradual return toward baseline, there was no statistical association between gland size grouping and recovery of sexual function, bother, or intercourse. Finally, the authors emphasize the importance of more comprehensive validated questionnaires, such as the EPIC versus IIEF-5.

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IMAGING

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Is apparent diffusion coefficient associated with clinical risk scores for prostate cancers that are visible on 3-T MR images?

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Radiology. 2011; 258: 488-95

Purpose: To investigate whether apparent diffusion coefficients (ADCs) derived from diffusion-weighted (DW) magnetic resonance (MR) imaging at 3 T correlate with the clinical risk of prostate cancer in patients with tumors that are visible on MR images, with MR imaging/transrectal ultrasonography (US) fusion-guided biopsy as a reference.
Materials and Methods: Forty-eight consecutive patients (median age, 60 years; median serum prostate-specific antigen value, 6.3 ng/mL) who underwent DW imaging during 3-T MR imaging with an endorectal coil were included in this retrospective institutional review board-approved study, and informed consent was obtained from each patient. Patients underwent targeted MR imaging/transrectal US fusion-guided prostate biopsy. Mean ADCs of cancerous target tumors were correlated with Gleason and D'Amico clinical risk scores. The true risk group rate and predictive value of the mean ADC for classifying a tumor by its D'Amico clinical risk score was determined by using linear discriminant and receiver operating characteristic analyses.
Results: A significant negative correlation was found between mean ADCs of tumors in the peripheral zone and their Gleason scores ($P = 0.003$; Spearman $\rho = -0.60$) and D'Amico clinical risk scores ($P < 0.0001$; Spearman $\rho = -0.69$). ADC was found to distinguish tumors in the peripheral zone with intermediate to high clinical risk from those with low clinical risk with a correct classification rate of 0.73.
Conclusion: There is a significant negative correlation between ADCs and Gleason and D'Amico clinical risk scores. ADCs may therefore be useful in predicting the aggressiveness of prostate cancer. Supplemental material: http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.10100667/-/DC1

Editorial Comment

The authors showed that endorectal 3T diffusion-weighted MR imaging (D-WMRI) and the calculated apparent diffusion coefficient (ADC), can be useful in the assessment of the aggressiveness of the peripheral zone prostate cancer lesions that are visible on conventional T2-weighted images. A significant negative correlation was found between mean apparent diffusion coefficients (ADCs) of prostate cancers in the peripheral zone and their Gleason score and D'Amico clinical risk score. As we know, D-WMRI is dependent on Brownian motion of water in biologic tissues. Since prostate cancerous tissues have higher cellularity and fibrosis than the non-cancerous tissue, restriction on Brownian motion of water tissue occurs and can be quantified by measurements the ADCs values. In this manuscript it was found that the mean ADC of tumors had a significant negative correlation with tumor Gleason scores and that a significant difference was also observed between mean ADCs values of low, intermediate, and high clinical risk tumors. Thus, ADCs values obtained from D-WMRI at endorectal 3 T were significantly lower in prostate cancers with intermediate and high clinical risk scores and higher Gleason scores. According to their results, ADC maps can be used to assess the aggressiveness of a prostate cancer lesion, potentially as an adjunct to information from other clinical sources (Gleason score, PSA, lesion size, lesion stage) to help select candidates for active surveillance and to follow these patients eventually replacing biopsies.

This study has some limitations. First, they evaluated the role of D-WMRI only in patients presenting cancer of the peripheral zone. Patients with cancer in the transition zone were not included. Second, the authors used a home made system to quantify ADCs values of prostate cancer, thus comparison with similar studies that uses commercially available ADCs measurement system is not possible. Third, they compared only findings observed on conventional T2-weighted image and DWI. It has been shown that prostate cancer assessment by MRI is better accomplished with the combination of results of multiparametric studies (conventional T2-weighted images, spectroscopy, diffusion-weighted images and contrast perfusion studies).

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Role of intraoperative US in the decision for radical or partial nephrectomy

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Radiology. 2011; 258: 283-90

Purpose: To investigate the effect of intraoperative ultrasonographic (US) findings on the decision for the type of nephrectomy to be performed in patients who had renal tumors that were preoperatively evaluated by using magnetic resonance (MR) imaging, with pathologic results as the reference standard.
Materials and Methods: The institutional review board approved the study protocol, and informed consent was obtained. Between June 2008 and September 2009, 44 patients (25 men, 19 women; mean age, 56.6 years; range, 28-76 years) with 46 renal tumors were prospectively assessed by using intraoperative US examinations to demonstrate tumor relationship with the nontumoral intact parenchyma. Findings at preoperative MR examinations were retrospectively evaluated by two radiologists to determine the type of surgery that would be recommended. The reference standard was results of pathologist's review of gross specimens and postoperative reports. The observers assigned their decisions as follows: score group 1, radical nephrectomy should be (should have been) performed; score group 2, partial nephrectomy can be (could have been) attempted; and score group 3, partial nephrectomy should be (should have been) performed.
Results: Radical nephrectomy was performed in 36 lesions. In all cases, the intraoperative US observer and the pathologist were concordant in the decision that radical nephrectomy versus partial nephrectomy could or should have been performed. MR observers 1 and 2 overcalled the need for radical nephrectomy in seven and four cases, respectively. Compared with pathologic results, the overall correlation of intraoperative US was 0.991, and the correlation for MR observer 1 was 0.786 and that for MR observer 2 was 0.731.
Conclusion: Intraoperative US can be suggested as a valuable examination method in patients with tumors at a central location with suspicious renal sinus extension demonstrated by using MR imaging. The close cooperation of urologist and radiologist in renal tumor work-up could reduce performance of unnecessary radical nephrectomy.

