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## **UROLOGICAL SURVEY**

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#### **STONE DISEASE**

## Long-Term Outcome of Endopyelotomy for the Treatment of Ureteropelvic Junction Obstruction: How Long Should Patients be Followed Up?

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Purpose: To evaluate the long-term success rate of endopyelotomy for the treatment of ureteropelvic junction (UPJ) obstruction.

Patients and Methods: Between January 1995 and December 2003, 85 endopyelotomies (10 percutaneous, 75 retrograde) were performed in 77 patients with a mean age of  $35.2 \pm 13.9$  years. The mean number of procedures per patient was 1.14, with 69 patients undergoing a single procedure. Endopyelotomies were performed using either a cold knife (N = 26), Ho:YAG laser (N = 47), or hook electrode (N = 12). Treatment success was defined as symptomatic relief with radiographic resolution or stabilization of renal function, as judged by an excretory urogram or diuretic renogram. Kaplan-Meier analysis was used to determine the long-term probability of success. Results: With a median follow-up of 37.3 months (range 3-98 months), the overall success rate was 67.5%, and the median time to failure was 7.7 months (range 1-50 months). Kaplan-Meier estimates of success were 87.8% at 6 months, 76.9% at 12 months, 72.2% at 18 months, 68.7% at 24 months, 64.8% at 36 months, and 61.6% at 60 months. The success rate was not significantly affected by the etiology, surgical approach, or incisional method. Similarly, the degree of preoperative hydronephrosis or renal function did not affect the success rate. Conclusions: The success rate of endopyelotomy decreases as the follow-up increases. Although most failures were detected within 1 year of the procedure, it appears that follow-up of at least 36 months is required for patients who have undergone endopyelotomy for UPJ obstruction.

#### **Editorial Comment**

This study lacks standardization in surgical technique. As the cutting modality and size and duration of stenting varied, it is difficult to make recommendations regarding best surgical practices. Yet this study does address a question that has eluded us to date. How long should endopyelotomies be followed?

While the median time to failure was 8 months, only 7% of patients failed beyond 2 years. This suggests that one could focus postoperative imaging during the period when failure is most likely to occur. However, the authors do not report the presentation of the 7% of patients who failed beyond 2 years – were they symptomatic or silent obstruction? Answering this question is critical if one wishes to eliminate radiographic follow-up at 2 years postoperative.

The authors report that the degree of hydronephrosis and preoperative renal function did not predict success with endopyelotomy. Indeed, the authors report a 60% success rate in kidneys with less than 25% function. This is in sharp contrast to the body of evidence that supports the use of these two variables in patient selection for endopyelotomy.

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## Impact of Shockwave Coupling on Efficacy of Extracorporeal Shockwave Lithotripsy

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Purpose: To evaluate the impact of a slow gated treatment rate on the efficacy of extracorporeal shockwave lithotripsy (SWL).

Patients and Methods: From August 1990 to July 2002, 40,462 SWL procedures were performed using the slow frequency electrocardiography (ECG)-gated lithotripter (82.5%) and fast frequency ECG-ungated (17.5%) modes for the Medstone STS lithotripter. Treatment characteristics, including the mode of SWL, location and size of the stone, re-treatment status, auxiliary procedures required, perioperative complications, and treatment outcomes, were recorded. The stone-free rate was reported by the treating physician on the basis of the finding of no residual stone fragments on a plain radiographic image.

Results: The treatment rate for the slow mode was a mean of 79.6 shocks/min, while the rate for the fast mode was 120/min. The total procedure time was 47.0 minutes for the slow mode and 40.6 minutes for the fast. The overall stone-free rate was higher for slow (66.9%) than fast (63.6%) procedures (P < 0.001). The stone-free rate for 1- to 10-mm stones was higher for the slow procedures (75.7%) than the fast procedures (70.7%; P < 0.001). Upper-ureteral stones responded better to slow treatment in terms of stone-free rate (79.5% v 72.6%; P < 0.001), re-treatment rate (6.5% v 8.0%, P = 0.05), auxiliary-procedure rate (6.1% v 8.9%; P = 0.01), and efficiency quotient (71 and 62). There was no significant difference in complication rates overall between slow and fast treatment. Conclusions: With a minimal increase in procedure time, greater efficacy can be obtained for the treatment of radiopaque stones with a slower shock-delivery rate. In particular, upper-ureteral calculi and calculi <10 mm benefit from a slower treatment rate.

#### **Editorial Comment**

Treating at a gated setting has been demonstrated to decrease the risk of cardiac dysrhythmias from 20% to 0.3% (Reference 15 in the article). In vitro and clinical trials have demonstrated that stone fragmentation and stone-free rates are superior with a slower (60 shocks/min) versus faster (120 shocks/min). This study suggests that a practical approach to slower treatments is to revert back to gating shockwave to the cardiac rhythm – thereby improving stone-free rates while preventing cardiac morbidity. Stones greater than 3 cm in size and distal ureteral stones did not benefit from a slower treatment protocol – as such, these stones are better suited for an endoscopic procedure.

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## ENDOUROLOGY & LAPAROSCOPY

**Reoperative Laparoscopic Pyeloplasty in Children: Comparison with Open Surgery** Piaggio LA, Noh PH, Gonzalez R.

Department of Surgery, Division of Urology, A. I. duPont Hospital for Children, Wilmington, Delaware, and Department of Urology, Thomas Jefferson University, Philadelphia, Pennsylvania J Urol. 2007; 177: 1878-82

Purpose: We assessed the feasibility of pediatric redo laparoscopic pyeloplasty in comparison to redo open pyeloplasty for safety, efficacy, operative time, blood loss, postoperative analgesic requirements, length of hospitalization, complications, need for readmission and subsequent procedures.

Materials and Methods: We performed a retrospective chart review of consecutive patients undergoing reoperative pyeloplasty between June 2003 and July 2006.

Results: A total of 10 patients (11 redo pyeloplasties) were divided into 2 groups, ie those undergoing redo open (4) and laparoscopic (6) pyeloplasty. Groups were similar in age, sex, weight, laterality, and number and type of prior interventions to repair ureteropelvic junction obstruction. Surgical time for redo laparoscopic pyeloplasty was longer than for redo open pyeloplasty (290 vs 203 minutes, p <0.05). Success rate was the same in both groups (80%). The redo laparoscopic pyeloplasty group had a shorter hospital stay (mean 2.5 vs 4.6 days, p <0.05), decreased use of parenteral narcotics (0.2 vs 5 mg/kg, p <0.01), and a trend toward decreased oral narcotics (0.2 vs 2.1 mg/kg, p = 0.09) and fewer complications (0 vs 4, p <0.05).

Conclusions: We confirm the feasibility of redo laparoscopic pyeloplasty in the pediatric population. In experienced hands pediatric redo laparoscopic pyeloplasty can be performed safely with a success rate similar to that of open surgery, and it may provide a faster recovery with decreased narcotic requirements and morbidity. Further studies are needed to better define the role of laparoscopic pyeloplasty for secondary ureteropelvic junction obstruction in the pediatric population.

## **Editorial Comment**

Historically, laparoscopy in pediatric urology was very controversial. It raised several questions about feasibility, safety and outcome. Time demonstrated that even in complex cases such as, the redo pyeloplasties, the laparoscopic approach maybe performed offering faster recovery time, decreased hospitalization and morbidity, as well as, less use of narcotics compared to the open approach.

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## Laparoscopic Extraperitoneal Radical Prostatectomy in Complex Surgical Cases

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Purpose: Patients with a high body mass index, previous pelvic surgery or large prostate size are not considered ideal candidates for radical prostatectomy. We assessed the impact of body mass index, previous pelvic surgery and prostate weight on perioperative and pathological outcomes in patients treated exclusively with laparoscopic extraperitoneal radical prostatectomy.

