International Braz J Urol
Vol. 35 (5): 610-632, September - October, 2009

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

Brent W. Snow
University of Utah
Salt Lake City, Utah, USA

STONE DISEASE

Use of renal ultrasound to detect hydronephrosis after ureteroscopy

Manger JP, Mendoza PJ, Babayan RK, Wang DS
Department of Urology, Boston University School of Medicine, Boston, Massachusetts, USA
J Endourol. 2009; 23: 1399-402

Introduction: Ureteral obstruction is a potentially serious complication after ureteroscopy. Postoperative imaging with intravenous urogram and CT has been described as a means to detect asymptomatic or "silent" obstruction. We sought to evaluate the use of renal ultrasound to diagnose hydronephrosis after ureteroscopy in a large, contemporary series.
Materials and Methods: Of the 438 ureteroscopies performed by one staff surgeon at our institution from August 2003 to June 2008, 289 underwent a strict follow-up protocol that included renal ultrasound at approximately 1 month from the date of operation in patients without a stent or 1 month from the date of stent removal in patients with a stent.
Results: Of the 289 patients with proper follow-up, 27 (9.3%) had sonographic evidence of hydronephrosis. Fourteen patients were asymptomatic, and 13 patients experienced ipsilateral flank pain. A total of 4.8% of the patients (14/289) had silent hydronephrosis. The negative predictive value and positive predictive value of ipsilateral flank pain for hydronephrosis were 94% and 35%, respectively. There was no difference between the symptomatic and asymptomatic groups with respect to need for further surgery (38% vs. 21%, $p = 0.42$). The number of asymptomatic patients after ureteroscopy needing renal ultrasound to diagnose one case of hydronephrosis was 18.
Conclusions: This study demonstrates that hydronephrosis is present in a small percentage of patients after ureteroscopy. Hydronephrosis can be present in both symptomatic and asymptomatic patients and may warrant further surgery. Renal ultrasonography at 1 month after ureteroscopy permits appropriate detection of hydronephrosis and should be considered as an imaging option.

Editorial Comment

The authors excluded patients who underwent alternative postoperative imaging (CT scan, antegrade nephrostogram) - it would have been useful to report why these patients underwent imaging (ex. symptoms) and what the findings were. The authors did not evaluate intraoperative factors that could help predict those who may benefit from postoperative imaging (ex. impacted stones, ureteral perforation, need for balloon dilation). It is possible that a more selective approach to postoperative imaging could be considered. As one-third of patients with hydronephrosis had subsequent spontaneous resolution, it is possible that delaying ultrasonography to 6-8 weeks is warranted. The degree and chronicity of preoperative hydronephrosis might guide the need for nuclear renography instead of ultrasonography to define obstruction as opposed to calyectasis. This issue is not addressed by the authors, though they note that 15% of patients with hydronephrosis on ultrasonography were determined on follow-up to have chronic dilation as opposed to obstruction.

Dr. Manoj Monga
Professor, Department of Urology
University of Minnesota
Edina, Minnesota, USA
E-mail: endourol@yahoo.com

Treatment outcomes after endopyelotomy performed with or without simultaneous nephrolithotomy: 10-year experience

Berkman DS, Landman J, Gupta M
Department of Urology, Columbia University, College of Physicians and Surgeons, New York, New York, USA
J Endourol. 2009; 23: 1409-13

Introduction: The incidence of renal calculi associated with ureteropelvic junction obstruction (UPJO) has been reported to be as high as 20%. Although it has been suggested that simultaneous stone removal be performed with endopyelotomy (EP) for patients with UPJO, no crossing vessel, and renal calculi, there are no large series to date reporting in a rigorous fashion the success rate for resolution of the UPJO. This study intends to determine if stone extraction performed with EP increases failure rate.
Materials and Methods: A retrospective review was performed for all patients who underwent EP by a single surgeon between August 1996 and November 2006. One hundred forty-six procedures for UPJO were done in 139 patients. Success rate was compared in 105 cases (72%) of isolated UPJO and 41 (28%) cases with UPJO and ipsilateral calculi. Determination of overall success required subjective improvement and objective data based on intravenous pyelogram, computed tomography, and/or nuclear scintigraphy.
Results: Overall success rate was 71% in patients undergoing EP only and 90% in 41 patients who had simultaneous nephrolithotomy ($p = 0.04$). The odds ratio of failure after EP was 2.9 for severe/massive preoperative hydronephrosis. When considered alone and after adjusting for the severity of preoperative hydronephrosis and/or renal function, simultaneous nephrolithotomy did not increase the EP failure rate.
Conclusion: This study demonstrates that UPJO resolves at an equal rate after EP performed with or without ipsilateral renal calculi. Patients with UPJO and renal calculi should undergo stone extraction and EP in the same setting with the expectation of excellent results.

Editorial Comment

Traditionally a staged approach (stone extraction; re-evaluation; endopyelotomy) has been recommended for stones at the ureteropelvic junction as it is difficult to establish the presence of a primary UPJ obstruction versus the possibility of secondary obstruction due to edema that will resolve following stone extraction. Indeed, such patients were excluded from analysis in this study. Concerns are raised with regards to the possibility of fragment migration through the endopyelotomy incision if the two procedures are performed simultaneously. Unfortunately, the authors did not compare success rates for those undergoing intracorporeal lithotripsy to those undergoing intact stone removal, nor do they correlate success with stone size. Similarly, the authors do not report the presence of residual fragments or fragments in the retroperitoneum on postoperative imaging. The study could be criticized due to the lack of standardization in preoperative and postoperative imaging. The authors do not discuss their preoperative imaging to assess for crossing vessels, and whether the identification of crossing vessels impacted their treatment algorithm.

Dr. Manoj Monga
Professor, Department of Urology
University of Minnesota
Edina, Minnesota, USA
E-mail: endourol@yahoo.com

ENDOUROLOGY & LAPAROSCOPY

Initial experience with robot assisted partial nephrectomy for multiple renal masses

Boris R, Proano M, Linehan WM, Pinto PA, Bratslavsky G
Urologic Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland, USA
J Urol. 2009; 182: 1280-6

Purpose: We evaluated the feasibility of performing robot assisted partial nephrectomy in patients with multiple renal masses and examined the results of our initial experiences.
Materials and Methods: We reviewed the records of 10 patients with multiple renal masses who underwent attempted robot assisted partial nephrectomy within the last 2 years. Demographic information, and intraoperative, perioperative and renal function outcome data on these patients were reviewed.
Results: A total of 24 tumors in 9 patients were removed with robot assistance. There was 1 open conversion with successful completion of partial nephrectomy. Of the patients 70% had a known hereditary renal cancer syndrome and the remainder had multifocal disease with unknown germline genetic alterations. Frozen section from the tumor bed evaluated in 5 of 10 cases was negative. One patient experienced urinary leak postoperatively, which resolved by postoperative day 9 without intervention. Of the 24 robotically resected masses 22 were malignant. Our most recent 3 patients underwent successful partial nephrectomy without hilar clamping, obviating the need for warm ischemia. Overall renal function was unchanged at most recent followup with a minimal decrease in operated kidney differential function.
Conclusions: Robot assisted partial nephrectomy for multiple renal masses was feasible in our early experience. Patient selection is paramount for successful minimally invasive surgery. Robot assisted partial nephrectomy without hilar clamping, especially in the hereditary patient population in which repeat ipsilateral partial nephrectomy may be anticipated, appears promising but requires further evaluation.