Editorial Comment

The authors review their experience in 44 patients with renal tumors and compared how recommendations obtained from different radiologist from preoperative MRI and intraoperative US studies would impact the surgeon's decision whether to perform radical or partial nephrectomy. The findings of preoperative MRI and intraoperative US were compared with pathologist's gross specimens review and post- operative reports.

Previous studies have demonstrated the utility of the association of preoperative CT studies and intraoperative US. Correlation of these methods is useful for the localization of non-palpable central tumors, particularly those with deep extension. In this original study, the authors compare the performance of preoperative MRI evaluation and intraoperative ultrasound in patients that underwent open renal surgery. As already mentioned by the authors, open surgery facilitates the use of large convex ultrasound probes, thus allowing visualization of the entire kidney and its vasculature. Smaller transducer, with smaller field of view would be necessary for example for laparoscopic nephron sparing surgery. The authors nicely show that whenever pre-operative MRI demonstrates central tumor suspicious for renal sinus fat invasion, the complimentary use of intraoperative US is very useful. In this study the diagnostic accuracy of intraoperative US and MRI for detection of tumor sinus extension, was 98% and 70%, respectively. We agree with the authors regarding their assumption that the same superiority of intraoperative US would be also observed if preoperative evaluation done with CT. Similarly to other studies the authors emphasizes that the close cooperation of urologist and radiologist is important to accomplish better surgical results, thus avoiding for example, unnecessary radical nephrectomy.

Intraoperative US for renal tumors can also be used also to identify satellite lesions, assess for peritumoral vascularity, determine renal vein invasion and also to demonstrate the cranial extension of tumor thrombus within the inferior vena cava. Radiofrequency ablation and cryoablation can also be monitored by intraoperative ultrasound.

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PATHOLOGY

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Active surveillance program for prostate cancer: an update of the Johns Hopkins experience

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J Clin Oncol. 2011; 4. [Epub ahead of print]

Purpose: We assessed outcomes of men with prostate cancer enrolled in active surveillance.
Patients and Methods: Since 1995, a total of 769 men diagnosed with prostate cancer have been followed prospectively (median follow-up, 2.7 years; range, 0.01 to 15.0 years) on active surveillance. Enrollment criteria were for very-low-risk cancers, defined by clinical stage (T1c), prostate-specific antigen density < 0.15 ng/mL, and prostate biopsy findings (Gleason score ≤ 6, two or fewer cores with cancer, and ≤ 50% cancer involvement of any core). Curative intervention was recommended on disease reclassification on the basis of biopsy criteria. The primary outcome was survival free of intervention, and secondary outcomes were rates of disease reclassification and exit from the program. Outcomes were compared between men who did and did not meet very-low-risk criteria.
Results The median survival free of intervention was 6.5 years (range, 0.0 to 15.0 years) after diagnosis, and the proportions of men remaining free of intervention after 2, 5, and 10 years of follow-up were 81%, 59%, and 41%, respectively. Overall, 255 men (33.2%) underwent intervention at a median of 2.2 years (range, 0.6 to 10.2 years) after diagnosis; 188 men (73.7%) underwent intervention on the basis of disease reclassification on biopsy. The proportions of men who underwent curative intervention (P = 0.026) or had biopsy reclassification (P < 0.001) were significantly lower in men who met enrollment criteria than in those who did not. There were no prostate cancer deaths.
Conclusion: For carefully selected men, active surveillance with curative intent appears to be a safe alternative to immediate intervention. Limiting surveillance to very-low-risk patients may reduce the frequency of adverse outcomes.

Editorial Comment

The authors studied the outcomes of men with prostate cancer enrolled in active surveillance comparing patients who did and did not meet very-low-risk criteria. Very-low-risk was defined according to the contemporary analysis of Bastian et al. for Epstein's criteria for insignificant cancer on needle biopsy: clinical stage

T1c, prostate-specific antigen density < 0.15 ng/mL, Gleason score ≤ 6, two or fewer cores with cancer, and ≤ 50% cancer involvement of any core.