Materials and Methods: From January 2004 to May 2005, 300 patients underwent laparoscopic extraperitoneal radical prostatectomy. Patients were divided into groups, including body mass index groups 1 (25 kg/m(2) or less), 2 (25.1 to 30), 3 (30.1 to 36) and 4 (greater than 36); prostate weight groups 1 (20 gm or less), 2 (20.1 to 40), 3 (40.1 to 60) and 4 (more than 60); and prior surgery groups 1 (no previous pelvic or prostatic surgery) and 2 (previous pelvic or prostatic surgery).

Results: Logistic regression demonstrated that body mass index, large prostate size and previous pelvic surgery did not affect margin status. The Kruskal-Wallis test was performed to analyze if body mass index, large prostate size and previous pelvic surgery had an effect on perioperative variables. Only prostate weight correlated with a delay in Foley catheter removal (3 days, p = 0.0005). The Wilcoxon rank sum test showed that patients with a higher body mass index had a slightly prolonged hospital stay (16 hours, p = 0.02). Patients with a prostate of more than 40 gm had slightly increased blood loss (56 cc, p = 0.03), which did not affect the transfusion rate.

Conclusions: Laparoscopic extraperitoneal radical prostatectomy can be performed in complex surgical cases without increased perioperative morbidity. Obese patients and those with a large prostate who prefer surgery as a treatment option for localized prostate cancer may benefit from the advantages that laparoscopic extraperitoneal radical prostatectomy offers.

#### **Editorial Comment**

The new era of minimally invasive surgery demonstrates the feasibility of laparoscopic retropubic radical prostatectomy in patients with high body mass index, previous pelvic surgery or large prostate size. In general surgery laparoscopic procedures are highly encouraged for patients that are more complex due to better outcomes compared to open surgery. In urology, we are still taken "baby steps" demonstrating slowly the advances in minimally invasive surgery. The authors should be congratulated for the elegant manuscript demonstrating the feasibility and good outcome of laparoscopic surgery in complex surgical patients.

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## IMAGING\_

# Diagnostic Yield of 58 Consecutive Imaging-Guided Biopsies of Solid Renal Masses: Should We Biopsy All That Are Indeterminate?

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Objective: The purpose of our study was to report the diagnostic yield of 58 consecutive imaging-guided biopsies of solid renal masses.

Materials and Methods: We retrospectively reviewed all percutaneous renal biopsies of solid masses performed at our institution over 83 consecutive months from May 1998 to March 2005 through a query of our radiology department procedure database. Fifty-five CT and three sonographic biopsies were performed at our institution during this time. A solid renal mass was documented prior to biopsy by contrast-enhanced CT (n = 48), gadolinium-enhanced MRI (n = 6), or sonography (solid noncystic masses, n = 4). The average maximal mass diameter was 3.1 cm (range, 1.0-11.0 cm). Forty-seven (81%) of the 58 biopsies were performed

immediately before percutaneous ablation. Forty-four (76%) of the biopsies were performed using a coaxial technique with side-cutting automated biopsy needles (16-20 gauge), and 14 (24%) were fineneedle aspirations with a Franseen needle (20 gauge) using a tandem technique. In 19 cases, immunohistochemistry or histochemistry (Hale colloidal iron stain) was used to establish or confirm the diagnosis. Medical records and radiology and pathology reports were reviewed for all patients.

Results: An adequate sample size was obtained in 55 (95%) of 58 renal masses and led to a definitive diagnosis in 52 (90%) of the 58. Renal cell carcinoma accounted for 36 (69%) of 52 diagnostic biopsies. The diagnosis of a benign lesion was made in 14 (27%) of 52 biopsies. Lymphoma (1/58) and metastatic disease (1/58) accounted for the remaining two diagnostic biopsies. Three biopsy samples obtained inadequate sample volumes, and an additional three samples were thought to have adequate sample volume but were not diagnostic. A single false-negative biopsy result was identified after growth was seen on follow-up imaging and subsequent nephrectomy revealed renal cell carcinoma.

Conclusion: Imaging-guided biopsy of a solid enhancing renal mass was diagnostic in 52 (90%) of 58 consecutive biopsies. The diagnosis of a benign lesion was made in 27% of diagnostic biopsies. Because of the advances in biopsy and histology techniques, the role of imaging-guided biopsy should be reconsidered.

#### **Editorial Comment**

Nowadays percutaneous renal mass biopsy is indicated more frequently due to several reasons: a) increased incidental detection of malignant and benign renal masses; b) improvement on cytologic and immunohistochemistry techniques and c) the increasing role of percutaneous renal ablation. The overall sensitivity of biopsy for diagnosis for malignancy is high ranging from 80%-92%. Classically renal biopsy is indicated in patients with renal mass and primary extrarenal tumor (to exclude or confirm metastases); to confirm the radiologic findings of an unresectable renal cancer; in patients with pulmonary or cardiac comorbidity and in patients with possible primary manifestation of lymphoma in the kidneys (1). Emerging indications for renal biopsy are: presence of multiple/bilateral solid renal masses without history of cancer; prior to renal mass ablation and in patients with small (< 3 cm) solid, hyperattenuating, homogeneously enhancing renal mass. These small lesions are indistinct and may be oncocitoma, angiomyolipoma without macroscopic fat (5% of AMLs) or more rarely a papillary renal cell carcinoma. As we know, modern diagnostic imaging techniques, allows the correct diagnosis of the majority of renal mass. There is no prospective study showing the incidence of incidentally detected benign renal mass among the lesions presumably considered renal cancer. Recent studies, however, done in patients who underwent radical nephrectomy or imagingguided tumor ablation presumably for renal cell carcinoma detected 12.8% to 37% of benign renal lesions. The authors of this study, found benignity in 27% of 58 small solid renal lesions. It would be interesting to know, how many of these lesions were part of that small group of hyperattenuating, homogeneously enhancing renal mass.

As pointed out by the authors one important limitation of this study is that 81% of their biopsies were performed before percutaneous ablation. As we know the ideal evaluation of the biopsy specimens is made by histologic ,cytologic and immunohistochemistry evaluation. Biopsy specimens analyzed as frozen sections and hematoxylin-eosin staining, usually done prior ablation, is rapid but usually incomplete. For this reason, to establish a definitive diagnosis immunohistochemical staining was necessary, in 17 (89%) of 19 nondiagnostic samples using hematoxylin-eosin staining. This is very important information of this publication. Biopsy results are crucial in some situations where the urologist has to decide whether the lesion should be removed or clinically followed. We agree with the authors conclusion that there is a definite role for imaging-guided biopsy of small solid renal masses before intervention, particularly those hyperattenuating and homogeneous. In our opinion when surgery is contemplated, and biopsy is not performed, enucleation or partial nephrectomy should be the primary indication in this small group of lesions.

#### Reference

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## Diagnosis of Prostate Cancer in Patients with an Elevated Prostate-Specific Antigen Level: Role of Endorectal MRI and MR Spectroscopic Imaging

Costouros NG, Coakley FV, Westphalen AC, Qayyum A, Yeh BM, Joe BN, Kurhanewicz J *Department of Radiology, University of California, San Francisco, San Francisco, CA, USA* AJR Am J Roentgenol. 2007; 188: 812-6

Objective: The objective of our study was to determine the accuracy of endorectal MRI and MR spectroscopic imaging (MRSI) in the diagnosis of prostate cancer in patients with an elevated serum prostate-specific antigen (PSA) level.

Materials and Methods: We retrospectively identified 40 patients with an elevated serum PSA level and without a histologic diagnosis of prostate cancer who underwent endorectal MRI and MRSI at our institution. On the basis of MRI findings alone and then combined MRI and MRSI findings, a single experienced observer rated the presence or absence of prostate cancer in each side of the prostate on a 5-point scale (1 = definitely absent, 5 = definitely present). Areas under the receiver operating characteristic (ROC) curve were calculated using the hemiprostate as the unit of analysis. The presence or absence of cancer on subsequent endorectal sonographically guided sextant biopsy was used as the standard of reference.

Results: Biopsy revealed no cancer in 24 patients, bilateral cancer in 11, and unilateral cancer in five. The areas under the ROC curve for the diagnosis of prostate cancer by hemigland was 0.70 for MRI alone and 0.63 for combined MRI and MRSI (no significant difference, p = 0.32).