Editorial Comment

Since the first laparoscopic partial nephrectomy was performed to by Winfield et al. and subsequently perfected by Kavoussi, Gill and others, the nephron-sparing surgery evolved with better technology, i.e. intraoperative ultrasound, vascular clamps, articulating needle holders, absorbable clips, etc. Ultimately, the use of robotic assisted surgery has been performed by the authors with comparable results as the laparoscopic partial nephrectomy. The advantages of the robot seem clear in terms of the intuitive use of the robot for intracorporeal suturing and the 7 degree of freedom of the laparoscopic devices, but one should be aware of the cost involved and the learning curve that could be different from surgeon to surgeon if the previous laparoscopic experience is minimal, which is not the case in this particular report. Furthermore, other methods of nephron-sparing surgery may be used to manage small renal masses, i.e. cryoablation or other ablative techniques that may yield the same oncological and functional outcomes as partial nephrectomies. The strength of this manuscript is the large experience of this group with previous management of malignant renal masses and complex laparoscopic oncological procedures performed laparoscopically in a single institution. Moreover, the complication rates of robotic assisted partial nephrectomies are comparable to open technique even when the complexity of the cases increased.

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

Assessment of laparoscopic suturing skills of urology residents: A Pan-European study

Kroeze SG, Mayer EK, Chopra S, Aggarwal R, Darzi A, Patel A
Department of Urology, St Mary's Campus, Imperial College Healthcare NHS Trust, London, UK
Eur Urol. 2009; 56: 865-73

Background: It has been acknowledged that standardised training programmes are needed to improve laparoscopic training of urologic trainees. Previous studies have suggested that simulator-based laparoscopic training can improve performance during real laparoscopic procedures.
Objective: To determine if there are performance differences for the completion of a simulated laparoscopic suturing task among urology residents based on their postgraduate year of training (PGY).
Design, Setting, and Participants: Using a validated scoring checklist, two independent observers objectively scored the completion of a standardised laparoscopic suturing task in a bench-top laparoscopic box trainer. PGY and previous exposure to laparoscopic surgery and laparoscopic simulated training was obtained from self-administered questionnaires. Data acquisition was undertaken at the European Urological Residents Education Programme (EUREP) 2007, run by the European School of Urology, and included a pan-European cohort of 201 urology residents.
Measurements: Reliability among those rating the suturing tasks was excellent (Cronbach's alpha=0.83). Each resident was scored for the suturing task. Residents were categorised into three groups based on their PGY status (junior [n=8]; intermediate [n=37]; senior [n=156]). The Kruskal-Wallis test was used to measure trend across the PGY; the Mann-Whitney U test was used to determine variation among categorised PGY groups.
Results and Limitations: Laparoscopic suturing skill was significantly different across PGY levels (p=0.032), and between junior residents and both intermediate and senior residents (p=0.008 and p=0.012, respectively). There was no significant difference between intermediate and senior residents (p=0.697). Only 12% of participants rated their existing volume of laparoscopic operative cases as sufficient, while 55% of participants had no regular opportunities, and 32% of participants had not performed laparoscopic procedures as primary surgeon. Most residents (96%) reported the use of laparoscopic simulators to be beneficial in training, although current European training programmes appear to provide <50% of residents with the opportunity to train with them.
Conclusions: A discernable relationship existed between the score obtained for a laparoscopic suturing task and year of resident training. Modular simulator training as part of a formal training programme may help to overcome some of the shortfall in residents' exposure to laparoscopic procedures as primary surgeon.

Editorial Comment

The optimal educative tools and transfer of knowledge in laparoscopic urological procedures have not been established yet. The authors have evaluated the acquisition of laparoscopic suturing techniques performed by different levels of European residents (201 residents) in different programs. The evaluation and data acquirement was performed by the European Urological Residents Education Program and the residents had to answer a survey. The conclusion of this study revealed that laparoscopic suturing skill was significantly different between junior residents and both intermediate and senior residents but there was no significant difference between intermediate and senior resident. Only 12% of trainees felt that they had enough laparoscopic operative experience, while 55% of participants had no regular opportunities, and 32% of participants had not performed laparoscopic procedures as primary surgeon. Most residents (96%) reported the use of laparoscopic simulators to be beneficial in training, although current European training programs appear to provide less than 50% of residents with the opportunity to train with them. In conclusion, there is a clear direct relationship between the skill level of laparoscopic suturing task and year of resident training and the residents perceive that laparoscopic

simulators may help formal laparoscopic training to overcome the lack of exposure to laparoscopic procedures as primary surgeons.

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

T1 hyperintense renal lesions: characterization with diffusion-weighted MR imaging versus contrast-enhanced MR imaging

Kim S, Jain M, Harris AB, Lee VS, Babb JS, Sigmund EE, Rueff LE, Taouli B
Department of Radiology, New York University Medical Center, New York, NY, USA
Radiology. 2009; 251: 796-807

Purpose: To compare the performance of apparent diffusion coefficient (ADC) measurement obtained with diffusion-weighted (DW) magnetic resonance (MR) imaging in the characterization of non-fat-containing T1 hyperintense renal lesions with that of contrast material-enhanced MR imaging, with histopathologic analysis and follow-up imaging as the reference standards.
Materials and Methods: Institutional review board approval was obtained for this HIPAA-compliant retrospective study, and the informed consent requirement was waived. Two independent observers retrospectively assessed MR images obtained in 41 patients with non-fat-containing T1 hyperintense renal lesions. The MR examination included acquisition of DW and contrast-enhanced T1-weighted images. For each index lesion, the observers assessed the (a) mean (+/- standard deviation) of ADC, (b) enhancement ratio, and (c) subtracted images for the presence of enhancement (confidence score, 1-5). Histopathologic analysis of renal cell carcinomas (RCCs) and follow-up imaging for benign lesions were the reference standards. ADCs of benign lesions and RCCs were compared. Receiver operating characteristic (ROC) curve analysis was performed to assess the accuracy of DW imaging, enhancement ratio, and subtraction for the diagnosis of RCC.
Results: A total of 64 lesions (mean diameter, 3.9 cm), including 38 benign T1 hyperintense cysts and 26 RCCs, were assessed. Mean ADCs of RCCs were significantly lower than those of benign cysts ([1.75 +/- 0.57] x 10(-3) mm(2)/sec vs [2.50 +/- 0.53] x 10(-3) mm(2)/sec, P < .0001). ADCs of solid and cystic portions of complex cystic RCCs were significantly different ([1.37 +/- 0.55] x 10(-3) mm(2)/sec vs [2.45 +/- 0.63] x 10(-3) mm(2)/sec, P < .0001). When data from both observers were pooled, area under the ROC curve, sensitivity, and specificity were 0.846, 71%, and 91%, respectively, for DW imaging; 0.865, 65%, and 96%, respectively, for enhancement ratio (at the excretory phase); and 0.861, 83%, and 89%, respectively, for subtraction (P = .48 and P = .85, respectively). The combination of DW imaging and subtraction resulted in area under the ROC curve, sensitivity, and specificity of 0.893, 87%, and 92%, respectively, with significantly improved reader confidence compared with subtraction alone (P = .041).
Conclusion: The performance of DW imaging was equivalent to that of enhancement ratio in the characterization of T1 hyperintense renal lesions, with both methods having lower sensitivity than image subtraction without reaching significance.

Editorial Comment

On MR imaging, most renal masses are hypointense on T1 and hyperintense on T2, thus comparison between T1-weighted image pre and post intravenous injection of contrast readily shows variable degree of hyperintensity of the lesions due to contrast enhancement (particularly hypervascular ones). Some lesions, however, are hyperintense in T1-weighted images making the perception of contrast enhancement a very difficult task. These hyperintense lesions on T1-weighted images are either benign (hemorrhagic cyst, hematoma, vascular lesion or oncocitoma) or malignant masses (papillary renal cell carcinoma). Image subtraction technique is very useful for the demonstration of subtle contrast enhancement in hyperintense T1 lesions. Image subtraction however can be of limited value in patients with irregular respiratory movements, which precludes adequate images subtraction.

DW imaging has been used to assess several renal disorders: infection, ischemia, obstruction and masses. The authors of this manuscript show that DW imaging can be of value to characterize non-fat-containing T1 hyperintense lesions. They found that the diffusion is more restricted in renal cell carcinoma (lower ADC values) than in benign hemorrhagic or proteinaceous cyst. Although with lower sensitivity than that image subtraction, the authors recommend DW imaging as an alternative to contrast-enhanced MRI in patients with chronic renal insufficiency that are at risk for development of nephrogenic system fibrosis secondary or associated with gadolinium-containing agent.

