
UROLOGICAL SURVEY

Francisco J.B. Sampaio
Urogenital Research Unit
State University of Rio de Janeiro

Athanase Billis
State University of Campinas
Campinas, SP, Brazil

Andreas Böhle
Helios Agnes Karll Hospital
Bad Schwartau, Germany

Steven B. Brandes
Washington University in St. Louis
St. Louis, Missouri, USA

Sean P. Elliott
University of Minnesota
Minneapolis, MN, USA

Fernando J. Kim
Univ Colorado Health Sci Ctr
Denver, Colorado, USA

Manoj Monga
University of Minnesota
Edina, MN, USA

Steven P. Petrou
Mayo Medical School
Jacksonville, Florida, USA

Adilson Prando
Vera Cruz Hospital
Campinas, SP, Brazil

M. Chad Wallis
University of Utah
Salt Lake City, Utah, USA

STONE DISEASE

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Chronic kidney disease affects the stone-free rate after extracorporeal shock wave lithotripsy for proximal ureteric stones

Hung SF, Chung SD, Wang SM, Yu HJ, Huang HS

Department of Urology, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taipei, Taiwan

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Objective: To investigate the effect of renal function on the stone-free rate (SFR) of proximal ureteric stones (PUS) after extracorporeal shock wave lithotripsy (ESWL), as urinary obstruction caused by PUS can impair renal function, and elevated serum creatinine levels are associated with decreased ureteric stone passage.

Patients And Methods: From January 2005 to December 2007, 1534 patients had ESWL for urolithiasis, 319 having ESWL in situ for PUS; they were reviewed retrospectively. Patients requiring simultaneous treatment of kidney stones, placement of a double pigtail stent, or percutaneous pigtail nephrostomy tube were excluded. We divided patients into groups by chronic kidney disease (CKD) stage according to the estimated glomerular filtration rate (eGFR) of ≥ 60 and < 60 mL/min/1.73 m². Stone-free status was defined as no visible stone fragments on a plain abdominal film at 3 months after ESWL. A logistic regression model was used to evaluate the possible significant factors that influenced the SFR of PUS after ESWL, and to develop a prediction model.

Results: The overall SFR of PUS (276/319 patients) was 86.5%; the SFR was 93% in patients with an eGFR of ≥ 60 and 50% in those with an eGFR of < 60 ($P < 0.001$). After univariate and multivariate analysis, the three significant factors affecting SFR were an eGFR of ≥ 60 , stone width, and gender, with odds ratios (95% confidence intervals) of 19.54 (8.25-46.30) ($P < 0.001$), 0.67 (0.55-0.82) ($P < 0.001$) and 0.16 (0.05-0.50) ($P = 0.002$), respectively. A logistic regression model was developed to estimate the probability of SFR after ESWL, the equation being $1/(1 + \exp[-(3.8137 - 0.3967 \times (\text{stone width}) + 2.9724 \times \text{eGFR} - 1.8120 \times \text{Male})])$, where stone width is the observed value (mm), eGFR = 1 for eGFR ≥ 60 and 0 for < 60 , and male = 1 for male, 0 for female.

Conclusions: Gender, eGFR ≥ 60 and a stone width of > 7 mm were significant predictors affecting the SFR after one session of ESWL for PUS.

Editorial Comment

The authors do not state at what time point was the serum creatinine obtained that was utilized to calculate the estimated GFR. This is a critical omission. Ideally the serum Cr and GFR would have been evaluated after resolution of the obstructing calculus. This would identify those with true chronic kidney disease. In contrast, if these values were evaluated at the time of obstruction; the abnormality may have been post-renal. Indeed, if they have selected those patients with renal insufficiency due to severe obstruction, one would anticipate that these may be patients with more severe hydronephrosis or longer duration since onset of pain and obstruction; both of which could be independent predictors of failure of SWL. The observation that stone width is more critical than stone length in determining shockwave success may be important to consider when counseling patients.

Dr. Manoj Monga*Department of Urology**Cleveland Clinic Foundation**Cleveland, Ohio, USA**E-mail: endourol@yahoo.com*

Novel in vitro model for studying ureteric stent-induced cell injury

Elwood CN, Lange D, Nadeau R, Seney S, Summers K, Chew BH, Denstedt JD, Cadieux PA

Lawson Health Research Institute, University of Western Ontario, London, Canada.

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Objective: To develop a novel in vitro model for the study of bladder and kidney epithelial cell injury akin to stent movement, as ureteric stents are associated with urinary tract complications that can significantly add to patient morbidity. These sequelae may be linked to inflammation triggered by stent-mediated mechanical injury to the urinary tract.

Materials and Methods: T24 bladder and A498 kidney cell line monolayers were damaged mechanically by segments of either Percuflex Plus (PP) or Triumph (triclosan-eluting) stents (both from Boston Scientific Corporation Inc. Natick, MA, USA) and the resulting expression profiles of several pro-inflammatory cytokines and growth factors were analysed.

Results: After control injury using the PP stent, supernatants of both cell lines had significantly increased levels of interleukin (IL)-6, IL-8, basic fibroblast growth factor and platelet-derived growth factor BB, and A498 cells also had increased tumour necrosis factor alpha. In almost all cases, the presence of triclosan within the media abrogated the pro-inflammatory cytokine increases, while its effects on growth factors varied.

Conclusion: This study suggests that stent-related symptoms in the bladder and kidney may be partially due to a local inflammatory response to epithelial damage caused by the presence and movement of the stent. Future stent design should take these inflammatory responses, with respect to physical injury, into consideration, using either more biocompatible materials or anti-inflammatory compounds such as triclosan.

Editorial Comment

The authors have previously evaluated ketorolac coated stents - noting no significant improvement in patient symptoms. It would be of value to test the anti-inflammatory properties of ketorolac-coated stents in this novel in vitro model. It would be interesting to develop epithelial: smooth muscle co-cultured matrices to evaluate the impact of stromal: epithelial interactions following stent irritation on the expression of inflammatory markers and growth factors. The concept of uroepithelial cell disruption as a cause for stent pain may suggest that those patients undergoing long ureteroscopic procedures with forceful irrigation may experience more stent discomfort due to the hydrodistension of the upper collecting system and subsequent stimulation of the inflammatory response. It would be important to evaluate inflammatory markers in urine after ureteroscopy and with urinary stents.