Conclusion: Endorectal MRI and MRSI are reasonably accurate for the diagnosis of prostate cancer in patients with an elevated serum PSA level, but the remaining limitations suggest that MRI and MRSI should be used as a supplement rather than a replacement for biopsy using the current technology and diagnostic criteria.

#### **Editorial Comment**

The authors present a retrospective study to determine if conventional and 3D-spectroscopic endorectal magnetic resonance imaging (3D-MRSI) techniques are accurate for the diagnosis of prostate cancer in patients with an elevated PSA. They had a 63% accuracy using conventional MRI and 3D-MRSI. Previous study on this subject has demonstrated an accuracy ranging from 67% to 79% (1). One important limitation of this study is related to the fact that the cancer was determined to be present or absent in each hemiprostate on the basis of the presence or absence of an ipsilateral positive biopsy result, on a subsequent endorectal sonographically guided biopsy. These biopsies were performed within 2 years of MRI and MRSI. In other words, the standard sextant sonographically guided biopsy was performed without the knowledge of the results obtained with the MRI and 3D-MRSI are projected on the film containing the conventional axial T2 sequence, and external and internal prostate landmarks obtained from these images are used during transrectal ultrasound examination to adequate biopsy the areas containing the suspicious voxels. As we have already pointed out this process has

limitation since is not an easy task, but allows an accuracy of 67% in patients with grade 4 (possible cancer) and accuracy of 79% in patients presenting at least one voxel grade 5 (cancer is definite present).

Although the author's conclusion is that addition of MRSI to MRI alone does not significantly improve the diagnostic accuracy for prostate cancer detection they also concluded that MRI and MRSI might still serve as a useful supplement to endorectal sonographically guided biopsy on an individual basis. A repeat biopsy could target regions that show an abnormality on MRI and MRSI to help improve the diagnostic yield of endorectal sonographically guided biopsy, as we have previously shown.

#### Reference

1. Prando A, Kurhanewicz J, Borges AP, Oliveira EM Jr, Figueiredo E: Prostatic biopsy directed with endorectal MR spectroscopic imaging findings in patients with elevated prostate specific antigen levels and prior negative biopsy findings: early experience. Radiology. 2005; 236: 903-10.

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## UROGENITAL TRAUMA

## Nonoperative Management Outcomes of Isolated Urinary Extravasation Following Renal Lacerations Due To External Trauma

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J Urol. 2006; 176 (6 Pt 1): 2494-7

Purpose: Urinary extravasation is a common finding in grade 4 and 5 renal injuries. To date there has been little written about the natural course of urinary extravasation following renal trauma. We reviewed data on the outcomes of urinary extravasation in the traumatized kidney when managed nonoperatively.

Materials and Methods: A retrospective review of the prospectively entered urological trauma database from San Francisco General Hospital was performed from 1979 to 2005. All patients with urinary extravasation after sustaining traumatic injury to the kidney as seen on computerized tomography were included in analysis. Results: A total of 61 patients with urinary extravasation were identified. Of these patients 27 (44%) were treated operatively (26 of 27 underwent immediate and 1 of 27 underwent delayed open surgery). All (100%) operatively treated patients underwent renal exploration and repair at primary surgical management of associated abdominal and/or vascular injuries. Open surgical exploration resulted in nephrectomy in 5 of 27 (19%) patients. Of the 34 (56%) patients treated nonoperatively only 3 (9%) had persistent, nonprogressing urinary extravasation by computerized tomography 3 to 7 days after injury. All 3 (100%) of these patients underwent uncomplicated endoscopic ureteral stent placement followed by complete resolution of urinary extravasation.

Conclusions: Nonoperative management of urinary extravasation in patients sustaining traumatic injury to the kidney without associated abdominal or vascular injury is safe and results in resolution in more than 90%. In patients with persistent urinary leakage endoscopic ureteral stent placement may be needed and is successful.

#### **Editorial Comment**

This article by Alsikafi et al., reports on the experience from San Francisco General Hospital over a 26-year period. This article further illustrates that the paradigm of blunt renal trauma management is typically conservative and expectant. American Association for the Surgery of Trauma grade IV injuries with extravasation of contrast are merely relative indications for renal exploration. The only absolute indications for renal exploration are grade V injuries that are life threatening due to massive bleeding. All other types of kidney trauma have a relative indication. Further points illustrated are that the treatment algorithm of nonoperative management of urinary extravasation is bed rest till the urine clears, serial hematocrits, followed by repeat CT a couple of days after initial injury. Extravasation that is stable or worse (i.e. an expanding urinoma) warrants ureteral stenting for 4 to 6 weeks. Extravasation that improves on subsequent imaging should be followed. Overall, 90% of grade IV renal injuries without major associated vascular or abdominal injuries are managed successfully without intervention.

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## **Delayed Diagnosis of Traumatic Ureteral Injuries**

Kunkle DA, Kansas BT, Pathak A, Goldberg AJ, Mydlo JH Departments of Urology and Surgery, Temple University Hospital, Philadelphia, PA, USA J Urol. 2006 Dec; 176(6 Pt 1): 2503-7

Purpose: We review our experience with traumatic ureteral injuries missed at exploration. We also conduct meta-analysis to define factors contributing to missed injury, comparing outcomes of early vs late diagnosis. Materials and Methods: Our genitourinary trauma database was retrospectively reviewed from 1995 through 2004. A total of 40 ureteral injuries were identified including 5 with delayed diagnosis. Previously published series of ureteral trauma were then analyzed for injuries with delayed diagnosis, with data extracted and collated for meta-analysis.

Results: A total of 40 patients with traumatic ureteral injuries was identified, all of whom underwent laparotomy. Five (12.5%) injuries were discovered at a mean of 6.0 +/- 3.0 days after laparotomy. The number of associated injuries for early and delayed diagnosis was 3.2 and 2.6 (p = 0.25), respectively. Mean hospital stay was 19.2 vs 36.6 days (p = 0.18) for those with immediate vs delayed diagnosis, respectively. Only 2 of 5 (40%) patients achieved satisfactory results during initial hospitalization. Literature review revealed 48 missed ureteral injuries, representing 11.1% of all patients with ureteral injuries who underwent laparotomy. Rates of nephrectomy for early and late diagnosis were 2.4% and 18.4% (p = 0.0001). Mortality related to traumatic injuries occurred in 6.1% with early diagnosis and 13.2% with missed injuries (p = 0.089).

Conclusions: Despite preoperative studies and intraoperative inspection, ureteral injury may remain undiagnosed until after laparotomy. We report intraoperative exploration to have a sensitivity of 88.9% across multiple series for traumatic ureteral injuries. Delayed diagnosis of ureteral injuries produces an association with prolonged hospital stay, and meta-analysis reveals a statistically significant increase in the rate of nephrectomy when ureteral injury is missed at exploration.

#### **Editorial Comment**

Kunkle et al. report on their experience with missed ureteral injuries at a busy inner city trauma center. This is a well written and comprehensive paper on delayed diagnosis. Tables 3 and 4 are nice metanalyses demonstrating that roughly 11% of ureteral injuries are missed at laparotomy, resulting in an overall nephrectomy rate of 18% and death at 13%. Even in the busiest of trauma centers, external ureteral injuries are rare, typically with fewer then 10 injuries seen per year. In the literature, there are only a few series with a sizable experience, and they are all retrospective, cover long study periods (10-40 years), and are mostly treated by heterogeneous groups of physicians. Most external ureteral injuries occur from gunshot wounds. Missile path even in proximity to the ureter can cause significant delayed tissue destruction. Such injuries can be difficult to identify initially and often present in a delayed fashion. Penetrating ureteral injuries are almost always associated with multiple intra-abdominal organ injuries (such as, small bowel, colon, liver and iliac vessels. Associated injuries are often more obvious and overshadow the ureteral injury. Ureteral injuries from blunt trauma are equally rare. They usually occur in children during rapid deceleration, causing excessive hyperextension and disruption at the ureteropelvic junction. Such patients are usually poly-traumatized and have associated multiple organ injuries (mostly liver, spleen and skeletal system).

