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UROLOGICAL SURVEY

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EDITORIAL COMMITTEE

STONE DISEASE

Percutaneous nephrolithotomy for caliceal diverticular calculi: a novel single stage approach

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Purpose: Current percutaneous treatment of symptomatic caliceal diverticular calculi involves renal access, stone removal, dilation of the diverticular communication, fulguration of the cavity and placement of a nephrostomy tube. We reviewed the outcomes of patients undergoing a novel single stage percutaneous nephrolithotomy technique for radiopaque caliceal diverticular stones that eliminates ureteral catheterization and entry into the renal collecting system.

Materials and Methods: A total of 21 patients (8 male and 13 female including 1 bilateral) with a mean age of 42.4 years underwent percutaneous nephrolithotomy for caliceal diverticular stones from February 2001 to May 2003. Of the diverticula 12 were upper pole, 4 were interpolar and 6 were lower pole. Infracostal access was established by the urologist directly onto the radiopaque stones without the aid of a ureteral catheter. After balloon tract dilation a 30Fr Amplatz sheath was placed and following stone removal the diverticulum was fulgurated. The infundibulum was neither cannulated nor dilated. A 20Fr red rubber catheter or an 8.5Fr Cope loop was placed into the diverticulum. Stone-free status was assessed by noncontrast computerized tomography on postoperative day 1 (POD1). The drainage tube was removed if there was no urine drainage and the kidney was stone-free. Excretory urography was performed at 3 months to evaluate diverticular resolution.

Results: Of 21 patients 20 were discharged home tubeless on POD1 and 18 of 21 (85.7%) renal units were stone- free on POD1 noncontrast computerized tomography. Mean operative time was 58.5 minutes and mean stone burden was 138.9 mm. Mean stone diameter was 11.6 mm and mean diverticular diameter was 15.3 mm. Of 22 renal units 16 had followup excretory urography. All diverticula decreased in size and 14 (87.5%) had complete resolution.

Conclusions: In patients with symptomatic radiopaque caliceal diverticular stones, a single stage procedure without the need for ureteral catheterization combined with direct infracostal diverticular puncture allows for a rapid procedure with little morbidity.

Editorial Comment

A variety of minimally invasive treatment options is available for the treatment of stone-bearing caliceal diverticula, including SWL, ureteroscopy, PCNL and laparoscopy. Among these, the percutaneous approach has been shown to offer the most consistent stone-free, symptom-free and diverticulum-free results. However, there is no consensus as to the optimal technique for management of the diverticulum or the diverticular neck. While most investigators recommend fulguration of the diverticulum, some additionally advocate identification and treatment of the diverticular neck with dilation or endoincision to assure drainage from a persistent diverticular cavity in the event ablation fails. Others, however, feel that treatment of the cavity is sufficient and recommend no treatment of the neck, since treatment adds time and risk to the procedure, primarily by way of bleeding, and generally necessitates placement of a transdiverticular drainage tube for a few days to a week to assure a patent tract.

Although outcomes with the various percutaneous approaches have been excellent, Kim and colleagues challenge the need for additional retrograde access to facilitate identification and treatment of the diverticular neck by advocating simple subcostal access to the diverticulum, fragmentation/removal of the stone and fulguration of the cavity without addressing the diverticular neck. With this approach, a stone free rate of 86% was achieved,

and in 88% of cases the diverticulum resolved completely or was reduced in size. This approach has the advantage of avoiding a supracostal approach in most cases of upper pole diverticula since access into the collecting system is not necessary and consequently a cephalad-directed access tract, below the 12th rib, will provide adequate access to the diverticulum. Although symptomatic outcomes were not addressed in this study, it is probably safe to assume that at least the 88% of patients rendered stone free and in whom the diverticulum resolved are symptom-free. Of note, the key to the success of these difficult cases is in the access. Provided the stone is visible to provide a target for percutaneous puncture, this approach can be successful. However, in some cases the diverticulum is difficult to identify fluoroscopically without the aid of retrograde instillation of contrast to opacify the diverticulum, in which case, a ureteral catheter or occlusion balloon can be a welcome aid.