During the follow-up period the proportions of men who underwent curative intervention ($p = 0.026$) or had biopsy reclassification (more than 2 cores, Gleason score > 6, or > 50% cancer involvement of any core) ($p < 0.001$) were significantly lower in men who met very-low-risk criteria. There were also no prostate cancer deaths in this cohort of patients.

The authors conclude that for carefully selected men, active surveillance limited to patients with very-low-risk cancers according to Epstein's criteria for insignificant cancer may significantly reduce the frequency of adverse outcomes.

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Testicular Vasculitis: A Series of 19 Cases

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Objectives: Because of limited reported cases, it is unknown how often testicular vasculitis represents isolated or systemic disease.
Methods: We report 19 cases (15 consultation; 4 in-house cases) of localized testicular infarction with associated vasculitis spanning 24 years.
Results: All were orchiectomy specimens; detailed clinical information was available in 16 cases. Mean age was 38 years. Clinical presentation was testicular pain in 13 and mass in 3 patients. Preoperative impression was testicular cancer in 13 cases. In all cases, localized testicular infarction associated with vasculitis was present and in none was tumor identified. Most cases (n = 14) showed polyarteritis nodosa (PAN)-like features with transmural necrotizing inflammation of small-medium arteries. In 4 cases, vasculitis was granulomatous (2 necrotizing; 2 non-necrotizing) and in 1 case was lymphocytic. An infectious etiology was excluded clinically and by special stains. Four patients were subsequently confirmed with systemic vaculitis: one with PAN, one with Wegener vasculitis, one with vasculitis not otherwise specified and one with subclinical systemic vasculitis. Two of those 4 patients had testicular PAN-like vasculitis and 2 had granulomatous vasculitis.
Conclusions: Testicular vasculitis can cause localized infarction that clinically mimics cancer. Although testicular vasculitis is an isolated finding in most patients an associated systemic vasculitis is not a rare event (4/16, or 25%), especially if the vasculitis is granulomatous (50% in this series). All patients should be clinically investigated for systemic disease.

Editorial Comment

This is a large series of a rare condition in the testis. Testicular vasculitis can cause localized infarction that clinically may mimic cancer (1). Testicular vasculitis may be an isolated finding, however, in most patients is associated with systemic vasculitis. All patients should be clinically investigated for systemic disease. In this series of 19 cases the mean age was 38 years and most cases (n = 14) showed polyarteritis nodosa-like features with transmural necrotizing inflammation of small-medium arteries (2). The pathologist must be aware of this condition and look for vasculitis whenever a patient with an infarcted testis has no history of torsion or trauma.

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UROLOGICAL ONCOLOGY

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Lymph node dissection at the time of radical nephrectomy for high-risk clear cell renal cell carcinoma: indications and recommendations for surgical templates

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Eur Urol. 2011; 59: 18-23.

Background: Observational studies suggest a proportion of patients with lymph node metastases will benefit from lymph node dissection (LND) at the time of nephrectomy for clear cell renal cell carcinoma (RCC).
Objective: Our aim was to report the performance of five previously identified high-risk pathologic features assessed by intraoperative examination on prediction of lymph node metastases and propose a template for LND based on locations of lymph node involvement.
Design, Setting, and Participants: The study included a historical cohort of consecutive patients from a single institution who received LND in conjunction with nephrectomy for high-risk clear cell RCC between 2002 and 2006.
Interventions: All patients underwent nephrectomy and LND.
Measurements: Patients were considered high risk for nodal metastasis if two or more of the following features were identified during intraoperative pathologic assessment of the primary tumor: nuclear grade 3 or 4, sarcomatoid component, tumor size ≥10cm, tumor stage pT3 or pT4, or coagulative tumor necrosis. Based on these

features, LND was performed at the time of nephrectomy, and the numbers and sites of regional lymph node metastasis were recorded for each patient.
Results and Limitations: Of the 169 high-risk patients, 64 (38%) had lymph node metastases. All patients with nodal metastases had nodal involvement within the primary lymphatic sites of each kidney prior to involvement of the nodes overlying the contralateral great vessel. A limitation of the study is the lack of a standardized LND performed throughout the study period.
Conclusions: Pathologic features of renal tumors are associated with the risk of regional lymph node metastases and lymph node metastases that appear to progress though the primary lymphatic drainage of each kidney. Based on these findings we recommend that when performing LND the lymph nodes from the ipsilateral great vessel and the interaortocaval region be removed from the crus of the diaphragm to the common iliac artery.

Editorial Comment

The landing zone of lymph node metastasis and hence the extent of lymph node dissection in renal cancer is not very well defined. The authors report on a historical cohort of patients with high-risk renal cancer and demonstrate the extent of lymph node metastases. Several clinically important conclusions can be drawn from these data. First, in 66% of patients with metastases these were suspected meaning that roughly one third of lymph node metastases were unsuspected. So clearly, lymphadenectomy (LND) should be performed in all high-risk patients. But to which extent? Interestingly, 45% of metastatic patients had no peri-hilar lymph node involvement. Furthermore, no patient with a right-sided tumor had para-aortic metastases without other retroperitoneal involvement, and no patient with a left-sided tumor had paracaval involvement without involvement of para-aortic or inter-aortocaval lymph nodes.