In the acute trauma setting, therefore, the diagnosis of ureteral injury can be difficult. When the ureteral injury is missed and not diagnosed till late or the primary repair fails, the complication rate increases considerably, including renal loss and even death.

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#### PATHOLOGY\_

## Are There Morphologic Correlates of Prostate Cancer Associated with TMPRSS2-ERG Molecular Abnormalities?

SW Fine, A Gopalan, M Leversha, SK Tickoo, HA Al-Ahmadie, S Olgac, W Gerald, VE Reuter *Memorial Sloan Kettering Cancer Center, New York, NY, USA* Mod Pathol. 2007; 20 (suppl 2): 146A

Background: Recent studies have shown that TMPRSS2-ERG fusion is common in prostate cancer, varying from 30-70% of cases in published series. The molecular abnormalities include formation of a fusion gene, in a majority of cases due to deletion of a region on chromosome 21. While the histologic features of these tumors have not been elucidated, it has been suggested that these molecular genetic events may be associated with distinct morphologic characteristics, such as cribriform architecture and the presence of blue mucin.

Design: Blinded histologic review was conducted on 67 cases comprising two tissue microarrays (TMA) on which fluorescent in situ hybridization (FISH) had previously been performed to delineate molecular abnormalities.

Results: By FISH, 37/67 cases showed molecular abnormalities, including 21 deletions, 5 translocations, and 11 cases with other abnormalities. The other 30 cases were negative on FISH analysis. 8/37 (16.7%) cases with and 9/30 (30%) cases without molecular abnormalities showed cribriform glands or glomerulations. Intralumi-

nal blue mucin was present in 15/37 (40.5%) cases with and 11/30 (36.7%) cases without genetic events. Overall, 19/30 (63.3%) cases without FISH abnormalities showed no specific morphologic features. Cribriform glands/ glomerulations were present in 8/17 cases with molecular changes and 9/17 FISH negative cases. Conclusions: In this analysis, we observe that TMPRSS2-ERG-related abnormalities do not correlate with specific tumor histology. Similarly, cribriform architecture is seen equally in cases with and without these genetic

events. These findings suggest a lack of association between FISH-detected molecular changes and these morphologic findings. Further studies in larger cohorts of tissue are in progress to confirm these observations.

#### **Editorial Comment**

The paper by Fine SW et al. from the Memorial Hospital (New York) is at odds with the paper by Mosquera MJ et al. from the Brigham and Women's Hospital (Boston). Fine SW et al. observed that TMPRSS2-ERG abnormalities did not correlate with any specific or peculiar feature of prostate adenocarcinoma. One of the reasons for the discrepancy between the two papers may be related to the sophisticated techniques used in cancer molecular cytogenetic analysis.

So far, the TMPRSS2-ERG fusion is detected by molecular cytogenetic analysis available only in research laboratories. Future efforts will be directed at characterizing the expressed protein products of this gene fusion which may be detected by immunohistochemistry. This latter technique is available to all routine laboratories of pathology.

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## **Morphological Features of TMPRSS2: ERG Fusion Prostate Cancer**

JM Mosquera, S Perner, F Demichelis, MD Hoffer, KD Mertz, P Paris, J Simko, C Collins, T Bismar, MA Rubin.

Brigham and Women's Hospital, Boston, MA; Harvard Medical School, Boston, MA; University of Ulm, Ulm, Germany; SRA Division Bioinformatics Group, Povo, Trento, Italy; University of California, San Francisco, CA; McGill University, Montreal, QC, Canada; MIT and Harvard Medical School, Cambridge, MA; Dana Farber Harvard Comprehensive Cancer Center, Boston, MA, USA Mod Pathol. 2007; 20 (suppl 2): 165A

Background: TMPRSS2:ETS fusion prostate cancers (PCA) comprise 40-50% of the PSA screened hospital based PCA examined to date making it the most common genetic rearrangement in human cancer. The most common variant involves TMPRSS2 and ERG. Emerging data from our group and others suggests that TMPRSS2:ERG PCA is associated with higher tumor stage and PCA specific death. The goal of this study was to determine if this common somatic alteration is associated with a morphologic phenotype.

Design: We assessed 253 PCA cases for TMPRSS2:ERG fusion status using FISH. Tumors were assessed for presence or absence of 8 morphologic features. The reviewers were blinded to the fusion status. Statistical analysis was performed to look for significant associations between morphologic features and TMPRSS2:ERG fusion status.

Results: Five morphologic features were associated with TMPRSS2:ERG PCA: blue-tinged mucin (85% of cases, n = 23/27), cribriform growth pattern (68%, n = 50/74), macronucleoli (78%, n = 39/50), intraductal tumor spread (88%, n = 38/43), and signet-ring cell-like features (82%, n = 9/11) all with p-values < 0.05. Only 24% (n = 30/125) of tumors without any of these features displayed the TMPRSS2:ERG fusion. In contrast, 55% (n = 38/69) of cases with one feature (RR = 3.88), 86% (n = 38/44) of cases with two features (RR = 20.06), and 93% (n = 14/15) of cases with three or more features (RR = 44.33) were fusion positive (p < 0.001). Conclusions: This is the first study to our knowledge that demonstrates a significant link between a molecular alteration in PCA and distinct phenotypic features. The strength of these findings is similar to BRCA-1/2 breast cancers and HNPCC colon cancer. The biologic effect of TMPRSS2:ERG overexpression may drive pathways that favor these common morphologic features that pathologists observe on a daily basis. These features should also be helpful in diagnosing TMPRSS2:ERG fusion PCA which may have both prognostic and therapeutic implications. Validation studies are underway.

#### **Editorial Comment**

A central aim in cancer research is to identify altered genes that play a causal role in cancer development. Possible rearrangements are of two general types. In the first, the promoter and/or enhancer elements of one gene are aberrantly juxtaposed to a proto-oncogene, thus causing altered expression of an oncogenic protein. In the second, the rearrangement fuses two genes, resulting in the production of a fusion protein that may have a new or altered activity. In 2005, Tomlins SA et al. (1) identified recurrent gene fusions of the region of TMPRSS2 to ERG or ETV1 in prostate cancer tissues. These fusions may have important implications for understanding prostate cancer tumorigenesis and developing novel diagnostics and targeted therapeutics.

TMPRSS2 (21q22.2) is a prostate-specific gene that is present in normal and neoplastic prostate tissue and is strongly induced by androgen in androgen-sensitive prostate cell lines. ERG (21q22.3) and ETV1 (7p21.2) are genes that encode ETS family transcription factors. TMPRSS2:ERG fusion is more frequent and occurs due to a deletion of a region on chromosome 21. TMPRSS2:ETS fusion prostate cancers comprise 40-50% of the PSA screened hospital based prostate carcinoma examined to date, making it the most common genetic rearrangement in human cancer. Emerging data suggest that TMPRSS2:ERG prostate cancer is associated with higher tumor stage and prostate specific death. Therefore, this fusion may be a marker for aggressive prostate cancer.

The aim of the study by Mosquera JM et al. was to find morphological features of TMPRSS2:ERG fusion prostate cancer that may indicate more aggressive tumors. The authors found that tumors with bluetinged mucin, cribriform growth pattern, macronucleoli, intraductal spread and signet-ring cell-like features were frequently associated with the fusion. When 3 or more features were combined, 93% of the cases presented TMPRSS2:ERG fusion.

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## INVESTIGATIVE UROLOGY \_

## Urethral Replacement Using Epidermal Cell-Seeded Tubular Acellular Bladder Collagen Matrix

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Objectives: To investigate the feasibility of replacing urinary epithelium cells with foreskin epidermal cells to reconstruct engineered anterior urethra with an acellular collagen matrix.