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

Imaging appearance of granulomatous disease after intravesical Bacille Calmette-Guerin (BCG) treatment of bladder carcinoma

Ma W, Kang SK, Hricak H, Gerst SR, Zhang J
Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
AJR Am J Roentgenol. 2009; 192: 1494-500

Objective: The purpose of our study is to present the radiographic findings in a series of 16 patients with complications associated with intravesical bacille Calmette-Guérin (BCG) treatment of bladder cancer.
Conclusion: Intravesical BCG-related complications such as granulomatous disease may show imaging findings mimicking primary or metastatic tumors in patients with bladder cancer. Radiologists should consider this possibility when imaging abnormalities are encountered in bladder cancer patients treated with intravesical BCG so that appropriate management can be administered and unnecessary procedures avoided.

Editorial Comment

Intravesical therapy with bacillus Calmette-Guérin (BCG) has proved to be more effective in the prophylaxis and treatment of superficial bladder tumors and carcinoma in situ than most chemotherapeutic agents. Some complications however may occur with this treatment. Granulomatous reaction may occur either in the urinary tract or sporadically outside the urinary tract (hepatitis, disseminated infection, miliary tuberculosis and polyarthritis).

This manuscript calls the attention of radiologists and urologists regarding the imaging manifestations of these complications. As it shown by the authors, granulomatous reaction may resemble focal primary renal or bladder tumors and focal or diffuse prostatic tumors. Since instillation of BCG is indicated for treatment of

superficial bladder cancer, the finding of focal nodularity in the bladder wall is very difficult to differentiate from bladder cancer and bladder biopsy or surgical pathology is necessary. Similarly, transrectal biopsy of the prostate is mandatory to exclude prostate cancer in these patients.

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

UROGENITAL TRAUMA

Impact of obesity in damage control laparotomy patients

Duchesne JC, Schmieg RE Jr, Simmons JD, Islam T, McGinness CL, McSwain NE Jr
Section of Trauma and Critical Care Surgery, Department of Surgery and Anesthesia, Tulane University School of Medicine, New Orleans, Louisiana, USA
J Trauma. 2009; 67: 108-12

Background: Obesity is an independent predictor of increased morbidity and mortality in critically injured trauma patients. We hypothesized that obese patients in need of damage control laparotomy (DCL) will encounter an increase incidence of postsurgical complications with a concomitant increase mortality when compared with a cohort of nonobese patients.
Methods: All adult trauma patients who underwent DCL during a 4-year period at a Level I Trauma Center were retrospectively reviewed. Patients were categorized into nonobese (body mass index [BMI] < or = 29 kg/m), obese (BMI 30-39 kg/m), and severely obese (BMI > or = 40 kg/m) groups. Outcome measures included the occurrence of postoperative infectious complications, failure of primary abdominal wall fascial closure, acute respiratory distress syndrome, acute renal insufficiency, multiple system organ failure, days of ventilator support, hospital length of stay, and death.
Results: During a 4-year period, 12,759 adult trauma patients were admitted to our Level I Trauma Center of which 1,812 (14.2%) underwent emergent laparotomy. Of these, 104 (5.7%) were treated with DCL: nonobese, n = 51 (49%); obese, n = 38 (37%); and severely obese, n = 15 (14%). In a multivariate adjusted model, multiple system organ failure was 1.82 times more likely in severely obese (95% CI: 1.14-2.90) and 1.74 times more likely in the obese patients (95% CI: 1.14-2.66) when compared with patients with normal BMI after DCL ($p < 0.01$). In the severely obese patients undergoing DCL, significantly elevated prevalence ratios (PR) for development of postoperative infectious complications, acute renal insufficiency, and failure of primary abdominal wall fascial closure were 1.75, 3.07, and 2.62, respectively. Days of ventilator support, length of stay, and mortality rates were significantly higher in severely obese patients (24 days, 27 days, and 60%) compared with obese (14 days, 14 days, and 21%) and nonobese (9.8 days, 14 days, and 28%) patients.
Conclusion: Severe obesity was significantly associated with adverse outcomes and increased resource utilization in trauma patients treated with DCL. Measures to improve outcomes in this vulnerable patient population must be directed at multiple levels of health care.

Body mass index affects time to definitive closure after damage control surgery

Haricharan RN, Dooley AC, Weinberg JA, McGwin G Jr, MacLennan PA, Griffin RL, Rue LW 3rd, Reiff DA
Section of Trauma, Burns and Surgical Critical Care, Department of Surgery, School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama, USA
J Trauma. 2009; 66: 1683-7

Background: A growing body of literature demonstrates that irrespective of the mechanism of injury, obesity is associated with significantly worse morbidity and mortality after trauma. Among patients requiring damage control laparotomy (DCL), clinical experience suggests that obesity affects time to definitive closure though this association has never been demonstrated quantitatively.
Methods: All patients at an academic Level I trauma center requiring a DCL between January 2002 and December 2006 (N = 148) were included. Information pertaining to demographic, injury, and clinical characteristics was abstracted from patient medical records. The risk of specific complications including pneumonia, renal failure, and sepsis was compared between normal and overweight/obese patients, as measured by body mass index (BMI). The lengths of intensive care unit (ICU) stay and mechanical ventilation as well as time to abdominal closure were also compared.
Results: The risk of pneumonia, sepsis, and renal failure was 2.05-times, 1.77-times, and 2.84-times higher among overweight patients compared with patients with a normal BMI. The risk of pneumonia, sepsis, and renal failure was 2.01-times, 4.24-times, and 1.85-times higher among obese patients compared with those with a normal BMI. Obese patients also had a significantly longer ICU length of stay (28.7 days vs. 15.1 days; $p < 0.0001$), longer hospitalization (39.3 days vs. 27.0 days; $p = 0.008$), and time to definitive closure (8.4 days vs. 3.9 days; $p = 0.03$) compared with patients with a normal BMI.
Conclusions: Among patients requiring DCL, those who are overweight or obese have a prolonged time to definitive closure. These patients also experience a significantly longer ICU course and a higher risk of pneumonia.

Editorial Comment

Obesity has reached epidemic proportions in the US and across the globe. Surgical management of the morbidly obese is difficult and time consuming, and prone to more complications and prolonged hospitalizations. In the trauma literature, obesity is an independent factor in a negative impact as to overall morbidity and mortality.

The concept of damage control is rarely discussed in the urologic literature but is an important management method that all Urologists should be familiar with. Urology and damage control were first championed by Michael Coburn of Ben Taub Hospital, a major trauma center in Houston, Texas. The concept entails that patients that are critically injured are best managed by temporizing surgical measures to quickly stop bleeding, and fecal and urinary leakage, avoid definitive reconstruction, and plan on a later staged operation, after the patient has been resuscitated in the Intensive Care Unit. The concept is that the fatal triad of a cold, coagulopathic and acidotic patient has a high degree of dying – and that such patients need to have surgery aborted and the adverse parameters corrected. To minimize the time on the operating room table a quick abdominal closure is needed. During the drug wars in the early 1990s in Bogotá, Colombia, the surgery services were overwhelmed and decided to do damage control surgeries and not to close the fascia, but instead sew an opened 3-liter saline bag to the skin edges. By not closing the fascia avoids intra abdominal compartment syndrome and allows the bowel edema time to resolve and allow for delayed closure. The use of the "Bogotá bag" was a major advance in the management of the critically ill patient. The "Bogotá bag" has been modified in to the current use of the "VAC PAC". This entails taking the fluoroscopy cover plastic sheet and fenestrating it with multiple small slits. The sheet in then placed under the fascia. Two lap pads are placed on top of the plastic sheet and 2 JP drains placed on top of the lap pads, and then covered with gauze. At the skin level a large adhesive VY drape is stuck to the skin and the JPs placed to wall suction. Making the "VAC PAC" takes less then 5 minutes and helps

control peritoneal fluid and bowel edema. In the critically injured Urology patients, the "VAC PAC" should be more liberally used. The use of damage control in urology mainly applies to the injured ureter, where the ureter can either be ligated, or a pediatric feeding tube or ureteral stent placed up the cut ureteral edge and the stent pulled quickly through the skin. Here, definitive measures such as a Psoas hitch or Boari flap are deferred to another day when the patient is stable. Attempting definitive repairs in the critically injured patient is unwise and risks death.