Dr. Manoj Monga

Department of Urology

Cleveland Clinic Foundation

Cleveland, Ohio, USA

E-mail: endourol@yahoo.com

ENDOUROLOGY & LAPAROSCOPY

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Complications of renal cryoablation: a single center experience

Sidana A, Aggarwal P, Feng Z, Georgiades CS, Trock BJ, Rodriguez R

The James Buchanan Brady Urological Institute and Department of Radiology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

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Purpose: We describe perioperative complications associated with renal cryoablation and identify potential risk factors for certain complications.

Materials and Methods: We retrospectively analyzed the medical records of patients with unifocal renal masses treated with cryosurgery at a single center between 1997 and 2007. All complications associated with these procedures were documented and classified into grades 1 to 5 by the Clavien surgical complication classification. In-depth analysis was done to identify potential risk factors for the most common complications.

Results: We evaluated 101 percutaneous, 52 laparoscopic and 9 open procedures. Complications were noted in 38 procedures (23.5%), including grades 1 to 4 in 19 (11.7%), 8 (4.9%), 5 (3.1%) and 6 (3.7%), respectively, as the severest complication. The most common complication was flank pain (11 procedures), followed by perinephric hematoma and cardiovascular complications (10 each). Mass size ($p = 0.001$), number of cryoablation probes ($p < 0.001$) and chronic anticoagulation ($p < 0.05$) were associated with an increased incidence of significant hematoma. Cardiovascular complications were more common when upper pole lesions were treated, and when an open approach was used (each $p < 0.05$). Respiratory complications occurred in 7 procedures and were associated with patient age ($p < 0.05$) and mass size ($p < 0.01$).

Conclusions: Cryoablation is a relatively safe procedure with a low complications rate in properly selected patients. We identified potential risk factors that may help identify patients most at risk for certain complications and consequently assist in preprocedural planning and counseling.

Editorial Comment

The management of small renal masses has evolved from total removal of the kidney to nephron-sparing surgery. Recently, renal cryoablation has emerged as a new treatment modality for small renal cancer. Although long-term results have not been established yet, it is clear that this novel surgical modality reveals low complication rates when compared to other minimally invasive surgery for management of small renal masses.

Complications were noted in 38 procedures (23.5%) from a total of 162 procedures, including 101 percutaneous, 52 laparoscopic and 9 open procedures. The complications were graded from 1 to 4 in 19 (11.7%), 8 (4.9%), 5 (3.1%) and 6 (3.7%), respectively, as the severest complication.

Interestingly, cardiovascular complications were more common when upper pole lesions were treated, and when an open approach was used (each $p < 0.05$); while respiratory complications occurred in 7 procedures and were associated with patient age ($p < 0.05$) and mass size ($p < 0.01$).

Dr. Fernando J. Kim*Chief of Urology, Denver Health Med. Ctr.**Associate Professor, Univ. Colorado Health Sci. Ctr.**Director of Minimally Invasive Urol. Oncology, UCHSC**Denver, Colorado, USA**E-mail: fernando.kim@dhha.org*

Transperitoneal laparoscopic radical nephrectomy for patients with dialysis-dependent end-stage renal disease: an analysis and comparison of perioperative outcome

Bird VG, Shields JM, Aziz M, De Los Santos R, Ayyathurai R, Ciancio G

Department of Urology, Division of Transplantation, University of Miami Miller School of Medicine, Miami, Florida, USA

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Objectives: To evaluate LRN as treatment for high risk patients. Laparoscopic radical nephrectomy (LRN) is performed for renal tumors not amenable to nephron-sparing treatments. Indications are increasing to include higher risk patients including those with end-stage renal disease (ESRD) necessitating dialysis.

Methods: We performed a retrospective analysis of a patient cohort with clinical stage T1 renal tumors undergoing transperitoneal LRN. Parameters examined included patient demographics, medical comorbidities, tumor characteristics, operative outcomes, and complications.

Results: One hundred eighty-nine patients underwent 195 LRN. Sixteen patients (8.5%) had preexistent ESRD requiring dialysis. A higher American Society of Anesthesiologists score ($P<.05$), higher age-adjusted Charlson comorbidity index ($P=.003$), higher incidence of previous abdominal surgery ($P=.012$), and higher incidence of hypertension ($P=.025$) were found for the ESRD group. Mean blood loss was 153.0 and 132.0 mL ($P=.71$) in the ESRD patients and non-ESRD patients, respectively. A longer stay ($P=.02$) was noted for ESRD patients. Mean tumor size in the ESRD patients and non-ESRD patients was 2.6 and 4.2 cm ($P<.05$), respectively. Renal cell carcinoma was the most common pathology in 14 of 20 (70.0%) ESRD patient renal units and 167 of 175 (95.4%) non-ESRD patient renal units ($P=.001$). Intraoperative and postoperative complication rates were 6.3% and 31.3% respectively for ESRD patients ($P=.05$), and 8.7% and 21.4% respectively for non-ESRD patients ($P=.35$). Most postoperative complications were minor.

Conclusions: LRN, for the treatment of renal tumors in ESRD patients requiring dialysis, is feasible and safe with acceptable intraoperative and postoperative complication rates.

Editorial Comment

Laparoscopic radical nephrectomy (LRN) has become standard of care for renal tumors not amenable to nephron-sparing surgery. LRN is a safe procedure associated with low morbidity for treatment of renal cell carcinoma.

The authors report their experience with LRN as treatment modality for renal masses in high-risk patients. Particularly, patients with end-stage renal disease (ESRD) requiring hemodialysis demonstrated little to no wound complications. Moreover, the authors demonstrated that papillary subtype RCC was more frequent in the ESRD than the non-ESRD population (30% ESRD versus 13.1% of non-ESRD patients).

The transperitoneal laparoscopic approach has shown to be safe and effective to manage high-risk patients with different techniques of CO₂ insufflation.

Dr. Fernando J. Kim*Chief of Urology, Denver Health Med. Ctr.**Associate Professor, Univ. Colorado Health Sci. Ctr.**Director of Minimally Invasive Urol. Oncology, UCHSC**Denver, Colorado, USA**E-mail: fernando.kim@dhha.org*

IMAGING

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MRI in the characterization and local staging of testicular neoplasms

Tsili AC, Argyropoulou MI, Giannakis D, Sofikitis N, Tsampoulas K

Department of Clinical Radiology, University Hospital of Ioannina, Ioannina, Greece

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Objective: The purpose of this study was to assess the role of MRI in the preoperative characterization and local staging of testicular neoplasms.