Thus, the surgical recommendation in high-risk tumors is that in patients with right-sided tumors LND should involve all para-caval and inter-aortocaval nodes, whereas in left-sided tumors para-aortic and inter-aortocaval lymph nodes should be removed.

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Sequential intravesical chemoimmunotherapy with mitomycin C and bacillus Calmette-Guérin and with bacillus Calmette-Guérin alone in patients with carcinoma in situ of the urinary bladder: results of an EORTC genito-urinary group randomized phase 2 trial (30993)

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Eur Urol. 2011; 59: 438-46

Background: Bacillus Calmette-Guérin (BCG) is the intravesical treatment of choice for carcinoma in situ (CIS).
Objective: Our aim was to assess if sequential mitomycin C (MMC) plus BCG after transurethral resection (TUR) is worthy of further study in non-muscle-invasive bladder cancer patients with CIS.
Design, Setting, and Participants: In a noncomparative phase 2 study, 96 patients with primary/secondary/concurrent CIS of the urinary bladder were randomized to sequential MMC plus BCG or to BCG alone after TUR.

Intervention: Patients received six weekly instillations of MMC followed by six weekly instillations of BCG or six weekly instillations of BCG, 3 wk rest, and three further weekly instillations of BCG. Complete responders received three weekly maintenance instillations at 6, 12, 18, 24, 30, and 36 mo in accordance with the initial randomization.
Measurements: End points were complete response (CR) rate at the first control cystoscopy 16-18 wk after start of treatment, disease-free interval, overall survival, and side effects.
Results and Limitations: Ninety-six patients were randomized, 48 to each treatment group. Ten patients were ineligible, and three did not start treatment. In all randomized patients, CR rates on MMC plus BCG and BCG alone were 70.8% and 66.7%, respectively. In 83 eligible patients who started treatment, CR rates were 75.6% and 73.8%, respectively. Based on a median follow-up of 4.7 yr, 25 patients (52.1%) on MMC plus BCG and 22 patients (45.8%) on BCG alone were disease free. Twelve patients stopped treatment due to toxicity: three during induction (two MMC plus BCG, one BCG) and nine during maintenance (three MMC plus BCG, six BCG).
Conclusions: In the treatment of patients with CIS, sequential chemoimmunotherapy with MMC plus BCG had acceptable toxicity. CR and disease-free rates were similar to those on BCG alone and to previous publications on sequential chemoimmunotherapy.
Trial Registration: This study was registered with the US National Cancer Institute clinical trials database (protocol ID: EORTC-30993). ttp://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=68869&version=HealthProfessional&protocolsearchid=7920643.

Editorial Comment

Carcinoma in situ (CIS) of the bladder is relatively rare, still an aggressive disease and treatment options are scarce. Intravesical BCG has proven to be better than chemotherapy in several trials. The authors sought to clarify if a combination of both would improve the outcome. Interestingly, they used an unusual statistical method and claimed their study a phase 2 noncomparative trial in which randomization was not done for the purpose of making a treatment comparison but to provide a simultaneous screening of the two treatments. Thus, no p values were given for the end points.

The differences between both treatment arms were small, if any. Side effects were mostly local and not severe. 48.6% of patients had recurred after 5 years on mitomycin C + BCG versus 56.4% on BCG alone.
The authors conclude correctly that the present study and data from the literature do not support the use of sequential intravesical chemotherapy and BCG of CIS.

Furthermore, this study design and conduct shows that if applied carefully, interesting alternatives for large-scale randomized trials do exist.

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Effect of dutasteride on prostate biopsy rates and the diagnosis of prostate cancer in men with lower urinary tract symptoms and enlarged prostates in the combination of avodart and tamsulosin trial
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Eur Urol. 2011; 59: 244-9