Dr. Steven B. Brandes
Associate Professor, Division of Urologic Surgery
Washington University in St. Louis
St. Louis, Missouri, USA
E-mail: brandess@wudosis.wustl.edu

PATHOLOGY

Does perineural invasion on prostate biopsy predict adverse prostatectomy outcomes?

Loeb S, Epstein JI, Humphreys EB, Walsh PC
James Buchanan Brady Urological Institute and the Department of Urology, Johns Hopkins Medical Institutions, Baltimore, MD, USA
BJU Int. 2009 Aug 19. [Epub ahead of print]

Objective: To determine the relationship between perineural invasion (PNI) on prostate biopsy and radical prostatectomy (RP) outcomes in a contemporary RP series, as there is conflicting evidence on the prognostic significance of PNI in prostate needle biopsy specimens.
Patients and Methods: From 2002 to 2007, 1256 men had RP by one surgeon. Multivariable logistic regression and Cox proportional hazards models were used to examine the relationship of PNI with pathological tumour features and biochemical progression, respectively, after adjusting for prostate-specific antigen level, clinical stage and biopsy Gleason score. Additional Cox models were used to examine the relationship between nerve-sparing and biochemical progression among men with PNI.
Results: PNI was found in 188 (15%) patients, and was significantly associated with aggressive pathology and biochemical progression. On multivariate analysis, PNI was significantly associated with extraprostatic extension and seminal vesicle invasion ($P < 0.001$). Biochemical progression occurred in 10.5% of patients with PNI, vs 3.5% of those without PNI (unadjusted hazard ratio 3.12, 95% confidence interval 1.77-5.52, $P < 0.001$). However, PNI was not a significant independent predictor of biochemical progression on multivariate analysis. Finally, nerve-sparing did not adversely affect biochemical progression even among men with PNI.
Conclusion: PNI is an independent risk factor for aggressive pathology features and a non-independent risk factor for biochemical progression after RP. However, bilateral nerve-sparing surgery did not compromise the oncological outcomes for patients with PNI on biopsy.

Editorial Comment

The significance of perineural invasion by carcinoma in needle prostatic biopsies is controversial (1,2). Presence of perineural invasion in needle prostatic biopsies may influence the indication of resection of neurovascular bundle. Loeb's et al. study showed that perineural invasion on prostate biopsy was not a significant independent predictor of biochemical progression on multivariate analysis and nerve-sparing surgery did not adversely affect biochemical progression even among men with perineural invasion.

In a recent study, we found that perineural invasion in needle prostatic biopsies significantly predicted prostatectomy stage > pT2 in univariate ($p < 0.01$) but not in multivariate analysis ($p = 0.38$). In multivariate analysis preoperative PSA, Gleason grading and percentage of linear extent of cancer in mm in the needle biopsy were the significant variables predictive of > pT2.

We agree with Loeb's et al. conclusion that nerve-sparing surgery does not adversely affect biochemical progression even among men with perineural invasion.

References

1. Bastacky SI, Walsh PC, Epstein JI: Relationship between perineural tumor invasion on needle biopsy and radical prostatectomy capsular penetration in clinical stage B adenocarcinoma of the prostate. Am J Surg Pathol. 1993; 17: 336-41.
2. Egan AJM, Bostwick DG: Prediction of extraprostatic extension of prostate cancer based on needle biopsy findings: Perineural invasion lacks significance on multivariate analysis. Am J Surg Pathol. 1997; 21: 1496-500.

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

A pathological reassessment of organ-confined, Gleason score 6 prostatic adenocarcinomas that progress after radical prostatectomy

Miyamoto H, Hernandez DJ, Epstein JI
The Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
Hum Pathol. 2009 Aug 13. [Epub ahead of print]

Prior studies of radical prostatectomies have reported a small percentage of men with biochemical progression after radical prostatectomy showing organ-confined, Gleason score 6. One might predict that this should virtually never occur. We identified 2551 (1983-2005) radical prostatectomies coded by the urologists at our institution as pathologically organ-confined, Gleason score 6 cancer with more than 1 year of follow-up. We re-examined histopathogically the serially sectioned and completely embedded radical prostatectomy specimens of 38 men who developed biochemical recurrence defined as a single prostate-specific antigen level of 0.2 ng/mL or greater. In 27 (71%) of 38 of cases, pathology re-review showed higher grade or stage than coded by the urologists. These included 10 cases of organ-confined with Gleason pattern 4 as either the primary or secondary pattern; 9 cases of organ-confined, Gleason score 6 with tertiary pattern 4 (in 4 cases, tertiary pattern 4 was described in the initial pathology report); 5 cases of Gleason score 7 plus extraprostatic extension; 1 case of Gleason score 6 with focal extraprostatic extension; and 2 cases with positive margins due to intraprostatic incision (listed in the initial pathology report). The remaining 11 cases were true organ-confined, Gleason score 6 tumors, but none of the patients developed systemic disease. Most prior reports of organ-confined, Gleason score 6 with progression are undergraded (upgrading with revision of Gleason system), understaged (difficulty recognizing focal extraprostatic extension), or suffer from situations with ambiguous staging (intraprostatic incision) or grading (tertiary pattern 4 or 2 + 4 = 6). Even for the rare true organ-confined, Gleason score 6 (no pattern 4) tumor with supposed biochemical progression, some may be false-positive progression based on low post-radical prostatectomy prostate-specific antigen levels and minute tumors that seem highly improbable to progress. With accurate pathologic evaluation, men with organ-confined, Gleason score 6 (no pattern 4) prostate cancer can be told that their risk of progression is very rare (0.4%).

Editorial Comment

This study may be intriguing for the urologist. From a total of 38 patients reported as having organ-confined cancer who developed biochemical recurrence defined as a single prostate-specific antigen level of 0.2 ng/mL or greater, pathology re-review showed that only 11 cases were true organ-confined. How does it happen?

Pathologists use strict criteria for diagnosis however there are many interpretative dilemmas. Experience and specialization are important considerations. One example is the Gleason grading reproducibility that can be categorized as intraobserver or interobserver. Exact interobserver agreement may vary from 36% to 81%; interobserver agreement + 1 score unit from 69% to 86%; and, the kappa values from 0.13 to 0.78 (slight to substantial agreement) (1).

Another example refers to criteria for extraprostatic extension. In the posterior, posterolateral and lateral aspects of the prostate gland, tumor admixed with periprostatic fat is the most recognized manifestation of extraprostatic extension. However, tumor in fat is not synonymous with extraprostatic extension and pathologists should be aware that intraprostatic adipocytes will be found in up to 5% of radical specimens. Another more common problem relates to the desmoplastic reaction that sometimes occurs in a tumor invading the adipose tissue replacing it. In this circumstance is difficult to evaluate extraprostatic extension. A bulging contour beyond the normal contour of the gland indicates extraprostatic extension (2). However, this finding may also be interpretative.

References

1. Amin MB, Grignon DJ, Humphrey PA, Srigley JR: Gleason Grading of Prostate Cancer. A Contemporary Approach. Philadelphia, Lippincott Williams & Wilkins. 2004.
2. Epstein JI, Amin M, Boccon-Gibod L, Egevad L, Humphrey PA, Mikuz G, et al.: Prognostic factors and reporting of prostate carcinoma in radical prostatectomy and pelvic lymphadenectomy specimens. Scand J Urol Nephrol. 2005; 39 (Suppl 216): 34-63.