Subjects and Methods: MRI was performed on 33 patients referred because a testicular mass had been detected clinically and sonographically. Both T1- and T2-weighted sequences were performed with a 1.5-T MRI unit. Gadolinium chelate was administered IV in all cases. We recorded the presence of a lesion and whether the histologic diagnosis of testicular malignancy could have been predicted on the basis of MRI features. For testicular neoplasms, local extension of disease was studied. The MRI findings were correlated with the surgical and histopathologic results.

Results: Histologic examination revealed 36 intratesticular lesions, 28 (78%) of which were malignant and eight benign. Thirteen malignant testicular tumors (46%) were confined within the testis, 12 (43%) had invaded the testicular tunicae or epididymis, and three (11%) had invaded the spermatic cord. The sensitivity and specificity of MRI in differentiating benign from malignant intratesticular lesions were 100% (95% CI, 87.9-100%) and 87.5% (95% CI, 52.9-97.7%). The rate of correspondence between MRI and histologic diagnosis in the local staging of testicular tumors was 92.8% (26/28).

Conclusion: MRI is a good diagnostic tool for the evaluation of testicular disease. It is highly accurate in the preoperative characterization and local staging of testicular neoplasms.

Editorial Comment

High-resolution sonography (US), with color or power Doppler has become the imaging modality of choice for the evaluation of scrotal abnormalities. US is an accurate method in distinguishing intratesticular from extratesticular lesions, a key point in the diagnostic evaluation of scrotal disease. Most intratesticular solid lesions are malignant, whereas extratesticular lesions are usually benign. Although sonography cannot accurately differentiate seminomatous from non-seminomatous tumors, their findings when combined with clinical information allow us to narrow the differential diagnosis of the majority of scrotal masses. Sonography can also be useful for local staging of testicular tumors, although it has limitation for the detection of the invasion of the spermatic cord (1). In such situation, very large scrotal mass or in inclusive sonographic studies, MRI should be performed as a complimentary tool.

The authors of this study nicely show that MRI is an efficient diagnostic tool to evaluate testicular masses and accurately differentiate between benign and malignant intratesticular tumors. With MRI, 87.5% of benign intratesticular mass lesions were characterized correctly. The overall accuracy of MRI in estimating the local extent of malignant testicular tumors was 93%. Contrary to US, MRI was adequate tool for the demonstration of invasion of the spermatic cord by the intratesticular tumor. Unfortunately, similarly to what happens with sonography, focal granulomatous orchitis may also simulate testicular tumor on MRI studies. The authors pointed out one major limitation of this study; they did not compare the diagnostic performances of sonography and MRI in the diagnosing and characterization of testicular disease. Although high-resolution sonography continues to be the imaging modality of choice, MRI is an efficient technique for testicular imaging.

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Dr. Adilson Prando

*Head, Department of Radiology and
Diagnostic Imaging, Vera Cruz Hospital
Campinas, São Paulo, Brazil
E-mail: adilson.prando@gmail.com*

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Imaging of prostate cancer local recurrences: why and how?

Rouvière O, Vitry T, Lyonnet D
Université de Lyon, Lyon, France
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Objective: Because prostate cancer local recurrences can be efficiently treated by salvage therapies, it becomes critical to detect them early.

Methods: The first alert is the rise of the prostate specific antigen (PSA) level after the post-treatment nadir, which can correspond to a distant recurrence, a local recurrence or both. This so-called biochemical failure (BF) is defined as PSA level > 0.2 ng/ml after radical prostatectomy (RP) and PSA level > nadir + 2 ng/ml after radiotherapy. There is no consensual definition of BF after cryotherapy, high-intensity focused ultrasound (HIFU) ablation or brachytherapy.

Results: Local recurrences after RP are treated by radiotherapy, those after radiotherapy by RP, cryotherapy, brachytherapy or HIFU ablation. Recurrences after cryotherapy or HIFU ablation can be treated by a second session or radiotherapy. Recurrences after brachytherapy are difficult to treat. In patients with BF, MRI can detect local recurrences, whatever the initial treatment was. Dynamic contrast-enhanced MRI seems particularly accurate. The role of spectroscopy remains controversial. Ultrasound-based techniques are less accurate, but this may change with the advent of ultrasonic contrast media.

Conclusion: These recent advances in imaging may improve the outcome of salvage therapies (by improving patient selection and treatment targeting) and should open the way to focal salvage treatments in the near future.

Editorial Comment

The authors should be congratulated for reviewing this important issue on uro-oncology. Important aspects of local recurrence after radical prostatectomy (RP), external-beam radiotherapy (EBRT), HIFU ablation, cryotherapy and brachytherapy are presented and discussed. For each modality of local treatment of prostate cancer, the authors define biochemical failure and discuss treatment options and the role of imaging techniques for the detection of tumor recurrence.

In our experience, dynamic-contrast enhanced MRI is the best modality for the detection of local recurrence after RP. For local recurrence after EBRT our better results are obtained with spectroscopy although dynamic-contrast enhanced MRI can also be useful in most cases. We also prefer to use spectroscopy for the detection of local tumor recurrence after brachytherapy. The quality of dynamic-contrast enhanced MRI stud-

ies in post-brachytherapy glands may be impaired due to the presence of several false-positive results. In our institution we have no experience with MRI for the detection of local tumor recurrence after HIFU ablation or cryotherapy.

Dr. Adilson Prando

Head, Department of Radiology and
Diagnostic Imaging, Vera Cruz Hospital
Campinas, São Paulo, Brazil
E-mail: adilson.prando@gmail.com

PATHOLOGY

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Prostate-specific antigen kinetics during follow-up are an unreliable trigger for intervention in a prostate cancer surveillance program

Ross AE, Loeb S, Landis P, Partin AW, Epstein JI, Kettermann A, Feng Z, Carter HB, Walsh PC
Departments of Urology and Pathology, The Johns Hopkins University School of Medicine, The James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, MD, USA
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Purpose: To assess the predictive ability of prostate-specific antigen (PSA) velocity (PSAV) and doubling time (PSADT) for biopsy progression and adverse pathology at prostatectomy among men with low-risk prostate cancer enrolled on an active-surveillance program.