Background: A 23% relative risk reduction (RRR) in prostate cancer (PCa) was shown in men receiving dutasteride in the 4-yr Reduction by Dutasteride of Prostate Cancer Events study, in whom biopsies were protocol dependent.
Objective: Our aim was to explore PCa risk reduction in men with benign prostatic hyperplasia (BPH) from the Combination of Avodart and Tamsulosin (CombAT) study, in which biopsies were undertaken for cause.
Design, Setting, and Participants: CombAT was a 4-yr randomized double-blind parallel group study in 4844 men ≥ 50 yr of age with clinically diagnosed moderate to severe BPH, International Prostate Symptom Score ≥ 12, prostate volume ≥ 30mL, and serum prostate-specific antigen (PSA) 1.5-10 ng/mL. Men underwent annual PSA measurement and digital rectal examination (DRE), and prostate biopsies were performed for cause.
Intervention: All patients took tamsulosin 0.4mg/d, dutasteride 0.5mg/d, or a combination of both.
Measurements: The primary end point was incidence of PCa. Secondary end points included postbaseline prostate biopsy rates and Gleason score of cancers.
Results and Limitations: Dutasteride (alone or in combination with tamsulosin) was associated with a 40% RRR of PCa diagnosis compared with tamsulosin monotherapy (95% confidence interval, 16-57%; p=0.002) and a 40% reduction in the likelihood of biopsy. There were similar reductions in low- and high-grade Gleason score cancers. The biopsy rate in the groups receiving dutasteride trended toward a higher diagnostic yield (combination: 29%, dutasteride: 28%, tamsulosin: 24%). One limitation was the lack of a standardized approach to PCa diagnosis and grading.
Conclusions: Dutasteride, alone or in combination with tamsulosin, significantly reduced the relative risk of PCa diagnosis in men with BPH undergoing annual DRE and PSA screening. Consistent with the increased usefulness of PSA for PCa detection, men receiving dutasteride had a numerically lower biopsy rate and higher yield of PCa on biopsy.
Trial Registration: Clinicaltrials.gov identifier: NCT00090103 (http://www.clinicaltrials.gov/ct2/show/NCT00090103).

Editorial Comment

This report from a large trial of dutasteride and/or tamsulosin (CombAT) focuses upon the cohort of men in which biopsies were undertaken for cause (suspicion of prostate cancer, PCa).

Men either received dutasteride, tamsulosin or both drugs. Thus, the results of the tamsulosin group may be seen as a control group for the effect of dutasteride. Altogether, PCa was detected in 2.3% in the combination group, in 2.6% in the dutasteride group and in 3.9% in the tamsulosin group. This may not seem impressive, but in pooling the dutasteride arm, there was a 1.5% absolute and a 40% relative risk reduction. Even more interestingly, Gleason sum scores were not significantly different between the groups (means Gleason scores were 6.3 in the combination group, 6.8 in the dutasteride group and 6.7 in the tamsulosin group; p = 0.12). In conclusion, these data underscore the clinical usefulness of dutasteride and even more, an important step toward the reduction of risk for prostate cancer.

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Simple enucleation is equivalent to traditional partial nephrectomy for renal cell carcinoma: results of a nonrandomized, retrospective, comparative study

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Purpose: The excision of the renal tumor with a substantial margin of healthy parenchyma is considered the gold standard technique for partial nephrectomy. However, simple enucleation showed excellent results in some retrospective series. We compared the oncologic outcomes after standard partial nephrectomy and simple enucleation.
Materials and Methods: We retrospectively analyzed 982 patients who underwent standard partial nephrectomy and 537 who had simple enucleation for localized renal cell carcinoma at 16 academic centers between 1997 and 2007. Local recurrence, cancer specific survival and progression-free survival were the main outcomes of this study. The Kaplan-Meier method was used to calculate survival functions and differences were assessed with the log rank statistic. Univariable and multivariable Cox regression models addressed progression-free survival and cancer specific survival.
Results: Median followup of the patients undergoing traditional partial nephrectomy and simple enucleation was 51 ± 37.8 and 54.4 ± 36 months, respectively ($p = 0.08$). The 5 and 10-year progression-free survival estimates were 88.9 and 82% after standard partial nephrectomy, and 91.4% and 90.8% after simple enucleation ($p = 0.09$). The 5 and 10-year cancer specific survival estimates were 93.9% and 91.6% after standard partial nephrectomy, and 94.3% and 93.2% after simple enucleation ($p = 0.94$). On multivariable analysis the adopted nephron sparing surgery technique was not an independent predictor of progression-free survival (HR 0.8, $p = 0.55$) and cancer specific survival (HR 0.7, $p = 0.53$) when adjusted for the effect of the other covariates.
Conclusions: To our knowledge this is the first multicenter, comparative study showing oncologic equivalence of standard partial nephrectomy and simple enucleation.

Editorial Comment

In this pioneering study, it is fundamental to emphasize important information regarding the limits of renal tumor simple enucleation – that could be the message for those meticulous readers with a less optimistic view.

The major point here is about the dubious clinical significance of simple enucleation in terms of less morbidity while it comes with the cost of worse cancer-specific survival, for Fuhrman grade 4 diseases, even with the enucleation group biased for lessen high grade tumors in this study, clearly showing that an additional margin of peri-tumor healthy renal parenchyma is necessary for high grade tumors better outcomes in short follow-up.

Given the limitations in renal biopsies, though increasingly progressing (1), further improvements in our capacity of identifying patients with high-grade disease and those at increased risk for poor outcomes would be essential to warrant widespread safe enucleations.