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

BASIC AND TRANSLATIONAL UROLOGY

Urodynamic and immunohistochemical evaluation of intravesical botulinum toxin A delivery using liposomes

Chuang YC, Tyagi P, Huang CC, Yoshimura N, Wu M, Kaufman J, Chancellor MB
Department of Urology, Chang Gung Memorial Hospital, Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan, Republic of China
J Urol. 2009; 182: 786-92

Purpose: Botulinum toxin A (Allergan, Irvine, California) is a high molecular weight neurotoxin used to treat hypersensitive bladder by direct injection to pass the urothelial barrier. We investigated the feasibility of intravesical botulinum toxin A delivery using liposomes (Lipella Pharmaceuticals, Pittsburgh, Pennsylvania), which

are phospholipid bilayered vesicles, and evaluated the urodynamic and immunohistochemical effect on acetic acid induced bladder hyperactivity in rats.
Materials and Methods: Liposomes (1 ml), botulinum toxin A (20 U/1 ml saline) or botulinum toxin A encapsulated in liposomes (lipotoxin, that is 20 U botulinum toxin A plus 1 ml liposomes) was administered in the bladder and retained for 1 hour on day 1 after baseline cystometrogram. Continuous cystometrogram was performed on day 1 by filling the bladder with saline and on day 8 by filling the bladder with saline, followed by 0.3% acetic acid. The bladder was then harvested. Cystometrogram parameters, histology, SNAP25 and calcitonin gene-related peptide expression were measured by Western blotting or immunostaining.
Results: The intercontraction interval was decreased 57.2% and 56.0% after intravesical acetic acid instillation in liposome and botulinum toxin A pretreated rats, respectively. However, rats that received lipotoxin showed a significantly decreased intercontraction interval response (21.1% decrease) to acetic acid instillation but without compromised voiding function. Also, lipotoxin pretreated rats had a better decrease in the inflammatory reaction and SNAP-25 expression, and increase in calcitonin gene-related peptide immunoreactivity than those in liposome or botulinum toxin A pretreated rats.
Conclusions: Intravesical lipotoxin administration cleaved SNAP-25, inhibited calcitonin gene-related peptide release from afferent nerve terminals and blocked the acetic acid induced hyperactive bladder. These results support liposomes as an efficient vehicle for delivering botulinum toxin A without injection.

Editorial Comment

It has been proved that Botulinum toxin A applied as cystoscopic guided injections into the bladder wall have a therapeutic effect on overactive bladder and interstitial cystitis / painful bladder syndrome. Nevertheless, we know well that bladder injection therapy has some limitations, including drug leakage outside the bladder, hematuria, pain at injection sites and uneven distribution. In this way, the authors have been searching for a simpler and lower risk method to deliver Botulinum toxin A without injection.

We know that it is difficult for Botulinum toxin A to access the submucosal nerve plexus in formal use with saline as a vehicle without direct injection to pass the urothelial barrier. Based on previous experience, the authors speculated that delivery using liposomes, which are phospholipid bilayered vesicles, and evaluated the urodynamic and immunohistochemical effect on acetic acid induced bladder hyperactivity in rats.
Their results show that Botulinum toxin A can be combined with liposomes to be administered as a liquid instillation without cystoscopic injection, with good therapeutic results in rats.

To our knowledge, this is the first report of the promise of liquid instillation of Botulinum toxin A. I strong recommend this paper to all physicians involved in research on neurourology.

Dr. Francisco J. B. Sampaio
Full-Professor and Chair, Urogenital Research Unit
State University of Rio de Janeiro
Rio de Janeiro, RJ, Brazil
E-mail: sampaio@urogenitalresearch.org

Shock wave induced kidney injury promotes calcium oxalate deposition

Xue YQ, He DL, Chen XF, Li X, Zeng J, Wang XY
First Affiliated Hospital of Medical College, Xi'an Jiaotong University, Xi'an, Shaanxi, China
J Urol. 2009; 182: 762-5

Purpose: Extracorporeal shock wave lithotripsy is the preferred treatment for upper urinary tract renal calculi. However, this treatment is associated with a high rate of recurrent renal calculi. Shock wave therapy can result

in renal epithelial cell injury, which in turn is a most important factor in calculus formation. We investigated the influence of kidney damage secondary to shock waves on Ca oxalate crystal retention in the kidney.
Materials and Methods: A total of 32 rats were randomly divided into 4 groups, including group 1--controls, group 2--sham treated rats given 25 ml 0.75% ethylene glycol per day for 14 days, group 3--rats given 15 kV 1 Hz shock waves 500 times to the left kidney, followed by 25 ml 0.75% ethylene glycol daily for 14 days, and group 4--rats with the same treatment as group 3 except the number of impacts was increased to 1,000. The 2 kidneys were removed at the end of the experiment. Ca oxalate crystals were observed by surgical microscopy in kidney sections stained with hematoxylin and eosin. Crystal morphology was determined using polarizing microscopy. Acidified kidney tissue homogenate was examined for Ca and oxalate content by colorimetry (Sigma).
Results: Kidney sections showed that kidneys that did not receive shock waves had fewer crystals than kidneys with shock waves, which had crystals in major areas. In the left kidney in groups 2 to 4 the mean +/- SD quantity of Ca was 16.88 +/- 6.41, 28.58 +/- 7.54 and 40.81 +/- 15.29 micromol/gm wet kidney and the mean quantity of oxalate was 8.44 +/- 6.80, 20.52 +/- 7.70, 31.76 +/- 14.14 micromol/gm wet kidney, respectively. Ca oxalate density increased with the number of shock wave impacts.
Conclusions: Kidney damage caused by shock wave treatment can increase Ca oxalate crystal retention in the kidneys of rats in this stone model.

Editorial Comment

The authors elegantly demonstrated in a rat model that shock wave therapy results in proximal tubular injury in a dose dependent manner. Also, this was associated with a markedly increased deposition of CaOx stones in kidney tissue.

The study is provocative, since we know that extracorporeal shock wave lithotripsy is associated with a high rate of stone recurrence. The main shortcoming of the study is the use of a rat model, which have a kidney very different from humans. Probably, further studies in pigs, which have kidneys very similar to human kidney, would better clarify this issue.

Dr. Francisco J. B. Sampaio
Full-Professor and Chair, Urogenital Research Unit
State University of Rio de Janeiro
Rio de Janeiro, RJ, Brazil
E-mail: sampaio@urogenitalresearch.org

RECONSTRUCTIVE UROLOGY

Urethral lengthening in metoidioplasty (female-to-male sex reassignment surgery) by combined buccal mucosa graft and labia minora flap

Djordjevic ML, Bizic M, Stanojevic D, Bumbasirevic M, Kojovic V, Majstorovic M, Acimovic M, Pandey S, Perovic SV
Belgrade Center for Genital Reconstruction, University of Belgrade, Serbia
Urology. 2009; 74: 349-53

Objectives: To develop a technique for urethral reconstruction using a combined labia minora flap and buccal mucosa graft. Urethral lengthening is the most difficult part in female transsexuals and poses many challenges.
Methods: From April 2005 to February 2008, 38 patients (aged 19-53 years) underwent single-stage metoidioplasty. The technique starts with clitoral lengthening and straightening by division of both clitoral ligaments

dorsally and the short urethral plate ventrally. The buccal mucosa graft is quilted to the ventral side of the corpora cavernosa between the native orifice and the tip of the glans. The labia minora flap is dissected from its inner surface to form the ventral aspect of the neourethra. All suture lines are covered by the well-vascularized subcutaneous tissue originating from the labia minora. The labia majora are joined in the midline and 2 silicone testicular implants are inserted to create the scrotum. The neophallus is covered with the remaining clitoral and labial skin.
Results: The median follow-up was 22 months (range 11-42). The median neophallic length was 5.6 cm (range 4-9.2). The total length of the neourethra was 9.4-14.2 cm (median 10.8). Voiding while standing was reported by all 38 patients, and temporary dribbling and spraying were noted by 12. Two fistulas and one urethral erosion resulted from the testicular implant and required secondary revision.
Conclusions: A combined buccal mucosa graft and labia minora flap present a good choice for urethral reconstruction in female-to-male transsexuals, with minimal postoperative complications.