Methods: We evaluated 290 men who met criteria for active surveillance (ie, PSA density < 0.15 ng/mL/cm³) and Gleason score < or = 6 with no pattern > or = 4, involving < or = 2 cores with cancer, and < or = 50% involvement of any core by cancer) with two or more serial PSA measurements after diagnosis from 1994 to 2008. Follow-up included twice-yearly digital rectal exam and PSA measurements and yearly surveillance biopsy. Treatment was recommended for biopsy progression (ie, Gleason score > or = 7, or > 2 positive cores, or > 50% core involvement). Sensitivity and specificity of postdiagnostic PSAV and PSADT were explored by using receiver operating characteristic (ROC) analysis.

Results: Overall, 188 (65%) men remained on active surveillance, and 102 (35%) developed biopsy progression at a median follow-up of 2.9 years. PSADT was not significantly associated with subsequent adverse biopsy findings (P = .83), and PSAV was marginally significant (P = .06). No PSAV or PSADT cut point had both high sensitivity and specificity (area under the curve, 0.61 and 0.59, respectively) for biopsy progression. In those who eventually underwent radical prostatectomy, PSAV (P = .79) and PSADT (P = .87) were not associated with the presence of unfavorable surgical pathology.

Conclusion: Postdiagnostic PSA kinetics do not reliably predict adverse pathology and should not be used to replace annual surveillance biopsy for monitoring men on active surveillance.

Editorial Comment

This is an important study concluding that postdiagnostic PSA kinetics do not reliably predict adverse pathology and should not be used to replace annual surveillance biopsy for monitoring men on active surveillance. At Johns Hopkins, the criteria for active surveillance are: PSA density < 0.15 ng/mL/cm³, Gleason score ≤ 6 with no pattern 4 or 5, involving ≤ 2 cores with cancer, and ≤ 50% involvement of any core by cancer (1).

At Stanford, the criteria are: Gleason score ≤ 6 with no pattern 4 or 5, one single core with cancer, linear extent of cancer ≤ 3 mm, and serum PSA is not considered (2). It is controversial whether percentage or linear extent is the best measure.

The follow-up included twice-yearly digital rectal exam and PSA measurements and yearly surveillance biopsy. Treatment was recommended for biopsy progression which was considered whenever Gleason score was ≥ 7 , > 2 positive cores, or $> 50\%$ core involvement. The important finding in Ross et al. study was that PSA double time was not significantly associated with subsequent adverse biopsy findings ($p = 0.83$) and PSA velocity was marginally significant ($p = 0.06$).

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Dr. Athanase Billis

Full-Professor of Pathology

State University of Campinas, Unicamp

Campinas, São Paulo, Brazil

E-mail: athanase@fcm.unicamp.br

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The value of mandatory second opinion pathology review of prostate needle biopsy interpretation before radical prostatectomy

Brimo F, Schultz L, Epstein JI

Department of Pathology, The Johns Hopkins Hospital Medical Institutions, Baltimore, Maryland, USA

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Purpose: We determined the value of mandatory second opinion pathology review to interpret prostate needle biopsy before radical prostatectomy.

Materials and Methods: In all cases referred to our institution for radical prostatectomy in 1 year we compared pathological parameters in original and reviewed pathology reports, including benign, atypical or malignant diagnosis, final Gleason score, positive core number, core highest cancer percent and perineural invasion or extraprostatic extension. A major Gleason score discrepancy was defined as a change to a different risk category (6,7 and 8-10). We defined a significant difference in the highest percent of cancer in a core as 30% or greater.

Results: Of the 855 cases originally diagnosed as prostatic adenocarcinoma cancer was confirmed in 844 (98.8%) by needle biopsy and prostatectomy, of which 9 (1%) were atypical and 2 (0.2%) were benign upon review. A major discrepancy in Gleason score was present in 124 cases (14.7%), of which 57 (46.0%) were upgraded and 67 (54%) were downgraded. Of cases with a final Gleason score of 6, 8.4% were originally diagnosed as 7 (7.8%) or 8-10 (0.6%), 21% with a final score of 7 had an original score of 6 (13.2%) or 8-10 (7.8%) and 21 of 61 (34%) with a score of 8-10 were originally diagnosed as 7 or less. There were 80 cases (64.5%) of disagreement between scores 6 and 7. Of the 777 cases with the positive core number in each

report 71 (9.1%) had discrepancies. After review the positive core number was higher in 45 cases (63.4%) and lower in 26 (36.6%). We noted a significant difference in the highest cancer percent in a core in 76 of 844 evaluable cases (9%) in which cancer was originally underestimated. In 60 of 76 cases (78.9%) cancer discontinuously involved the core on review. Review revealed perineural invasion in 138 of 844 cases (16.3%) that was not originally reported in 37 of 138 (26.8%). In 4 cases review showed extraprostatic extension on needle biopsy.

Conclusions: Compared to a smaller study more than 10 years ago at our institution the rate of unconfirmed cancer was identical (1.2%). To our knowledge this is the first study to analyze concordance upon review of the number of positive cores and maximum percent positive in a core (each discrepancy 9%). In a few cases mandatory second opinion on prostate needle biopsy results in significant differences that may affect therapy.

Editorial Comment

This article by Brimo et al. emphasizes the importance of a second opinion pathology review of prostate needle biopsy interpretation before radical prostatectomy. It may result in significant differences that may affect therapy. Of the 855 cases originally diagnosed as prostatic adenocarcinoma, cancer was confirmed in 844 (98.8%) by needle biopsy and prostatectomy. Therefore, the rate of unconfirmed cancer was 1.2%. Of these unconfirmed cases 1% were “suspicious but not diagnostic” and 0.2% were benign.

The most common benign lesion that simulates adenocarcinoma is partial atrophy. The lesion was reported in the periodic literature in 1998 (1). Architecturally, partial atrophy consists of crowded glands often with a disorganized growth pattern. In contrast to complete atrophy, which can typically be diagnosed at scanning magnification owing to the presence of well-formed glands with a very basophilic appearance, partial atrophy has pale cytoplasm lateral to the nuclei giving rise to pale staining glands that more closely mimic cancer. An additional difficulty in distinguishing cancer from partial atrophy is the positivity for alpha-methylacyl coenzyme A racemase (AMACR) in some acini (2-4).