Materials and Methods: Acellular collagen matrices were generated from allogeneic rabbit bladder submucosa. In nine rabbits, autologous foreskin epidermal cells were isolated, expanded in vitro, and labelled with 5bromo2'-deoxy-uridine (BrdU) before seeding onto a tubular acellular collagen matrix (1.5 x 1 cm). In male rabbits, a urethral mucosal defect was created, and urethroplasty performed with a tubular acellular collagen matrix seeded with epidermal cells (nine rabbits) or with a matrix with no cell seeding (nine rabbits; control group). Urethrography was done at 1, 2 and 6 months after grafting. The urethral grafts were harvested and analysed grossly and histologically.

Results: In the control group, gross views and urethrography revealed stricture of repaired defects at the different sample times. In the experimental group, a wide urethral calibre was maintained with no sign of strictures. Histology in the control group showed a single layer of epithelium cells with disorganized muscle fibre bundles in the submucosa layer at 1 month after grafting, and a transitional cell layer surrounded by disorganized muscle fibre bundles at 2 and at 6 months. Grafts seeded with epidermal cells formed a single-layer structure by 1 month, and at 2 and 6 months there were several layers of epidermal cells with abundant vessels in the submucosa. There was an evident margin between graft epidermal cells and host epithelium at 6 months. The implanted cells expressed keratin, shown by staining with anti-pancytokeratins. Immunofluorescence for BrdU confirmed the presence of implanted epidermal cells at 1 month after grafting; there were fewer positive cells at the implantation site at 2 months, there were several layers of epidermal cells with no signs of BrdU staining.

Conclusions: Urethral reconstruction was better with an acellular collagen matrix seeded with epidermal cells than with the acellular collagen matrix alone. Foreskin epidermal cells seem adequate in replacing urethral epithelium cells for urethral reconstruction.

#### **Editorial Comment**

It has been demonstrated that tissue engineering techniques are useful for urethral reconstruction and acellular collagen matrices derived from donor bladder submucosa have been used both experimentally and clinically for onlay urethral replacement with good success (1). Other materials have been also used with varied successful results, both for urethral and bladder replacement (2,3).

In the present study, the authors examined the feasibility of using an epidermal cell-seeded or -unseeded scaffold for tubularized urethral replacement in a rabbit model. It was found that the acellular collagen matrix had a structure of loose collagen with no nucleoli, and proposed that it might be important for avoiding rejection. Histological analysis shown that the mucosal membrane of the graft is thin, and strictures were formed in the unseeded group, with many disorganized muscle fiber bundles around the urethral lumen. On the other hand, the study demonstrated that seeded implants had a thin epidermal cell layer at 1month, with normal multiple layers of epidermal cells at 2 and 6 months. Repeated urethrograms demonstrated that a wide urethral caliber was maintained with no sign of strictures.

The authors must be commended for such well-designed experimental work, which provides more evidence in animal models that acellular matrix might be suitable for urethral repair. Nevertheless, it is still uncertain whether larger defects can be corrected with such a matrix.

Although promised, tissue engineered for urethral substitution remains arguable, since buccal mucosa is easy to obtain and the buccal defect heals well. Also, the buccal mucosal grafts are tough, resilient, easy to harvest, and leave no scar as demonstrated recently (4,5). Also, these homologous grafts appear to be an optimal substitute even for anterior and posterior long urethral strictures in repeated urethroplasty (5).

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#### The Penile Suspensory Ligament: Abnormalities and Repair

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Objective: To assess men presenting with abnormalities of the penile suspensory ligament (PSL) and its correction. Patients and Methods: In all, 35 men presenting with abnormalities of the PSL that were subsequently repaired were included in this series. The causes included; sexual trauma (15 men), congenital absence of the PSL/ congenital penile curvature (14), and two each with venogenic erectile dysfunction, Peyronie's disease and penile dysmorphic disorder. The diagnosis was made clinically by the presence of a palpable gap between the symphysis pubis and the penis, together with medical history and examination of penile torsion or instability. The surgical repair used nonabsorbable sutures placed between the symphysis pubis and the tunica albuginea of the penis.

Results: A 'good' surgical outcome was defined as correction of the penile deformity or instability and achieving normal sexual function. There was a good surgical outcome in 91% of men as defined, and 86% of the men were happy with the outcome. There were no significant complications, but three men needed a repeat PSL repair.

Conclusion: Men with abnormalities of the PSL can present with a variety of clinical symptoms, but when correctly diagnosed the repair is a simple technique with a successful cosmetic and functional outcome.

#### **Editorial Comment**

This is a welcome original contribution dealing with a neglected and poor recognized urological pathology. Anatomists and urologists well recognized that penile suspensory ligament (PSL) is important because it supports

and maintains the erect penis in an upright position during sexual intercourse, and its defect would cause significant deformations hindering normal erections and intercourse (1). Since 1979, patients with defects in the suspensory ligament were recognized in the urological literature (2), including congenital etiology. Nevertheless, the authors of the present paper, in the best of my knowledge, described systematically by the first time the clinical history, physical findings and treatment of suspensory ligament abnormalities.

Here, I would like to highlight some points described by the authors in the article. The PSL has susceptibility to trauma following sexual intercourse, particularly with forced downwards pressure, leading to penile instability, deformity and a variable degree of erectile dysfunction (ED). Penile pain was the predominant symptom in 11 of the 15 patients who presented after sexual trauma, and ED was the presenting symptom in 13 of the 35 men. Other symptoms were penile instability and deformity. Concerning diagnosis, the authors showed that it is made clinically, characterized by the presence of a palpable gap between symphysis pubis and the penis. Nevertheless, this is not always present, and in this series only 15 of the 35 men had this sign; thus, the authors emphasize that a supportive history such as penile trauma or evidence of penile deformity/instability on examination also helps in formulating the diagnosis. The surgical technique for treating PSL abnormalities presented here is simple and offers good results.

The authors pointed out that a fractured penis is one of the differential diagnoses to PSL trauma since the mechanism of injury is usually similar in both conditions and both can present with the patient complaining of hearing a "snap". Nevertheless, the authors teach us that men with a fractured penis usually have significant swelling and immediate detumescence; whereas men with PSL rupture usually do not have these signs.

The final message of the authors from the present series is that abnormality of the PSL is a subtle diagnosis and men with this injury could present with a variety of symptoms and a variable degree of ED.

I recommend this paper for all urologists involved with andrology and reconstructive surgery.

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#### **RECONSTRUCTIVE UROLOGY**

#### Fournier's Gangrene: A Review of 43 Reconstructive Cases

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Background: Fournier's gangrene is a rare and potentially fatal infectious disease characterized by necrotic fasciitis of the perineum and abdominal wall, along with the scrotum and penis in men and the vulva in women.

Fournier's gangrene is a true surgical emergency. Skin loss can be very incapacitating and difficult to repair. Methods: The authors reviewed retrospectively the clinical records of a series of 43 patients with Fournier's gangrene between the years 1985 and 2003 who, after initial treatment by the Departments of Urology and Surgery, were referred to the Department of Plastic Surgery for reconstruction. The following parameters were evaluated: age, gender, interval between onset of symptoms and diagnosis, clinical symptoms, lesion site, results of bacteriologic cultures, cause and predisposing factors, treatment and reconstructive procedures, length of hospital stay, and outcome.

Results: The mean patient age was 56.6 years. Fifteen patients (34.9 percent) had diabetes mellitus. The cause of Fournier's gangrene was found in 32 patients (74.4 percent). The most common presentation was scrotal swelling, and scrotal involvement was found in 40 cases (93.0 percent). All of the patients underwent surgical debridement, and several reconstruction techniques were used. The mean length of hospital stay was 73.6 days. Two patients died.

Conclusions: Management of this infectious entity should be aggressive. Several techniques that are used to reconstruct the lost tissue have shown good results. The superomedial thigh skin flap has proven to be a reliable method of resurfacing large scrotal defects. Reconstructive surgery makes the return to a normal social life possible in many cases.