Editorial Comment

Belgrade has established itself as one of the premier centers for urologic reconstruction. Specifically, they have pushed advances in female-to-male sex reassignment surgery. In this article, accompanied by several instructive photographs, they describe the technique and results of the metoidoplasty with urethral lengthening using buccal mucosa. This technique represents a departure from the radial forearm free flap technique. Instead, they rely on pre-operative clitoral lengthening with a combination of androgens and a vacuum pump. The enlarged clitoris is freed from its ligamentous attachments and the urethral plate is divided to achieve adequate length. This leaves a urethral defect of several centimeters, which is then bridged with a dorsal buccal graft, and a ventral onlay of labia minor flap.

From a reconstructive standpoint, this is really a sensible and beautiful operation. It employs techniques familiar to the urethral reconstructionist. Many of the men are able to obtain erections postoperatively, although none was sufficient for penetration. All were able to void in the standing position. Hopefully this variation of the metoidoplasty can offer a relief from the complications of urethral construction associated with previous female-to-male transsexual procedures. We look forward to hearing long-term results.

Dr. Sean P. Elliott
Department of Urology Surgery
University of Minnesota
Minneapolis, Minnesota, USA
E-mail: selliott@umn.ed

Urodynamic changes and initial results of the AdVance male sling

Davies TO, Bepple JL, McCammon KA
Eastern Virginia Medical School, Norfolk, USA
Urology. 2009; 74: 354-7

Objectives: To present the urodynamic changes and early results associated with the AdVance male sling. The AdVance male sling is a treatment option for postprostatectomy incontinence (PPI), with the goal of eliminating urinary incontinence without affecting voiding parameters. A concern of any procedure in treating men with PPI is whether the treatment induces obstruction and causes retention.
Methods: Data were prospectively collected from 13 patients undergoing AdVance male sling placement for PPI. Urodynamic testing was performed at baseline and repeated at 6 months postoperatively. A 24-hour pad

test and the Incontinence Quality of Life questionnaire were completed preoperatively and at 3 and 6 months postoperatively.
Results: The median age at the procedure was 63.3 years (range 44.7-74.7). The mean preoperative and 6-month postoperative patient-reported pad use was 4.52 and 1.04, respectively (2-tailed t test, P = .0009). The 24-hour pad test, performed preoperatively and at 6 months postoperatively, yielded a pad weight of 779.3 and 67.6 g, respectively (P = .03). The Valsalva leak point pressure improved significantly (P = .032), but the detrusor voiding pressure, postvoid residual urine volume, and maximal and average flow rates remained relatively unchanged. At 3 and 6 months postoperatively, the Incontinence Quality of Life scores had improved significantly compared with the preoperative scores (P < .01).
Conclusions: These results are encouraging, because this series has demonstrated a significant improvement in patient-reported pad use, 24-hour pad test weights, and Valsalva leak point pressure without signs of obstruction. The improvement in incontinence was accompanied without any changes in the other voiding parameters and with significant improvement in the quality-of-life measures. Ongoing studies with longer follow-up are pending to compare their results with these promising early results.

Editorial Comment

The authors present urodynamic data supporting the concept that the transobturator sling achieves continence by means other than compression. Original reports from developers of the sling (1) supported the concept that it achieved continence by lengthening of the membranous urethra. The current article does not shed light on whether that is indeed the mechanism but it does show that pressure-flows studies are not consistent with obstruction. Curiously, 2 of 13 patients had to perform intermittent catheterization postoperatively for urinary retention lasting up to 2 weeks. It would be interesting to know whether the urodynamic outcomes of these 2 patients were any different from the rest. With only 13 patients and large standard deviations around the variables of interest, the study is underpowered to test anything but an enormous difference in voiding parameters; however, with pre- and post-op flow rates and pressures so close to each other it is hard to believe the findings would be clinically significantly different even with a larger cohort. While the findings deserve to be validated by other centers, the conclusions remain important.

Reference

1. Rehder P, Gozzi C: Transobturator sling suspension for male urinary incontinence including post-radical prostatectomy. Eur Urol. 2007; 52: 860-6.

Dr. Sean P. Elliott
Department of Urology Surgery
University of Minnesota
Minneapolis, Minnesota, USA
E-mail: selliott@umn.ed

UROLOGICAL ONCOLOGY

Prostate cancer detection rate in patients with repeated extended 21-sample needle biopsy

Campos-Fernandes JL, Bastien L, Nicolaiew N, Robert G, Terry S, Vacherot F, Salomon L, Allory Y, Vordos D, Hoznek A, Yiou R, Patard JJ, Abbou CC, de la Taille A
Department of Urology, CHU Mondor, Créteil, France
Eur Urol. 2009; 55: 600-6

Background: Prevalence of prostate cancer (PCa) after a negative first extended prostate needle biopsy protocol is unknown.
Objective: To evaluate the prevalence of significant PCa in patients who have had a negative first extended prostate biopsy protocol.
Design, Setting, and Participants: Between March 2001 and May 2007, 2500 consecutive patients underwent an extended protocol of 21 biopsies. Of 953 patients who had a negative first extended prostate biopsy procedure, 231 patients underwent a second or more set of 21-core biopsies. Indications for repeated biopsies were persistently elevated prostate-specific antigen (PSA), PSA increase during the follow-up, or prior prostatic intraepithelial neoplasia (PIN), or atypical small acinar proliferation (ASAP).
Intervention: All participants underwent at least two extended prostate needle biopsy protocols.
Measurements: Clinical and pathologic factors (age, PSA, PSA doubling time, PIN, ASAP, digital rectal exam [DRE]) were analyzed for their ability to predict positive biopsy, and tumour parameters were assessed in patients undergoing radical prostatectomy.
Results and Limitations: Second, third, and fourth extended 21-sample biopsy procedures yielded a diagnosis of PCa in 18%, 17%, and 14% of patients respectively. Patients with prior PIN had 16% risk of prostate cancer; patients with ASAP had a 42% risk. The mean number of positive cores was 2.19. Prostate volume and PSA density were statistically significant predictors of positive biopsy ($p<0.05$). For the 43 patients who underwent radical prostatectomy, pathologic findings revealed mean Gleason score of 6.7 (6-8), pT2a-c in 72%, pT3a in16%, and pT4 in 7%. Mean cancer volume was 1.15 cc and 85.2% of tumours were clinically significant (tumour volume > 0.5 cc, Gleason > or = 7 and/or pT3).
Conclusions: Negative first extended biopsies should not reassure a patient of not having PCa. However, prostate cancers detected after two or more sets of extended procedures, appear to be localized (intracapsular disease) and well-differentiated prostate cancers, although they are still clinically significant.

Editorial Comment

The authors report on a large series of extended 21-sample needle biopsies in 2500 consecutive patients with suspect prostate cancer.

There are several interesting issues for the clinician. First, this procedure was done in an outpatient 2-hour setting with local anesthesia. Next, the results show that with each new round of biopsies roughly 15% of cancers are detected (18%, 17%, 14% for the second, third and forth biopsy procedure, respectively). This leads to the conclusion that in case of continued suspicion the urologist and his/her patient should not give up. Notably, most of these cancers were significant (82.5%). Of the 58 cancers diagnosed, 65% had PSA levels between 4 and 10 ng/ml. Seventy-six percent and 10% had biopsy Gleason sum 6 and 7a (3+4), respectively. Interestingly, of those 43 patients from this group who underwent radical prostatectomy 30% had Gleason sum score 6 and roughly 60% had Gleason sum score 7a, again suggesting an undergrading in core biopsies.

There are much more details and I recommend the paper for reading.