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Dr. Athanase Billis
Full-Professor of Pathology
State University of Campinas, Unicamp
Campinas, São Paulo, Brazil
E-mail: athanase@fcm.unicamp.br

RECONSTRUCTIVE UROLOGY

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Urethrotomy has a much lower success rate than previously reported

Santucci R, Eisenberg L

Detroit Medical Center and Michigan State College of Osteopathic Medicine, Detroit, Michigan, USA

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Purpose: We evaluated the success rate of direct vision internal urethrotomy as a treatment for simple male urethral strictures.

Materials and Methods: A retrospective chart review was performed on 136 patients who underwent urethrotomy from January 1994 through March 2009. The Kaplan-Meier method was used to analyze stricture-free probability after the first, second, third, fourth and fifth urethrotomy. Patients with complex strictures (36) were excluded from the study for reasons including previous urethroplasty, neophallus or previous radiation, and 24 patients were lost to followup.

Results: Data were available for 76 patients. The stricture-free rate after the first urethrotomy was 8% with a median time to recurrence of 7 months. For the second urethrotomy stricture-free rate was 6% with a median time to recurrence of 9 months. For the third urethrotomy stricture-free rate was 9% with a median time to recurrence of 3 months. For procedures 4 and 5 stricture-free rate was 0% with a median time to recurrence of 20 and 8 months, respectively.

Conclusions: Urethrotomy is a popular treatment for male urethral strictures. However, the performance characteristics are poor. Success rates were no higher than 9% in this series for first or subsequent urethrotomy during the observation period. Most of the patients in this series will be expected to experience failure with longer followup and the expected long-term success rate from any (1 through 5) urethrotomy approach is 0%. Urethrotomy should be considered a temporizing measure until definitive curative reconstruction can be planned.

Editorial Comment

Our understanding of the success rate of optical internal urethrotomy for urethral stricture disease has been primarily based on 2 studies both published in 1996. Pansadoro et al. (1) and Albers et al. (2) were both large retrospective series of optical internal urethrotomy performed with modern techniques. Both showed success rates to be 32-40% with follow-up longer than 24 months. Both demonstrated success to be highest for short segment strictures in the bulbar urethra: 42% (1) and 66% (2). Cost effectiveness analysis based on these data has suggested that a single urethrotomy should be attempted before urethroplasty (3). However, primary urethroplasty was preferred if the success rate of urethrotomy was to drop below 35%. Now, the current article by Santucci and Eisenberg demonstrates a much lower success rate for urethrotomy. In fact, the success rate is so low that it begs us to consider whether urethrotomy should be abandoned except in those unable to undergo urethroplasty. How can these data differ so dramatically and which study presents the most accurate assessment of the true success rate for urethrotomy? Several elements of the studies by Pansadoro (1) and Albers (2) may have led to an overestimate of the success rate: (1) Several patients in the Albers series were on self-obdurance postoperatively (2). Pansadoro et al only included those patients with at least 5 years of follow-up, thus excluding many who may have failed early and then lost to follow-up (3). The follow-up was not well-recorded in the Albers series. So, the article by Santucci and Eisenberg may indeed represent the true success rate of urethrotomy and should serve as a call to others to closely examine the efficacy of an often-performed but poorly-studied procedure.

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Dr. Sean P. Elliott

Department of Urology Surgery

University of Minnesota

Minneapolis, Minnesota, USA

E-mail: selliot@umn.edu

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Morbidity of oral mucosa graft harvesting from a single cheek

Barbagli G, Vallasciani S, Romano G, Fabbri F, Guazzoni G, Lazzeri M

The Centre for Reconstructive Urethral Surgery, Arezzo, Italy.

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Background: The oral mucosa (OM) is a popular substitute for urethroplasty.

Objective: The aim of this study was to investigate oral morbidity and patient satisfaction in a homogeneous group of patients who underwent OM harvesting.

Design, Setting, and Participants: This study is a prospective analysis of 350 patients who underwent OM harvesting from a single cheek.

Intervention: The graft was harvested in an ovoid shape with closure of the wound. Standard graft size was 4cm in length and 2.5cm in width.

Measurements: Self-administered, nonvalidated semiquantitative (0, absence of complications or symptoms; 3, the worst complication or symptom) questionnaire consisting of six questions was used to investigate early complications, with 13 questions designed to investigate late complications and patient satisfaction.

Results and Limitations: Early complications included bleeding, which occurred in 15 patients (4.3%); two patients required immediate surgical revision of the harvesting site. The majority of patients (85.2%) showed no pain, and only 3.7% of patients required use of anti-inflammatory drugs. The majority of patients (65.8%) showed slight or moderate swelling. With respect to late complications, most of the patients (73.4%) reported oral numbness for 1 wk, 22.9% for 1 mo, and 3.77% for 3 mo. Numbness resulting from scarring was absent or slight in most of patients. Changes in oral sensitivity occurred in 2.3% of patients. No difficulties opening the mouth or smiling was found in 98.3% and 99.7% of patients, respectively. Slight or moderate dry mouth was found in 97.1% of patients. In response to the question, "Would you undergo oral mucosa graft harvesting using this technique again," 343 patients (98%) replied "yes," and 7 patients (2%) replied "no."

Conclusions: The harvesting of an OM ovoid graft from a cheek with closure of the wound is a safe procedure with a high patient satisfaction rate.

Editorial Comment

Success rates of substitution urethroplasty with buccal mucosa graft are similar to those using genital skin as the graft material. The principal reason buccal mucosa has been embraced as the graft material of choice is because the graft harvest is believed to cause less morbidity than harvest from other donor areas. Thus, this

article represents an important study documenting the low morbidity of oral graft harvest. The questions asked by the authors cover a broad spectrum of possible symptoms. This confirms most surgeons' observations that oral mucosa harvest is well-tolerated. Still, in the absence of a study that directly compares the morbidity of oral mucosa harvest with that of genital skin harvest it is unclear whether oral mucosa harvest is safer than genital skin harvest.

Dr. Sean P. Elliott

Department of Urology Surgery

University of Minnesota

Minneapolis, Minnesota, USA

E-mail: selliot@umn.edu

UROLOGICAL ONCOLOGY

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A new multimodality technique accurately maps the primary lymphatic landing sites of the bladder

Roth B, Wissmeyer MP, Zehnder P, Birkhäuser FD, Thalmann GN, Krause TM, Studer UE

Department of Urology, University of Bern, Bern, Switzerland

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Background: Pathoanatomic studies have failed to map accurately the primary lymphatic landing sites of the urinary bladder.