#### **Editorial Comment:**

This long-term retrospective study underlines the importance of Fournier's gangrene, which is a rare but very lethal emergency that should be diagnosed early and treated aggressively. The article updates the clinical picture with the required knowledge to efficiently handle these cases.

There is no predicting age, but predisposing factors such as diabetes, colorectal disorders and/or alcohol abuse in addition to hypertension, obesity and cigarette consumption are frequently seen in the constellation with Fournier's gangrene. The authors found a predominant involvement of the scrotum with scrotal swelling or scrotal lesions in more than 90% of male cases. Surprisingly, however, Fournier's gangrene was also seen in 21% of females (1).

After hemodynamic stabilization, an aggressive surgical debridement is a must with corresponding infusion therapy. Frequently the repeated debridement is necessary before a reconstruction can be planned. In 80% of the cases, the cause of the gangrene was polymicrobic with Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa being the predominantly found microbial. In addition, the increasing role of methicilin resistant S. aureus (MRSA) in genitoperineal infection needs to be stressed (2).

Most of the time an orchiectomy or penectomy was not necessary. In the author's opinion, the superomedial skin flap was the most reliable method of reconstruction in large scrotal defects after formation of healthy granulation tissue. Fasciocutaneous or musculocutaneous flaps were performed only in special cases. For functional, physiological and psychological reasons, the reconstruction of the scrotum is essential and may require a multi-modal approach instead of split- and full-thickness skin grafts, which can be used only in minimal lesions.

With the regimen outlined in this paper, only one out of the 43 patients died due to multiple organ failure. Others have reported a mortality rate up to 67% (1) whereas a decreased mortality rate of 22.8% was achieved by using the Fournier's Severity Index (3).

From this and other reports it can be concluded that the earliest possible diagnosis and aggressive therapy, repeated surgical debridement, and combined aggressive broad-spectrum antibiotic coverage keeping in mind the increasing role of MRSA decrease morbidity and mortality of Fournier's gangrene. The reconstructive surgical approach helps to restore physiological function of external genitalia and thus a return to a normal social life.

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#### **Complications of Porcine Small Intestine Submucosa Graft for Peyronie's Disease**

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Purpose: We report outcomes and complications of the use of porcine small intestine submucosa for correcting penile curvature due to Peyronie's disease.

Materials and Methods: A retrospective study was performed in patients with severe penile curvature (greater than 60 degrees) requiring surgical correction for sexual function. Preoperatively all patients underwent evaluation, including history, physical and penile duplex ultrasound. Of these patients 19 underwent tunical grafting with 1-layer Surgisis small intestine submucosa. Postoperatively patients were evaluated with clinic visits and telephone interviews to assess results.

Results: A total of 19 patients 46 to 69 years old (mean age 54) were treated with tunical incision or excision and grafting with small intestine submucosa between March 2002 and July 2005. Average followup was 15 months (range 3 to 43). Patients reported less penile pain with intercourse after surgery. There was no difference in Sexual Health Inventory for Men scores. Preoperatively 12 men (63%) had erectile dysfunction, defined as Sexual Health Inventory for Men less than 21, while 10 (53%) reported postoperative erectile dysfunction. Seven of the 19 patients (37%) had recurrent penile curvature (greater than 10 degrees) and 5 (26%) had recurrent Peyronie's disease plaque. Our complication rate was 37%, including hematoma at the graft site in 5 cases (26%), graft infection in 1 (5%) and Peyronie's disease recurrence requiring plication in 1 (5%).

Conclusions: Small intestine submucosa carries potential for grafting applications because it is easy to use and readily available. Our experience resulted in a 37% complication rate, which exceeds those previously reported with saphenous vein graft repair.

#### **Editorial Comment**

The surgical management of penile deformations due to Peyronie's Disease with various types of grafts is still under discussion. Autologous tissue used for corporeal reconstruction include tunica vaginalis, fascia lata, fascia temporalis, rectus sheath, and venous patches, reports on heterologous tissue include cadaveric fascia and xenogenic tissue such as porcine small intestine submucosa (SIS, Stratasys<sup>®</sup>), dermal porcine collagen

(Permacoll<sup>®</sup>) (1), and bovine pericardium graft (2). Due to either limited availability or immunogenic problems bioabsorbable artificial materials such as tissue sealant coated collagen fleece (Tachosil<sup>®</sup>) (3) have been tested lately (4,5).

In the current report, the authors present a retrospective study dealing with complications in the application of small intestine submucosa (SIS). The treatment of 19 patients with a follow-up of 15 months is currently the largest study concerning xenogenic material in penile reconstruction. The use of SIS was successful in a recent report in 11 of 12 treated patients (6). The same author reported about straightening of the penis and reconstruction of tunica albuginea defects due to excised plaques with penile prosthesis implantation in conjunction with SIS (7). Contrary to this report, the authors in this paper reported a complication rate of 37% mainly due to hematoma, infection or disease recurrence.

Do we have a new standard for penile reconstructive surgery now with off the shelve bioartificial material such as small intestine submucosa available? Nineteen selected patients clearly cannot be representative for all patients with Peyronie's disease necessitating surgery. We need larger series with randomization, direct comparison of various materials, standardizations in the timing of surgery, selection of patients, surgical technique, postoperative management, and evaluation of the outcome. In addition, with a complication rate in more than a third of the patients in this study and an improvement in sexual function of merely 10 % (which is in 2 patients) there is ample room for better materials, advancements in surgical technique, and further studies.

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## UROLOGICAL ONCOLOGY\_

## Hydronephrosis as a Prognostic Marker in Bladder Cancer in a Cystectomy-Only Series

Bartsch GC, Kuefer R, Gschwend JE, de Petriconi R, Hautmann RE, Volkmer BG *Department of Urology, Faculty of Medicine, University of Ulm, Ulm, Germany* Eur Urol. 2007; 51: 690-7; discussion 697-8

Objectives: Hydronephrosis in patients with bladder cancer is caused by tumour at the ureteral orifice, secondary ureteral tumours, intramural or extravesical tumour infiltration, or compression of the ureter. This study investigated the prognostic impact of hydronephrosis in bladder cancer.

Methods: A series of 788 patients were treated with radical cystectomy with curative intent for transitional cell carcinoma of the bladder without neoadjuvant/adjuvant radiotherapy/chemotherapy between January 1986 and September 2003. All patients had a complete follow-up until death or until the study's end date. Survival rates were calculated using the Kaplan-Meier method. A multivariate analysis with a Cox regression model was performed with respect to potential influencing factors.

Results: A total of 108 patients (13.7%) had unilateral and 25 patients (3.2%) had bilateral hydronephrosis. The rate of organ-confined tumours was significantly higher in patients without hydronephrosis (67.9% vs. 37.6%; p<0.001). Forty-three (32.3%) of the 133 hydronephrotic patients had a tumour involving the ureteral orifice. In this group the rate of organ-confined tumours was significantly higher than in the other patients with hydronephrosis (53.5% vs. 30.0%; p=0.009). In the multivariate analysis, preoperative hydronephrosis was determined as an independent prognostic marker for recurrence-free survival besides the pT classification and lymph node status (p=0.0015). The etiology of hydronephrosis did not affect the tumour-specific survival. Conclusions: Hydronephrosis at the time of diagnosis of bladder cancer is associated with a high probability of

conclusions: Hydronephrosis at the time of diagnosis of bladder cancer is associated with a high probability of advanced tumours. It is an independent prognostic factor for recurrence-free survival.

#### **Editorial Comment**

The question if patients with concomitant hydronephrosis and bladder cancer have inferior prognosis is a matter of debate since long. Here, the authors stratify their patients into two cohorts, hydronephrosis without tumor at the ureteral orifice versus no hydronephrosis or hydronephrosis with tumor at the ureteral orifice. This stratification increases significantly the prognostic impact of hydronephrosis. According to their results, a patient with hydronephrosis without tumor at the orifice has a 70% risk of having non-organ confined disease and a 40% risk of lymph node metastases, in contrast to patients with visible tumor at the orifice having risks at 41.7% and 19.4%, respectively. This translates into different tumor-specific survival rates.