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

Analysis of T1c prostate cancers treated at very low prostate-specific antigen levels

Stephenson AJ, Jones JS, Hernandez AV, Ciezki JP, Gong MC, Klein EA
Section of Urologic Oncology, Glickman Urological and Kidney Institute, Department of Quantitative Health Sciences, Cleveland Clinic Foundation, Cleveland, Ohio, USA
Eur Urol. 2009; 55: 610-6

Background: The Prostate Cancer Prevention Trial (PCPT) has challenged the validity of recommended prostate-specific antigen (PSA) thresholds for prostate biopsy (> 2.5 ng/ml) given the 17% prostate cancer (pCA) detection rate at PSA of 1.1-2.0. The outcome of patients treated at PSA < or = 2.5 is poorly defined, and advantages associated with such an early diagnosis are uncertain.
Objective: Compare the outcome of patients with T1c pCA with pretreatment PSA < or = 2.5 and 2.6-4.0.
Design, Setting, And Participants: Since 1998, 351 patients with clinical stage T1c and PSA < or = 4.0 have been treated at our institution; 84 (24%) of those patients had PSA < or = 2.5. Clinical information was obtained from a prospective database. Treatment was radical prostatectomy (RP), brachytherapy, and external-beam radiotherapy (EBRT) in 261 (74%), 67 (19%), and 23 (7%) patients, respectively.
Intervention: Definitive therapy for clinically localized pCA.
Measurements: Progression-free probability and pathologic end points.
Results and Limitations: No significant differences between the groups were observed in terms of biopsy (18% vs 22%) or specimen Gleason score 7-8 (44% vs 56%), non-organ-confined cancer (11% vs 13%), indolent cancer (34% vs 24%), or 5-yr progression-free probability (89% vs 93%; p>0.1 for all). More biologically unimportant cancers (defined as pathologically organ-confined and Gleason < or = 6) were identified among patients with PSA < or = 2.5 (55% vs 41%, p=0.050), and indolent cancers were three times more frequent than non-organ-confined cancers among these patients (p=0.003).
Conclusions: The pathologic features and outcome of patients treated at low PSA levels are favorable and similar for patients with PSA < or = 2.5 versus 2.6-4.0. However, > 50% of the former have potentially biologically unimportant cancer. We failed to identify a therapeutic benefit to the diagnosis of cancers below accepted PSA thresholds for biopsy.

Editorial Comment

The debate of lowering the threshold for biopsy in patients with a low PSA is still active and gets some support from this paper. The authors compare the results from two cohorts of patients with low PSA, namely < 2.5 ng/ml and 2.5-4 ng/ml. They did not find any significant differences between these groups but further data in this paper are of interest. Taken together both groups, 21% of these patients had biopsy Gleason sum scores 7 or 8, whereas 53% had specimen Gleason scores 7-8, again suggesting undergrading in biopsies. 12% had non-organ confined cancers and 12 % had positive surgical margins.

Altogether these and other data (e.g. from the PCPT trial) suggest that the threshold for performing biopsies is rather low and should include more factors than PSA alone.

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

NEUROLOGY & FEMALE UROLOGY

Prevalence of Ureaplasma urealyticum and Mycoplasma hominis in women with chronic urinary symptoms

Baka S, Kouskouni E, Antonopoulou S, Sioutis D, Papakonstantinou M, Hassiakos D, Logothetis E, Liapis A
Department of Biopathology, Aretaieion Hospital, University of Athens, Athens, Greece
Urology. 2009; 74: 62-6

Objectives: To assess the prevalence of Ureaplasma urealyticum and Mycoplasma hominis in women experiencing chronic urinary symptoms.
Methods: Urine, vaginal, and urethral samples obtained from 153 women presenting with chronic voiding symptoms were tested for the presence of pathogens including U. urealyticum and M. hominis. Patients with positive cultures for Mycoplasma were treated with a single dose of 1 g azithromycin and followed up 1 month after therapy. Patients with persistent infection received 100 mg doxycycline orally, twice daily for 7 days, according to the results of the susceptibility test. The patients were asked to rate the severity of their symptoms at their initial visit and after treatment.
Results: U. urealyticum was detected from > or =1 site in 81 women (52.9%), and M. hominis was detected in 5 patients (3.3%), always in association with U. urealyticum. At follow-up, 77 patients (95.1%) initially positive for Mycoplasma had negative cultures; the cultures of 4 (4.9%) remained positive for U. urealyticum and became negative after the second therapeutic regimen. A significant improvement in all symptoms was observed in women with positive cultures for Mycoplasma after therapy.
Conclusions: A high prevalence of U. urealyticum was observed in women with unexplained chronic voiding symptoms. Testing for the presence of U. urealyticum and M. hominis in the urogenital tract could prove valuable for the management of a significant percentage of chronic urinary symptoms in women through appropriate treatment.

Editorial Comment

The authors present an excellent paper associating the presence of urinary tract infection with urinary symptoms. They denoted that with the appropriate diagnosis and therapy urinary symptoms would resolve. The authors noted that the presence of organisms usually associated with vaginal colonization in the urinary tract may represent an infection causing the urinary symptoms and that appropriate therapy of same with susceptibility testing would resolve these symptoms. This dogmatic approach to therapy helps reaffirm the need for appropriate and diligent clinical diagnosis and therapy in this patient population. It further bolsters the empirical approach previously described by Burkhard et al. (1). Both discuss the consideration for treatment of the sexual partner. It is hoped that future resistance patterns will not lesson the effectiveness of doxycycline, the antibiotic both reports found to be efficacious with this patient diagnosis.

Reference

1. Burkhard FC, Blick N, Hochreiter WW, Studer UE: Urinary urgency and frequency, and chronic urethral and/or pelvic pain in females. Can doxycycline help? J Urol. 2004; 172: 232-5

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

Complications of mid urethral slings: important outcomes for future clinical trials

Daneshgari F, Kong W, Swartz M
Department of Urology and Female Pelvic Surgery, Upstate Medical University, Syracuse, New York, USA
J Urol. 2008; 180: 1890-7

Purpose: Mid urethral slings are becoming the first line surgical treatment for stress urinary incontinence in women. We reviewed the complications of mid urethral sling placement and their potential pathophysiology.
Materials and Methods: We conducted a literature search on MEDLINE from 1995 to 2007 using the key words sling, complications, mid-urethral slings, transvaginal tape, transobturator tape, trials, pathophysiology and complications. The Cochrane database was also searched. The results were summarized according to the type of mid urethral slings reported.
Results: There were 928 MEDLINE citations for sling and complications, 279 for sling and complications and bladder, and 68 for sling and complications and voiding dysfunction. The reported complication rates ranged from 4.3% to 75.1% for retropubic and 10.5% to 31.3% for transobturator mid urethral slings. Complications included bladder perforation, hemorrhage, bowel injury, vaginal extrusion, de novo urgency and urge incontinence, urinary tract infections and voiding dysfunction. Retropubic mid urethral slings led to a higher occurrence of complications such as bladder perforation and hematoma. In addition, the retropubic approach resulted in serious complications such as bowel injury, major vascular injury and death. Groin pain was more common after the transobturator approach. Experimental studies indicated that the potential mechanisms for sling complications may include vaginal dissection, denervation injury and bladder remodeling.
Conclusions: Mid urethral slings result in bothersome complications which should not be minimized. Awareness of these complications should encourage improvements in patient counseling as well as further investigation of the underlying mechanisms. Decreasing complications should be considered an important outcome for future clinical studies of mid urethral slings.

Editorial Comment

A noted authority in the field presents a broad spanning review of potential complications of what has probably become the most popular method of treating female stress urinary incontinence. Though the authors did not report any instances of bowel perforation with a transobturator sling, our institution is preparing a case report on a colon injury associated with a transobturator tape procedure so this complication may and does occur. If history serves as a guide, with the increased used of mid urethral slings the breath and depth of complications reported will expand. Of note is the somewhat high rate of new onset urinary urge incontinence associated with a retropubic mid urethral sling. This relatively high rate of urinary urgency was previously noted in the past when reviewing the work of Alperin et al (1). This rate of de novo urgency should be taken in historical context and compared to discussions on this occurrence in the past (2).