Objective: To use single-photon emission computed tomography (SPECT) combined with computed tomography (CT) plus intraoperative gamma probe verification to map the primary lymphatic landing sites of the bladder.

Design, Setting, and Participants: Clinical trial of 60 consecutive cystectomy patients at a single centre.

Intervention: Flexible cystoscopy-guided injection of technetium nanocolloid into one of six non-tumour-bearing sites of the bladder for preoperative detection of radioactive lymph nodes (LNs) with SPECT/CT followed by intraoperative verification with a gamma probe. Backup extended pelvic LN dissection (PLND) for ex vivo detection of missed LNs.

Measurements: Three-dimensional projection of each LN site.

Results and Limitations: A median of 4 (range: 1-14) radioactive LNs were detected per site and patient. Ninety-two percent of all LNs were found distal and caudal to where the ureter crosses the common iliac arteries. Eight percent were found proximal to the uretero-iliac crossing, none without simultaneous detection of additional radioactive LNs within the endopelvic region. Extended PLND resected 92% of all primary lymphatic landing sites; limited PLND resected only 52%. A few LNs may have been missed despite preoperative SPECT/CT, intraoperative gamma probe verification, and extended backup PLND.

Conclusions: Multimodality SPECT/CT plus intraoperative gamma probe show the template of the bladder's primary lymphatic landing sites to be larger than is often thought. PLND limited to the ventral portion of the external iliac vessels and obturator fossa removes only about 50% of all primary lymphatic landing sites, whereas extended PLND along the major pelvic vessels, including the internal iliac, external iliac, obturator, and common iliac region up to the uretero-iliac crossing, removes about 90%.

Editorial Comment

The authors of this very interesting study try to answer the question on the extent of lymphadenectomy in bladder cancer surgery on a scientific base. They detect the lymph node landing site of radioactive material injected into several areas of the bladder. Their conclusion is scientifically and clinically sound. As only 8% of “positive” lymph nodes were found cephalad of the uretero-iliac junction, and none of these was without a positive node in the caudal locations very, it is justified to limit the lymphadenectomy to the level where the retracted ureters cross the common iliac vessels. Still, the area to be explored is not “limited” and includes all tissue up to, on, and behind the external and internal iliac vessels and anterior to the presacral space. This paper is recommended reading for all urologic surgeons dealing with invasive bladder cancer.

Dr. Andreas Bohle

Professor of Urology

HELIOS Agnes Karll Hospital

Bad Schwartau, Germany

E-mail: boehle@urologie-bad-schwartau.de

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Transurethral resection of non-muscle-invasive bladder transitional cell cancers with or without 5-aminolevulinic acid under visible and fluorescent light: results of a prospective, randomised, multicentre study

Schumacher MC, Holmäng S, Davidsson T, Friedrich B, Pedersen J, Wiklund NP

Department of Molecular Medicine and Surgery, Karolinska Institutet, Department of Urology, Stockholm, Sweden

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Background: Fluorescent light (FL)-guided cystoscopy induced by 5-aminolevulinic acid (5-ALA) has been reported to detect more tumours compared with standard white-light (WL) cystoscopy. Most reports are from single centres with relatively few patients.

Objective: To evaluate whether 5-ALA-induced FL and WL cystoscopy at transurethral resection (TUR) is superior compared with standard procedures under WL only with respect to tumour recurrence and progression in patients with non-muscle-invasive bladder cancer.

Design, Setting, and Participants: This randomised, multicentre, observer- and pathologist-blinded, prospective phase 3 clinical trial enrolled 300 patients, and of those patients, 153 were randomised to FL cystoscopy and 147 were randomised to standard WL cystoscopy.

Intervention: All patients were first inspected under WL and all lesions were recorded. Patients randomised to FL underwent a second inspection. TUR was carried out in both groups.

Measurements: Control cystoscopy under WL was performed in all patients every 3 mo during the first year after randomisation and biannually thereafter.

Results and Limitations: At the first TUR, the mean number of resection specimens per patient was 2.5 (FL: 2.5; WL: 2.4; $p=0.37$) and the resulting mean number of resected tumours was 1.7 with FL and 1.8 with WL ($p=0.85$). More patients were diagnosed with carcinoma in situ (CIS) in the WL group (13%) than in the FL group (4.2%). Within-patient comparison of FL patients only showed that FL detected more lesions than WL. Tumour lesions solely detected by FL cystoscopy that would not otherwise be detected by WL cystoscopy included 52% dysplasia, 33% CIS, 18% papillary neoplasms, 13% pT1, and 7% pTa. Outcome at 12 mo did not show any difference between groups with regard to recurrence-free and progression-free survival rates.

Conclusions: In this prospective, randomised, multi-institutional study, we found no clinical advantage of FL cystoscopy compared with WL cystoscopy and TUR.

Editorial Comment

This paper put some water into the wine of fluorescence-based cystoscopy and resection (TUR). 300 patients from 5 institutions were randomized and the outcome was compared in terms of resected material and, importantly, in terms of clinical outcome after 12 months. In short, no meaningful differences were detected between both groups and the clinical outcomes were similar. The authors argue that the more “positive” results of other groups in favour of fluorescence-based cystoscopy might be due to the monocentric approach of these groups. In conclusion, there is still the need for more objective analyses such as this one before fluorescence-based cystoscopy or TUR can be regarded as standard in urology.

Dr. Andreas Bohle
Professor of Urology
HELIOS Agnes Karll Hospital
Bad Schwartau, Germany
E-mail: boehle@urologie-bad-schwartau.de

NEUROLOGY & FEMALE UROLOGY

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Effect of amitriptyline on symptoms in treatment naïve patients with interstitial cystitis/painful bladder syndrome

Foster HE Jr, Hanno PM, Nickel JC, Payne CK, Mayer RD, Burks DA, Yang CC, Chai TC, Kreder KJ, Peters KM, Lukacz ES, FitzGerald MP, Cen L, Landis JR, Propert KJ, Yang W, Kusek JW, Nyberg LM; Interstitial Cystitis Collaborative Research Network

Department of Surgery, Section of Urology, Yale University, New Haven, Connecticut, USA

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Purpose: Amitriptyline is frequently used to treat patients with interstitial cystitis/painful bladder syndrome. The evidence to support this practice is derived mainly from a small, single site clinical trial and case reports.