Thus, hydronephrosis without visible tumor at the orifice is a very ominous prognostic factor.

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## Advanced Age Is Associated With Poorer Bladder Cancer-Specific Survival in Patients Treated With Radical Cystectomy

Nielsen ME, Shariat SF, Karakiewicz PI, Lotan Y, Rogers CG, Amiel GE, Bastian PJ, Vazina A, Gupta A, Lerner SP, Sagalowsky AI, Schoenberg MP, Palapattu GS; Bladder Cancer Research Consortium (BCRC) *The James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, Maryland, USA* Eur Urol. 2007; 51: 699-706; discussion 706-8

Objective: Bladder cancer (BCa) is a disease of older persons, the incidence of which is expected to increase as the population ages. There is controversy, however, regarding the outcomes of radical cystectomy (RC), the gold standard treatment of high-risk BCa, in patients of advanced chronological age. The aim of our study was to assess the impact of patient age on pathological characteristics and recurrence-free and disease-specific survival following RC.

Methods: The records of 888 consecutive patients who underwent RC for transitional cell carcinoma (TCC) were reviewed. Age at RC was analyzed both as a continuous (yr) and categorical (<or =60 yr old, n=240; 60.1-70 yr old, n=331; 70.1-80 yr old, n=266; >80 yr old, n=51) variable. Logistic regression and survival analyses were performed.

Results: Higher age at RC, analyzed as a continuous or categorical variable, was associated with extravesical disease and pathological upstaging (all p<0.02). Older patients were less likely to receive postoperative chemotherapy ( $< \sigma = 60$  yr: 32% vs. >80 yr: 14%, p=0.008). In both pre- and postoperative multivariate models, higher age at RC as a categorical variable was associated with BCa-specific survival (p<0.05). Patients >80 yr old had a significantly greater risk of disease recurrence than patients aged < or =60 yr (p<0.05).

Conclusion: Greater patient age at the time of RC for BCa is independently associated with adverse outcomes. Better understanding of factors associated with postoperative outcomes in this growing segment of the population is necessary. Prospective corroboration and further refinement of similar analyses in other large datasets is needed.

#### **Editorial Comment**

This manuscript gives the results of 888 patients from 4 large centers in the USA and Canada on bladder cancer in the elderly. Some figures may recall the aggressivity of bladder cancer in general e.g. 48% had non-organ confined disease, 42% had pathological upstaging.

Higher age was associated to worse prognostic factors such as risk of extravesical disease and pathological upstaging. In spite of more advanced disease, older patients were significantly less likely to receive adjuvant chemotherapy. The comment of M. Brausi to this paper is also advocated reading as it dissects the present bias in patient selection. In summary, this paper confers mainly well-known facts to urologists, still it is worthwhile reading as it may remind you not to wait too long to proceed with radical therapy as time may not play in favor of your elderly patients.

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## NEUROUROLOGY & FEMALE UROLOGY

**Comparison of Diagnostic Criteria for Female Bladder Outlet Obstruction** Akikwala TV, Fleischman N, Nitti VW *Department of Urology, New York University School of Medicine, New York, New York, USA* J Urol. 2006; 176: 2093-7

Purpose: There is no universally accepted definition of bladder outlet obstruction in women. We compared 5 contemporary urodynamic definitions and determined how well they correlated with each other and with clinical suspicion of bladder outlet obstruction.

Materials and Methods: A total of 154 women who underwent videourodynamics were prospectively evaluated. Clinical obstruction was suspected when history, physical examination, symptoms and basic testing before urodynamics raised the suspicion. Women were classified as having obstruction based on 5 contemporary definitions, including 3 pressure flow cutoff point criteria, videourodynamic criteria and the Blaivas-Groutz nomogram. The McNemar Test was used to compare each definition to the others and to suspicion of clinical obstruction.

Results: Of the women 91 were evaluable, including 26 (29%) with obstruction by videourodynamic criteria, 28 (31%) with obstruction by 1998 cut point criteria, 18 (20%) with obstruction by 2000 cut point criteria, 13 (14%) with obstruction by 2004 cut point criteria and 38 (42%) with obstruction by the Blaivas-Groutz nomogram. Videourodynamic and 1998 cut point criteria were not significantly different from each other (78.9% concordance) and each agreed with the clinically obstructed category in the comparison. Compared to the other criteria, the Blaivas-Groutz nomogram overestimated obstruction, while 2004 cut point criteria tended to underestimate it.

Conclusions: Each urodynamic definition of female bladder outlet obstruction has merit. Videourodynamic criteria and 1998 cut point criteria have the highest concordance. The Blaivas-Groutz nomogram overestimates obstruction compared to the other criteria. Therefore, it should not be used as the sole or standard definition of obstruction in women.

#### **Editorial Comment**

The authors prospectively reviewed a cohort of women who had clinical suspicion of bladder outlet obstruction. The patients underwent a full evaluation including fluoroscopic urodynamic studies. The data obtained was applied to five definitions for female bladder outlet obstruction. The application results were then compared to each other and then to the clinical situation at hand.

This is an excellent study was well planned and very illustrative of the difficulty in diagnosing bladder outlet obstruction in women in an absolute manner. The authors point out the challenge in diagnosing bladder outlet obstruction in females who have a current neurologic diagnosis or who do not generate a detrusor contraction during their urodynamic study. In addition, the results and discussion highlight the importance of combining clinical suspicion, physical examination, urodynamic evaluation as well as radiographic imaging during the diagnostic process. In our practice, though we incorporate multiple variables similar to this article in the evaluation of female bladder outlet obstruction, we do rely to a pronounced degree on the radiographic imaging during the patient's micturitional cycle. This is definitely a reference article for the urologic surgeon, especially those involved in tertiary evaluations in female urology.

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# Female Sexual and Hormonal Status in Patients with Bronchial Asthma: Relationship with Respiratory Function Tests and Psychological and Somatic Status

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Objectives: To assess the relationship among the sexual, hormonal, physical, and psychological status of women with bronchial asthma (BA) compared with that of healthy volunteers.

Methods: Thirty-eight women with BA were enrolled in the study. The patients were asked to complete the Female Sexual Function Index, General Health Questionnaire, and Medical Outcomes Study Short Form 36item Health Survey (SF-36). Using the answers on the SF-36, the mental and physical component summary scores were calculated. A total of 20 healthy women were enrolled in the study as the control group. The same questionnaires were given to this group as well. Statistical analysis was performed using the Mann-Whitney U test and Pearson correlation tests.

Results: At the end of the study, statistically significant differences were observed for all questionnaire scores (P <0.05). The most common female sexual dysfunction was diminished arousal (n = 30, 78.9%) in women with BA. In the correlation analysis, the total Female Sexual Function Index score had a statistically significant and positive correlation with the mental component summary score (r = 0.503, P = 0.001) and a negative correlation with the General Health Questionnaire score (r = -0.380, P = 0.020).

Conclusions: The results of our study have shown that BA, as a chronic medical condition, can be a cause of female sexual dysfunction with mental and psychiatric mechanisms.

#### **Editorial Comment**

The authors reviewed the association of bronchial asthma (BA) upon female sexual function and dysfunction. The study cohort consisted of 38 married, pre-menopausal women with a diagnosis of bronchial asthma and a control group of 20 healthy women who were also married and pre-menopausal. According to the American Thoracic Society, patients with bronchial asthma did suffer from symptoms of shortness of breath, wheezing and coughing. Patients were excluded if they were older than 50 years old or if their husbands had a sexual dysfunction. The questionnaire forms utilized did encompass quality of life, psychological status as well as sexual status. The female sexual function index included the categories of arousal, desire, orgasm, lubrication, pain and satisfaction. The authors found that the most common sexual problem associated with bronchial asthma was diminished arousal. They do note that though the initiation of sexual activity in women with bronchial asthma was difficult, if arousal and interest could be achieved then successful intercourse could be completed.