Although this study and others showing a small proportion of clinical recurrence for positive margin (2) encourage urologists to perform nephron-sparing surgery, even if the anticipated resection margin is close and touches the collecting system or renal hilum, an intensive surveillance with closer and longer follow-up is needed in such special situations, warranting timely rescue measures, being the cost and burden of serial imaging significant.

Moreover, residual cancer cells may require many years to become clinically apparent, since the average annual growth rate of radiographically visible masses can be as small as 0.13 cm/year (3) with rare but real potential to metastases, leaving concerning to longer follow-up.

While the benefits of nephron sparing surgery in terms of preventing chronic kidney disease and its associated cardiovascular morbidity and potential mortality are progressively clear (4,5), selection bias, variations in technique, tumor size and location make adequate evaluation of the enucleation and its comparison to standard partial nephrectomy difficult.

Additionally, it is well recognized the phenomenon that despite increased detection and treatment of small tumors, mortality from RCC did not decrease (6), suggesting a lead time bias which uniquely joins kidney and prostate cancer; most patients will very likely die with their cancer rather than of their cancer.

Further prospective, randomized and unbiased studies with technique standardization are necessary and advance in the identification of clinically significant tumors will be important in determining the renal masses needing treatment, as well as the well-adjusted treatment in each case. To the future, the answer needed is probably: when is enucleation necessary and safe?

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Association of hematuria on microscopic urinalysis and risk of urinary tract cancer

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Purpose: We determined the incidence of urinary tract cancer in patients with hematuria, stratified risk by age, gender and hematuria degree, and examined current best policy recommendations.

Materials and Methods: We performed a large, retrospective population based cohort study of patients who underwent microscopic urinalysis during 2004 and 2005 in a large managed care organization. Patients were followed for 3 years for urinary tract cancer.
Results: We identified 772,002 patients who underwent urinalysis during the study period. After exclusions due to previous hematuria, age less than 18 years, pregnancy, urinary tract infection, inpatient status and prior urinary tract cancer 309,402 patients were available for analysis, of whom 156,691 had hematuria. The overall 3-year incidence of urinary tract cancer in those with hematuria was 0.68%. Older age (greater than 40 years OR 17.0, 95% CI 11.2-25.7), greater hematuria (greater than 25 red blood cells per high power field OR 4.0, 95% CI 3.5-4.5) and male gender (OR 4.8, 95% CI 4.2-5.6) were associated with a higher risk of cancer. The American Urological Association definition of microhematuria had 50% sensitivity, 84% specificity and 1.3% positive predictive value.
Conclusions: The incidence of urinary tract cancer is low even in individuals with microhematuria. Thus, current best policy recommendations do not perform well. Since older age, male gender and greater hematuria are associated with a higher risk of cancer, future studies should evaluate strategies that target these populations.

Editorial Comment

Although under review, the last AUA Best Practice Policy Recommendations suggest evaluation in patients who have at least 2 urinalyses with 3 or more RBC/HPF within a 12-month period as well as those with gross hematuria (1).

The authors have proposed an approach of evaluating patients older than 40 years with at least 1 urinalysis showing greater than 25 RBC/HPF. Compared to the AUA method this alternative strategy could have spared 25,917 evaluations and detected 6 more cases of urinary tract cancer. Compared to the CUA approach (AUA restricted to patients > 40 years) it could have spared 11,584 evaluations and detected 16 more cases.

Older age, greater hematuria and male gender were predictors of urinary tract cancer, in accordance to a more restrictive protocol based on home dipstick testing to identify hematuria in a limited age spectrum (> 50 years), including only men with a proved beneficial impact on positive cases of bladder cancer (2).

However, future studies are to be greatly improved including evaluation of known risk factors, such as smoking history, occupational exposure to chemicals or dyes, gross hematuria, urological disease, irritative voiding symptoms, urinary tract infection, analgesic abuse and pelvic radiation in prospective, randomized trials of general population.

Furthermore, confounding clinical contexts, such as menstruation, vigorous exercise and cases of recent urinary tract instrumentation should be excluded and also the complete evaluation of urine cytology, upper tract imaging and cystoscopy are necessary for all patients to provide the best evidence for a safe actualization of the last recommendations that age 10 years.