Materials and Methods: We conducted a multicenter, randomized, double-blind, placebo controlled clinical trial of amitriptyline in subjects with interstitial cystitis/painful bladder syndrome who were naïve to therapy. Study participants in both treatment arms received a standardized education and behavioral modification program. The drug dose was increased during a 6-week period from 10 up to 75 mg once daily. The primary outcome was a patient reported global response assessment of symptom improvement evaluated after 12 weeks of treatment.

Results: A total of 271 subjects were randomized and 231 (85%) provided a global response assessment at 12 weeks of followup. Study participants were primarily women (83%) and white (74%), with a median age of 38 years. In an intent to treat analysis (271) the rate of response of subjects reporting moderate or marked improvement from baseline in the amitriptyline and placebo groups was 55% and 45%, respectively ($p = 0.12$). Of the subgroup of subjects (207) who achieved a drug dose of at least 50 mg, a significantly higher response rate was observed in the amitriptyline group (66%) compared to placebo (47%) ($p = 0.01$).

Conclusions: When all randomized subjects were considered, amitriptyline plus an education and behavioral

modification program did not significantly improve symptoms in treatment naïve patients with interstitial cystitis/painful bladder syndrome. However, amitriptyline may be beneficial in persons who can achieve a daily dose of 50 mg or greater, although this subgroup comparison was not specified in advance.

Editorial Comment

The authors review the efficacy of amitriptyline therapy on patients with interstitial cystitis/painful bladder syndrome. All patients treated in this study were naïve to therapy and once enrolled had dose escalation over a six week period up to 75mg per day. All patients while receiving medicine were synchronously enrolled in a behavioral modification program. If the patients withdrew from the study for any reason they were categorized as failures in the post study analysis.

When viewing the study population as a whole, the authors found that there was no significant improvement with the use of amitriptyline plus the behavior modification program over placebo. However, the segment of the group treated with dose escalation to a dose of more than 50 mg of amitriptyline per day had a better than placebo response.

Though these patients faced the onerous symptoms of interstitial cystitis, out of the over 2000 patients contacted, a significant number who passed their screening declined to participate because either they were not interested or had synchronous medical conditions. In addition, those patients in the study who took the placebo still recorded significant adverse events including 31% with constitutional symptoms of fatigue and malaise, 21% having neurologic adverse events consisting of dizziness or somnolence and in approximately one-third pain (primarily headache). That the placebo response was robust at 40% speaks as much as to placebo effect as for the potential efficacy of education and behavioral modification programs in this patient population. This article provides the reader with a clear understanding of the dosage efficacy of amitriptyline for the use of interstitial cystitis if one selects that medication therapy. In addition, the article makes a clear argument for the combination of behavioral modification and education to medical therapy for this patient population.

Dr. Steven P. Petrou

*Professor of Urology, Associate Dean
Mayo School of Graduate Medical Education
Jacksonville, Florida, USA
E-mail: petrou.steven@mayo.edu*

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Cost analysis of interventions for antimuscarinic refractory patients with overactive bladder

Watanabe JH, Campbell JD, Ravelo A, Chancellor MB, Kowalski J, Sullivan SD

Pharmaceutical Outcomes Research and Policy Program, University of Washington, Seattle, Washington

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Objectives: To estimate average, initial, and cumulative procedure related costs from a US payer perspective extending up to 3 years for the overactive bladder (OAB) interventions: sacral neuromodulation (SNM), intra-detrusor botulinum toxin A (BoNTA), and augmentation cystoplasty (AC) for antimuscarinic refractory patients.

Methods: Costs (2007 US dollars) were calculated using Current Procedural Terminology (CPT) codes, Ambulatory Payment Classification (APC) codes; Diagnosis Related Group (DRG) payments, and Healthcare Common Procedure Coding System (HCPCS) Level II Codes extracted from the literature and from the SNM device manufacturer. CPT codes were converted to costs using the Center for Medicare and Medicaid Services

(CMS) Relative Value Unit (RVU) fee schedule. Sensitivity analyses were performed to evaluate assumptions and uncertainty of results based on plausible variation in estimates of key cost drivers.

Results: The initial treatment cost was \$22,226, \$1,313, and \$10,252 for SNM, intra-detrusor injection of BoNTA, and AC respectively. The first-year cost was \$23,614, \$2626, and \$11,637 respectively. Three years after initiating treatment, the cumulative cost was \$26,269, \$7651, and \$14,337 respectively. Sensitivity analyses revealed that SNM persisted as the most costly intervention in all scenarios. The 3-year cumulative cost range produced by the sensitivity analyses for SNM, BoNTA, and AC was \$25,384-\$27,357, \$4586-\$11,476, and \$12,315-\$16,830, respectively.

Conclusions: All estimates of cost endpoints for SNM were greater than those for BoNTA and AC. These cost estimates, when combined with data on outcomes and risks, are important components of a robust health care technology assessment of antimuscarinic treatment failure options.

Editorial Comment

This article examines the cost of treating one of the most difficult populations with voiding dysfunction, those patients who have failed standard antimuscarinic medical therapy. The authors reviewed three of the most common treatments for this population: sacral neuromodulation, augmentation enterocystoplasty, and intra-detrusor botulinum toxin injections. The cost for the three year therapy was projected and compared among the three therapies.

One of the main challenges of the paper was the cost analysis for projecting the potential cost of botulinum toxin injections in view of its' non-FDA approved status. Regardless, the article makes an illuminating comment regarding the cost of sacral neuromodulation in comparison with the two other therapies. The summary cost of augmentation enterocystoplasty may be somewhat conservative in its estimation in view that the cost of lifelong self-catheterization may not be clearly accounted. Many surgeons who perform this operation understand that a significant segment of those patients treated will need to practice lifelong self intermittent catheterization secondary to their reconstruction. This is currently no small social cost in the United States in view that the self-catheterization is now supported by the government paying for one-time use disposable catheters. The manuscript has a very illustrative graph with projected costs over a time span. It will be interesting to note at what point the projected cost of botulinum toxin-A injections surpasses augmentation enterocystoplasty in overall cost in view of the steeper slope of the botulinum toxin injection line. In addition, the cost of botulinum toxin injections may vary in time with the potential addition of new manufacturers. Regardless, the utility and decreased comparative expense of botulinum toxin injections for this population should surely impress and excite the reader.