The topic of female sexual dysfunction is very popular in both the lay press as well as with professional study. This study excellently explores the effect of chronic disease upon a woman's sexual being. The authors do note that a positive mood and well being were the most important parameters controlling sexual activity in women. In view that there have been findings of difference in qualitative and quantitative difference in visually evoked sexual arousal between pre-menopausal and menopausal without bronchial asthma it would be interesting to see if this was mirrored in the population with bronchial asthma (1). In addition, in view that all the patients in this study were married, it would be of both scientific interest and great social commentary to see if a study cohort of unmarried women were more easily aroused than ones who were married when exposed to visual erotic stimuli and the areas of the brain affected (2).

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## PEDIATRIC UROLOGY\_

# Inflammation of the Testis and Epidididymis in an Otherwise Healthy Child: Is it a True Bacterial Urinary Tract Infection?

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Purpose: The exact etiology of acute gonadal inflammation (EO) in children is unknown. Bacterial infection and underlying urological abnormalities are thought to be the main causes, and hence antibiotic treatment and further invasive urinary tract imaging studies are usually recommended. The purpose of this study was to assess

the role of bacterial infection in pediatric acute EO.

Materials and Methods: We retrospectively searched our electronic medical archive for children under the age of 18 years with the diagnosis of acute EO between 1997 and 2002. Patients' charts were retrieved and reviewed for clinical and laboratory data.

Results: During 1997–2002, 193 patients with acute EO were treated. There were two subgroups according to the results of urinary cultures: 182 children (94.3%) had negative urine cultures and 11 (5.7%) had positive cultures. In the negative culture group, the mean age was  $9.8 \pm 3.2$  years (0.5–17). Medical history for urological disease was negative in all patients. Presenting symptom was scrotal pain in 165 (90.7%), and only three patients (1.6%) had accompanying urinary symptoms. Physical examination was normal besides tender gonad. Urinalysis was completely normal in 169 (92.9%) patients. Scrotal Doppler ultrasound (US) demonstrated nonspecific inflammatory process in 146 patients (80%), in nine (5%) torsion of the appendix testis was documented and in 27 (14.8%) scrotal US was normal. Follow up was available in 40% all of whom had an uneventful recovery with normal physical examination. In the positive culture group of 11 patients, the mean age was  $11 \pm 6.7$  years (3 months to 16 years), and eight patients (73%) had a known congenital urological abnormality. Presenting symptom was pain in five (45.4%) and pain with swelling in six (55.6%). Accompanying dysuria, frequency and urgency occurred in eight (72.7%) patients. Urinalysis was abnormal in 10 (90.9%). US demonstrated increased blood flow to the gonad in 10 (90.9%).

Conclusions: Negative history for urological disease, absence of urinary symptoms and normal urinalysis make the diagnosis of bacterial EO unlikely. In this setting, once testicular torsion was excluded, there is no justification for antimicrobial treatment or further imaging of the urinary tract.

#### **Editorial Comment**

This manuscript looks at patients under 18 years of age, between 1997 and 2002. They presented with the diagnosis of inflammation of the testis and epididymis. Charts were reviewed from children under the age of 18 from 1997 to 2002 and 193 patients were evaluated. They were divided into two groups, positive cultures and negative cultures. Hundred and eighty-two patients had negative cultures with a mean age of 9.8. The most common symptom in the culture negative group was scrotal pain and only 3 patients in this group had any urinary symptoms. Nearly 93% of these children had normal urinalysis with the other 13 children having scattered red cells or white cells. None was positive for protein, nitrites or leukocyte esterase. 80% of these culture-negative patients had ultrasounds of the scrotum with 9 patients having torsion of the appendix testis and follow up in 40% of the patients showed a normal physical exam. Eleven patients in the second group had positive urine cultures with a median age of 11 years. Five patients presented with pain and 6 with testicular swelling. The urinalysis was positive including red cells, white cells, protein nitrites and leukocyte esterase in 10 of the 11 patients with cultures being positive in all 11.

The authors rightly point out that only a minority of patients have positive urine cultures when epididymoorchitis is suspected and question whether antibiotics should be included as part of the treatment of patients whose urinalyses are negative.

The conclusion was that patients with a non-bacterial epididymo-orchitis are usually pre-pubertal children without positive history for urologic disease. Their presentation is without urinary symptoms yet there is no justification for antibiotic therapy or urinary tract imaging. They did caution that non-verbal children and infants might need to be excluded.

A few decades ago, urology textbooks suggested that epididymo-orchitis was due to urologic abnormalities such as ectopic ureters and that the entire urinary tract needed to be imaged. It is becoming more and more clear that the majority of epididymo-orchitis is not bacterial in origin and probably has a significant viral component. Somekh et al. (1) had a nice manuscript suggesting that a viral etiology may often be the cause. It is recognized that anti-inflammatory medications should be the main stay of treatment rather than antibiotics in epididymo-orchitis in kids.

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## Ureteroscopy In Children: Is There a Need for Ureteral Dilation and Postoperative Stenting?

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Introduction: Ureteroscopic stone manipulation and extraction is the standard of care for distal stone disease in the adult population. Recently, with refinements in instrumentation, these standards have been applied in pedi-

atrics. Here, we investigate the role of ureteral dilation and the need for postoperative stenting after ureteroscopy. Materials and Methods: Twenty-nine children (21 male, eight female) with a mean age of 11.0 (2.5–17.5) years underwent 34 ureteroscopic procedures (21 right, 13 left) to address ureteral stones in 27 (23 distal, 3 mid and 1 proximal), surveillance of the upper tract in six and a retained stent in one. Active ureteral dilation was not required in any of these patients. A Wolff 4.5-F or 6.5-F tapered semi-rigid ureteroscope was passed alongside a previously placed guidewire to access the upper collecting system. Proximal ureteral surveillance was performed after completion of the procedure; all but two patients had a diagnostic ureterogram. Four patients had preoperative placement of a JJ stent. Postoperative stents were placed in six patients, two had stents placed preoperatively for infection associated with either autonomic dysreflexia or stone impaction, two for extravasation or perforation, one for edema and one for subsequent ESWL.

Results: Mean follow up after ureteroscopy was 16.2 (0.3–48) months. Of the 27 procedures for stone disease, 15 (55%) stones required laser litholipaxy and 12 (45%) were managed with stone basket extraction. The overall re-treatment rate for stone disease was 4%. Diagnostic ureteroscopy was normal in six procedures. None of the procedures managed without a post-ureteroscopy stent required subsequent intervention.

Conclusion: Ureteroscopy is a safe, effective method to manage ureteral stones. Refinements in instrumentation allow its application to the pediatric population. Ureteroscopy including laser lithotripsy can be performed without ureteral dilation or postoperative stenting.

#### **Editorial Comment**

This article reviews a four-year consecutive series of ureteroscopies performed in children under the age of 18. Thirty-four ureteroscopic procedures were performed, 27 for renal stones, 6 for upper tract surveillance and 1 to remove a retained ureteral stent. All procedures were done under general anesthesia utilizing a guide wire, followed by a 4.5F or 6.5F tapered semi-rigid ureteroscope without the use of ureteral dilatation or a sheath. Twelve patients had stone basket extraction, while the remaining stone patients required Holmium: YAG laser and/or electrohydraulic litholapaxy with a retreatment rate of only 4%. Seventy-nine percent of the patients were managed as outpatients. Twenty-one percent were inpatients due to pre-operative pain or infections or a planned secondary procedure. The 23 (79%) patients who were managed as outpatients did not have a ureteral stent after the procedure. Two complications occurred. One was a small amount of extravasation from the perforation of the tip of a stone basket. The second had perforation migration and then impacted distal ureteral stone. The authors conclude that ureteroscopy in children is safe without ureteral dilatation and postoperative stenting.

Technology continues to bring improvements to pediatric urologic stone management. It has allowed for ureteral surgery that previously was not thought possible. This study shows a very low complication rate and a low stent usage rate demonstrating that with the refinements in the technology ureteral stone disease can be treated very similarly in children as is currently done for adult patients.

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