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NEUROLOGY & FEMALE UROLOGY

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The effect of testosterone treatment on urodynamic findings and histopathomorphology of pelvic floor muscles in female rats with experimentally induced stress urinary incontinence

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Objective: In recent studies, it has been observed that androgen receptors are densely located in pelvic floor muscles. We aimed to investigate the effect of testosterone on urodynamic findings and histopathomorphology of pelvic floor muscles in rats with experimentally induced stress urinary incontinence.
Materials and Methods: Twenty-eight adult female rats were randomized into four groups. Group I: rats in which SUI was induced and single-dose testosterone was administered 30 days later, group II: rats in which SUI was induced and single-dose testosterone was administered within the same session, group III: rats in which SUI was induced and saline was injected intramuscularly 30 days later, and group IV: the sham group. In order to demonstrate objectively the curative and preventive role of testosterone in experimental model of SUI, urodynamic examination and histopathomorphological evaluation of levator ani muscle were performed.
Results: Myofiber areas in groups I and II were detected to be significantly larger than those of the control group ($P < 0.001$). Another parameter was leak point pressure value by urodynamy. Regarding this parameter, LPP values in groups 1, 2 and 4 were observed to be significantly higher than those of group 3 ($P < 0.001$). The results of the comparison among groups 1, 2 and 4 revealed no significance ($P > 0.05$), which indicates that testosterone provides continence in a similar way to the group in which sciatic nerve section was not performed.
Conclusions: In the present study, it has been demonstrated that testosterone has both preventive and curative effects on rat models of experimental SUI.

Editorial Comment

The authors present a very elegant study in which the role of intramuscular exogenous testosterone is proven to enhance free serum testosterone levels and to partially restore striated muscle fiber atrophy secondary to sciatic nerve injury in female rats. Also, from a clinical perspective, urodynamics study shows improvement in leak point pressure (LPP) values for treated rats, although the reading technique resembles more a detrusor leak point pressure than a true Valsalva LPP.

This study reinforces the idea that the anabolic effect of testosterone may be a useful tool to treat female urinary incontinence in a non-surgical manner. Additional aspects other than muscle hypertrophy such as neurological and connective tissue changes may be implicated. It should be noted, however, that clinical studies are necessary to determine the ideal form of testosterone formulation and delivery method, associated side effects such as humor disturbances and virilization, ideal dosage and duration of therapy.

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Overactive and underactive bladder dysfunction is reflected by alterations in urothelial ATP and NO release

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ATP and NO are released from the urothelium in the bladder. Detrusor overactivity (DO) following spinal cord injury results in higher ATP and lower NO release from the bladder urothelium. Our aim was to study the relationship between ATP and NO release in (1) early diabetic bladders, an overactive bladder model; and (2) "diuretic" bladders, an underactive bladder model. To induce diabetes mellitus female rats received 65mg/kg streptozocin (i.v.). To induce chronic diuresis rats were fed with 5% sucrose. At 28 days, in vivo open cystometry was performed. Bladder wash was collected to analyze the amount of ATP and NO released into the bladder lumen. For in vitro analysis of ATP and NO release, a Ussing chamber was utilized and hypoosmotic Krebs was perfused on the urothelial side of the chamber. ATP was analyzed with luminometry or HPLC-fluorometry while NO was measured with a Sievers NO-analyzer. In vivo ATP release was increased in diabetic bladders and unchanged in diuretic bladders. In vitro release from the urothelium followed the same pattern. NO release was unchanged both in vitro and in vivo in overactive bladders whereas it was enhanced in underactive bladders. We found that the ratio of ATP/NO, representing sensory transmission in the bladder, was high in overactive and low in underactive bladder dysfunction. In summary, ATP release has a positive correlation while NO release has a negative correlation with the bladder contraction frequency. The urinary ATP/NO ratio may be a clinically relevant biomarker to characterize the extent of bladder dysfunction.

Editorial Comment

Munoz et al. report on the importance of urinary ATP/NO ratio as a biomarker of bladder dysfunction. Nitric oxide has gained importance over recent years as it has been shown to play an important role on the relaxant activity of different non striated muscle tissues including bladder, corpus cavernous and vessels wall. The end product of the nitrergic pathway is the activation of calcium channels, but a step before that, cyclic GMP is the trigger element.

Understanding the mechanisms involved in bladder contraction and relaxation at a molecular level opens new horizons for therapeutic targets and pharmacological treatments. Not only NO donors may be promising tools to promote bladder relaxation, but also NO-independent guanilate cyclase stimulators may become part of this armamentarium.

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PEDIATRIC UROLOGY

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Risk factors for progression to end-stage renal disease in children with posterior urethral valves