Dr. Steven P. Petrou

*Professor of Urology, Associate Dean
Mayo School of Graduate Medical Education
Jacksonville, Florida, USA
E-mail: petrou.steven@mayo.edu*

PEDIATRIC UROLOGY

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Urinomas protect renal function in posterior urethral valves--a population based study

Wells JM, Mukerji S, Chandran H, Parashar K, McCarthy L

Department of Paediatric Urology, Birmingham Children's Hospital, UK.

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Background/Purpose: Urinomas have been thought to protect renal function in boys with posterior urethral valves (PUVs), although recent reports have disputed this. This study tested the hypothesis that urinomas protect global renal function in boys with PUV.

Methods: A retrospective analysis of all boys with PUV presenting to a tertiary unit derived from a region with an estimated population of 5.5 million was performed. Comparisons of the initial nadir creatinine, current creatinine, and renal status score (RSS) were made between those with and without urinomas. The RSS was derived from nephrology assessment of current renal status (0 = normal to 4 = end-stage renal failure or transplantation). Results were given as median (range), except for RSS, which was given as mean +/- SEM. $P < \text{or} = .05$ was regarded as significant.

Results: During 1989-2009, 9 of 89 PUV boys were diagnosed with urinomas. Initial nadir creatinine was statistically lower in boys with urinomas (31 [18-44] vs 45 [20-574] $\mu\text{mol/L}$, $P < .01$). Length of follow-up was similar (5.1 [2.2-17.3] vs 5.9 [1.8-19.7] years, $P = .59$). Follow-up creatinine was significantly lower in urinoma boys (44 [25-77] vs 61 [29-1227] $\mu\text{mol/L}$, $P < .05$), as was the RSS (0.14 +/- 0.14 vs 0.91 +/- 0.14, $P < .01$). No urinoma boys progressed to end-stage renal failure or required transplant.

Conclusion: This population-based study of PUV boys demonstrates that urinomas reduce nadir creatinine and significantly protect long-term global renal function.

Editorial Comment

The authors reviewed their data on all patients presenting with posterior urethral valves in infancy to their tertiary care center over 20 years. They identified 89 patients, 9 of whom were diagnosed with urinomas. Long term follow-up (mean of 5 years) in 7 of these patients showed that both initial nadir creatinine and follow-up creatinine were significantly lower in boys with urinomas. Renal status score was also significantly better in these boys and none has progressed to end stage renal failure or transplantation. Two of the 9 patients did not have long term follow-up due to their young age.

Spontaneous decompression of the urinary tract in patients with posterior urethral valves has typically been thought to have a protective effect. As the authors point out, this notion has been challenged in the last decade. In response, this population based study is less likely to be tainted by selection bias seen in other reports and supports the hypothesis that decompression has a protective effect on renal function. Unfortunately, this hypothesis has not been uniformly supported by the use of vesicoamniotic shunting in the antenatal period. Perhaps this suggests that there are other factors which create a greater likelihood of spontaneous perforation that serve to protect long term renal function.

M. Chad Wallis
Division of Pediatric Urology
University of Utah
Salt Lake City, Utah, USA
E-mail: chad.wallis@hsc.utah.edu

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Predictive factors for acute renal cortical scintigraphic lesion and ultimate scar formation in children with first febrile urinary tract infection

Oh MM, Cheon J, Kang SH, Park HS, Lee JG, Moon du G

Department of Urology, Korea University Medical Center, Seoul, Korea

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Purpose: We assessed predictive factors for acute renal cortical scintigraphic lesion and ultimate scar formation in children with a first febrile urinary tract infection.

Materials and Methods: A total of 89 girls and 138 boys with a first febrile urinary tract infection were included in the study. We analyzed radiological (ultrasound, dimercapto-succinic acid scintigraphy, voiding cystourethrogram), clinical (age, gender, peak fever, therapeutic delay time) and laboratory (complete blood count with differential count, absolute neutrophil count, blood urea nitrogen, creatinine, urinalysis, Gram's stain, culture, C-reactive protein, erythrocyte sedimentation rate) variables. Dimercapto-succinic acid scintigraphy was performed within 5 days and at 6 months after diagnosis of urinary tract infection. Voiding cystourethrogram was performed after the acute phase of the urinary tract infection. Predictive factors for acute scintigraphic lesion and ultimate scar formation were assessed using logistic regression analysis.

Results: Of 227 patients enrolled 140 had a refluxing and 87 a nonrefluxing urinary tract infection. On logistic regression analysis therapeutic delay time ($p = 0.001$) and presence of reflux ($p = 0.011$) were predictive of acute scintigraphic lesion and ultimate scar formation ($p = 0.001$ and $p = 0.0001$, respectively) in children with a first febrile urinary tract infection.

Conclusions: Since vesicoureteral reflux is the common risk factor for acute scintigraphic lesion and ultimate scar formation, voiding cystourethrogram must be considered as an initial study in patients with acute febrile urinary tract infection.

Editorial Comment

This study examined 227 young children (mean age 9 months) who were hospitalized with their first febrile urinary tract infection. The authors were able to obtain a DMSA renal scan within 1 week of presentation and a subsequent scan at 5 to 7 months on all patients in the study. They also obtained laboratory values at the time of admission and reviewed VCUGs on all patients to determine reflux status. Multivariate logistic regression analysis demonstrated that both the presence of reflux and increased therapeutic delay time were predictive of an acute photon defect on the initial DMSA scan. They were also predictive of ultimate scar formation on follow-up DMSA scans, but the odds ratio was much higher for children with reflux (10.1 vs. 2.4).

The patients in this study were a select population in that they were all young patients and all required hospitalization for their first urinary tract infection. The authors did a nice job getting a complete set of data on their entire study population, which is often a difficult task. The role of imaging studies after urinary tract infections has been challenged in recent years and this study reminds us that reflux status remains a significant risk factor for renal scarring, particularly in this young patient population.

M. Chad Wallis
Division of Pediatric Urology
University of Utah
Salt Lake City, Utah, USA
E-mail: chad.wallis@hsc.utah.edu