References

1. Alperin M, Abrahams-Gessel S, Wakamatsu MM: Development of de novo urge incontinence in women post sling: the role of preoperative urodynamics in assessing the risk. Neurourol Urodyn. 2008; 27: 407-11.
2. McGuire E: Bladder instability and stress incontinence. Neurourol Urodyn. 1988; 7: 563-7.

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

Age at orchiopexy and testis palpability predict germ and Leydig cell loss: clinical predictors of adverse histological features of cryptorchidism

Tasian GE, Hittelman AB, Kim GE, DiSandro MJ, Baskin LS
Department of Urology, University of California-San Francisco, San Francisco, California, USA
J Urol. 2009; 182: 704-9

Purpose: We determined the relationship between clinical variables and testicular histopathological changes associated with decreased fertility potential in children with cryptorchidism.
Materials and Methods: Testis biopsies of 274 children who underwent orchiopexy and concurrent testicular biopsy between 1991 and 2001 were analyzed for germ and Leydig cell loss, and testicular fibrosis. Multivariable logistic regression was used to determine if age at orchiopexy (analyzed as continuous and ordinal variables), preoperative testis palpability, unilateral vs bilateral disease and/or side of undescended testis was predictive of these pathological outcomes.
Results: Age at orchiopexy was associated with germ and Leydig cell depletion. Each month of testis undescent was associated with development of moderate/severe germ cell depletion (OR 1.02 for each month of age, $p < 0.005$) and Leydig cell loss (OR 1.01 for each month of age, $p < 0.02$). Nonpalpable testes were associated with severe germ cell depletion. Children with palpable testes had lower odds of germ cell depletion than those with nonpalpable testes (OR 0.46, $p < 0.005$). This finding corresponds to a significant 2% risk per month of severe germ cell loss and 1% risk per month of Leydig cell depletion for each month a testis remains undescended, and a 50% greater risk of germ cell depletion in nonpalpable relative to palpable cryptorchid testes.
Conclusions: Testes that remain undescended are associated with progressive loss of germ and Leydig cells, and nonpalpable testes predict severe germ cell loss.

Editorial Comment

This is an 11-year study. Patients under 18 underwent orchiopexy with a concurrent testicular biopsy. The pathologic specimens were graded on the degree of tubular fibrosis, average number of germ cells per tubule and presence or absence of Leydig cells. Patients were grouped into 4 groups by age, 0-12 months, 13-24 months, 25-96 months, and greater than 96 months. They also had an ordinal statistical analysis.

Of the 274 patients included in the study, 68% had unilateral cryptorchidism and 32% had bilateral. The mean age was 43.6 months with a range of 1-209 months. 172 of the patients had palpable testes and 102 were non-palpable. Forty-five were intra-abdominal testes. After adjusting for variables, each month of undescended state of the testis was associated with germ cell depletion with an odds risk of 1.02 for each month. The p-value was less than 0.005 and Leydig cell loss had an odds risk ratio of 1.01 for each month with a p-value of 0.02. There was no association found between testis palpability and the absence of Leydig cells. Fibrosis was not associated with testis location or patient age. There was no pathologic correlation associated with laterality or with unilateral bilateral disease.

The results suggest a significant 2% risk per month for germ cell depletion and 1% risk per month for Leydig cell loss after the first year of life, this confirms current practice patterns of suggesting early orchiopexy for the best long-term results. Of note, the patient age in the study was older than usual practice with a mean of 43.6 months. I also wish that the authors and journal had included more data. Since 40% of their patients were younger than 18 months, this means that there was just over 1 patient per month in all of the months studied. It would be helpful to understand the statistics better and the data distribution to be certain that the statistical outcomes are correct.

The greatest concern for papers predicting outcome of undescended testes is that they are just that, predictions. It takes an extremely long study to actually document fertility and paternity and the threshold of Leydig cell depletion which affects adult hormone function is not clear.

Dr. Brent W. Snow
Division of Urology
University of Utah Health Sci Ctr
Salt Lake City, Utah, USA
E-mail: brent.snow@hsc.utah.edu

Abnormal renal scans and decreased early resolution of low grade vesicoureteral reflux

Nepple KG, Knudson MJ, Austin JC, Cooper CS
Division of Pediatric Urology, University of Iowa, Iowa City, Iowa, USA
J Urol. 2008; 180: 1643-7

Purpose: Limited studies suggest a relationship between scarring on renal scan and failure to resolve vesicoureteral reflux. We evaluated the impact of abnormal renal scans on early vesicoureteral reflux resolution.
Materials and Methods: The medical records and renal scans were reviewed of children diagnosed with primary reflux between 1988 and 2004. We defined an abnormal renal scan as renal scarring or relative renal function 40% or less. Reflux resolution was noted 1 and 2 years after diagnosis.
Results: Renal scan data were available on 161 children with vesicoureteral reflux, including 127 girls and 34 boys. Relative renal function was 15% or less in 7 children, 16% to 35% in 14, 36% to 40% in 18 and greater than 40% in 122. Of the 161 patients 79 (43%) had an abnormal renal scan, including 37% with grades 1 to 3 reflux. The rate of 2-year reflux resolution in the abnormal and normal renal scan groups was 13% vs 53%. Of children with grades II and III reflux those with an abnormal renal scan were less likely to have reflux resolution compared to those with normal renal scans (23% vs 55% and 4% vs 41, respectively, $p < 0.05$). The same relationship was present at 1 year for grades 2 and 3 (18% vs 49% and 4% vs 30, respectively, $p < 0.05$).
Conclusions: Abnormal renal scans are an important independent predictor of early failure to resolve vesicoureteral reflux. An abnormal renal scan should be considered when counseling families about the likelihood of early reflux resolution. Performing a renal scan may be indicated in select patients.

Editorial Comment

This research deals with 16 years of reflux studies in which patients had a renal scan and a VCUG. Demographic variables as well as voiding dysfunction were noted and compared. One hundred and sixty-one patients had a renal scan and all of the recurred data for the study. Four different kinds of renal scans were used over this long data collection period, including glucoheptonate, Mag3, DMSA and DPTA. Relative renal function was judged to be poor if it were less than 40% and abnormal renal scans were noted if there were renal scars, even if the relative renal function was normal.

Seventy children, 43.5%, had abnormal renal scans and 91 children had normal renal scans. Boys had a few more abnormal renal scans than girls did but this did not reach statistical significance. The incidence of voiding dysfunction between normal and abnormal renal scans was the same. Abnormal renal scans were more prevalent in higher grades of reflux and this reached a p value of less than 0.001. There was not a statistical difference between different kinds of renal scans.

Reflux spontaneous resolution rate was 29.8% at 1 year and 35.4% at 2 years and 33 children in the study group underwent corrective surgery within the first two years. Of the patients with diminished relative

renal function, 10% had VUR resolution and in the normal renal function group, 43% had resolution with p value of less the 0.001. Reflux grades were not compared in Grade IV and V patients because so many of them had abnormal renal scans and the resolution rate had a negative correlation with the abnormal renal scans in Grade I-III. None of the patients with abnormal renal scans and voiding dysfunction had resolution in the first 2 years.

The management of vesicoureteral reflux is multifaceted and the time where the greater the reflux allowed simple surgical decisions to be made is long past. This study shows that previous kidney scarring for relative poor kidney function has an impact on vesicoureteral reflux resolution at least in the first two years. This study unfortunately used four different kinds of renal scans but this did not seem to alter the statistics. It is probably best at this time to recognize that preventing the kidney scars is the purpose of reflux treatment and reflux is only one factor to consider among others such as kidney scarring and bladder dysfunction.

The longest follow up was two years and it would be most interesting to see what the five-year follow up data would be.

Dr. Brent W. Snow
Division of Urology
University of Utah Health Sci Ctr
Salt Lake City, Utah, USA
E-mail: brent.snow@hsc.utah.edu