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Objective: To identify the variables which affect long-term renal outcome in children with posterior urethral valves (PUV).
Materials and Methods: Retrospective analysis of 260 children with PUV who underwent ablation of valves in 1992-2008 at our tertiary care center. The following risk factors for progression to end-stage renal disease (ESRD) were analyzed: nadir serum creatinine greater than 1.0mg/dL, bilateral grade 3 or higher VUR at diagnosis, recurrent febrile UTIs, and severe bladder dysfunction. Patients were divided into two groups: those who developed ESRD (group 1) and those who did not (group 2).
Results: Forty (17.62%) patients had nadir serum creatinine > 1mg/dL. At time of initial presentation, high-grade VUR was seen in 63.1% and 33.5% of groups 1 and 2, respectively (P = 0.002). Overall, 77 (34%) of the boys developed breakthrough urinary tract infections: 37.03% and 33.5% in groups 1 and 2, respectively (P = 1). Fifty-nine (26%) patients were found to have severe bladder dysfunction: 77.8% and 19% in groups 1 and 2, respectively (P < 0.0001). Twenty-seven (11.89%) patients progressed to ESRD, at mean age of 11.21 years (5-16). On univariate analysis, the risk-predicting variables were: nadir serum creatinine value greater than 1mg/dL (P < 0.0001), bilateral high-grade VUR (P = 0.002) and severe bladder dysfunction (P < 0.0001). On multivariate logistic regression analysis, nadir serum creatinine greater than 1mg/dL (OR 23.79; CI 8.20-69.05) and severe bladder dysfunction (OR 5.67; CI 1.90-16.93) were found to be independent risk factors predictive of ultimate progression to ESRD.
Conclusions: Nadir serum creatinine and bladder dysfunction are the main factors affecting long-term renal outcome in cases of PUV. Early identification and treatment of bladder dysfunction may thus be beneficial.

Editorial Comment

This paper looked at a large series of children with posterior urethral valves in order to identify risk factors for end-stage renal disease. Patients were followed for a mean of 7.2 years. A total of 227 patients were eligible for inclusion in the review. The authors looked at age at presentation, nadir serum creatinine, presence of high-grade reflux, recurrent febrile urinary tract infections, and severe bladder dysfunction as variables. 30% of patients developed chronic kidney disease and 12% progressed to end-stage renal disease. On univariate analysis nadir creatinine greater than 1 mg/dL, bilateral high-grade reflux, and severe bladder dysfunction were found to be risk factors. On multivariate analysis; however, only nadir serum creatinine greater than 1 mg/dL and severe bladder dysfunction were predictive of progression to end-stage renal disease.

The strength of this study is the large number of patients at a single institution. Certainly longer follow-up would likely reveal a greater number of patients who progress to end-stage renal disease. Their findings are in line with another large series recently published which also demonstrated bladder dysfunction and nadir creatinine to be the only independent risk factors for end-stage renal disease using multivariate analysis (1). While nadir serum creatinine is not a modifiable risk factor, bladder dysfunction can certainly be managed aggressively in these at risk patients. This paper helps to reemphasize the importance of screening for bladder

dysfunction early on. It remains to be seen whether or not early and aggressive management of bladder dysfunction can have an impact on outcomes.

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Safety of shock wave lithotripsy for treatment of pediatric urolithiasis: 20-year experience

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Purpose: This retrospective study was designed to assess the impact of shock wave lithotripsy on the pediatric kidney using pretreatment and posttreatment (99m)technetium dimercapto-succinic acid renal scintigram.
Materials and Methods: A total of 182 patients 5 months to 19.8 years old (mean 5.3 years) were treated for renal calculi with shock wave lithotripsy during a 20-year period. Pretreatment evaluation included clinical assessment, urine culture, renal ultrasound and plain abdominal radiograph with or without excretory urogram. Dimercapto-succinic acid scintigram was performed before and 6 months after completion of treatment in 94 patients (52%).
Results: Patients underwent 1 to 4 sessions of shock wave lithotripsy per kidney with at least 1 month between treatments. Median number of shocks delivered per session was 3,000 (IQR 2,601 to 3,005). No new scars were observed on any posttreatment dimercapto-succinic acid scan. Regarding renal function, patients fell into 1 of 4 groups. Group 1 (66 patients, 70%) had normal function on dimercapto-succinic acid scan before and after treatment, group 2 (18, 19%) had decreased function in the affected kidney on pretreatment scan with no change after treatment, group 3 (2, 2%) had impaired function in the treated kidney that was transient (1) or permanent (1) and group 4 (7, 7%) had improved function in the treated kidney.
Conclusions: Shock wave lithotripsy is an effective treatment for renal calculi in children. Renal parenchymal trauma associated with extracorporeal shock wave lithotripsy does not seem to cause long-term alterations in renal function or development of permanent renal scars in children.

Editorial Comment

This retrospective study looked at 182 pediatric patients who were treated for renal stones over 20 years using shock wave lithotripsy. They had a low number of complications with steinstrasse developing in 2 patients and another 2 patients who developed pyelonephritis. Part of their preoperative assessment included a DMSA scan. What is remarkable about this study is that they were able to get posttreatment DMSA scans in 94 patients six months following lithotripsy. No new renal parenchyma scars were discovered on their follow-

up DMSA scans. In addition, 89% of the patients had no change in function. They had 7 patients who actually had increase in their relative function in the affected kidney and 3 patients that had a greater than 5% decrease in function. Only 1 of these had permanent deterioration of function which was felt by the authors to be more likely due to obstruction rather than the shock wave lithotripsy.

There has always been concern about the collateral parenchymal damage done with shock wave lithotripsy particularly in the pediatric population. The data from this paper would indicate that any damage sustained is temporary and typically resolves within six months of treatment.

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