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Emergency extracorporeal shockwave lithotripsy for acute renal colic caused by upper urinary-tract stones

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Purpose: To evaluate emergency SWL for the treatment of upper urinary-tract stones causing renal colic.

Patients and Methods: Between January 1999 and June 2003, 53 patients with a mean age of 46.6 years (range 22-65 years) were enrolled. The inclusion criteria were acute renal colic, radiopaque 5-mm to 1.5-cm calculi in the ureteropelvic junction (N=10) or upper ureter (N=43), and no evidence of urinary-tract infection or acute renal failure. The mean stone size was 7.14 mm (range 5-13 mm). Patients were randomly assigned to the control (N=28) and study (N=25) groups using previously prepared cards in envelopes. Patients in the study group underwent emergency SWL, while patients in the control group underwent scheduled SWL within 30 days. Stone status was evaluated 4 weeks after lithotripsy. There was no significant difference between the control and study groups with respect to age, sex, stone location or volume, renal obstruction, or days spent in the hospital for pain control. Available fragments of stones were sent for infrared spectroscopy. Preoperative and postoperative data were compared in the two groups using SPSS 10.0 statistical software.

Results: The SWL treatment lasted 50 +/-11 minutes. The stone-free rates were 72% and 64% and the efficiency quotients were 53% and 44% in study and control groups, respectively. Patients in the control group spent more time in the hospital (P=0.014) and in recovery at home (P=0.011).

Conclusion: Emergency SWL for acute renal colic caused by upper-ureteral stones is a safe procedure and offers effective release from pain and obstruction. It also decreases hospitalization days and hastens return to normal activity.

Editorial Comment

In most patients, acute renal colic resolves within 24-48 hours, and thus when treatment of an obstructing stone is deemed necessary, the procedure can be scheduled electively. However, symptoms may recur, are unpredictable and can necessitate repeat emergency room or office visits prior to planned treatment. As such, for patients experiencing acute renal colic who have a low likelihood of spontaneous stone passage, acute treatment may be desirable. However, it is not clear if SWL success rates are compromised by the state of acute colic or if pain resolves promptly with SWL treatment.

Kravchick and colleagues randomized 53 patients with acute renal colic due to 5 to 15 mm isolated UPJ or proximal ureteral calculi to undergo “emergency” SWL (within 48-72 hours) or elective SWL (within 30 days). Stone free rates, need for retreatment and auxiliary procedure rates were comparable between the 2 groups; however, the group treated “emergently” required fewer days in the hospital and missed fewer work days compared with the group treated electively. Furthermore, no patients treated “emergently” required upper tract drainage compared with 2 patients in the electively treated group. Unfortunately, time to resolution of obstruction was not addressed.

This study suggests that SWL treatment of patients during or within a short time of an episode of acute renal colic avoids unnecessary pain or need for intervention without compromising stone free rates. Other investigators have likewise demonstrated that SWL treatment of patients with high grade or complete obstruction is associated with acceptable stone free rates and results in resolution of the obstruction in most patients within 72 hours, thereby confirming the safety and efficacy of treatment under conditions of acute renal colic and/or obstruction (1,2).

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ENDOUROLOGY & LAPAROSCOPY

Evolution of hand-assisted laparoscopic surgery

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J Endourol. 2005; 19: 133-5

The authors described the history of the first hand assisted splenectomy and nephrectomy, as well as, then the development of hand assisted devices and laparoscopic equipment. The use of laparoscopic endo-GI staplers was not universally accepted among surgeons creating controversy, instrument that became standard in all major laparoscopic ablative surgery.

This manuscript also helps us to understand the importance of societies, associations and their specific publications to better disseminate information, ideas and technology.

Editorial Comment

Since the first laparoscopic procedure was performed in intrabdominal organs, technology and techniques evolved including the hand-assisted laparoscopic surgery. This paper describes the complexity of developing new surgical techniques and the roadblocks that one may encounter despite the efficient surgical team and

willingness of a group of surgeons and their institution. The authors also illustrate the importance of specific societies that can promote the dissemination of ideas and information.

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Laparoscopic radical prostatectomy

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Purpose: After the pioneering period when only few teams were performing the procedure, the laparoscopic approach to radical prostatectomy has become widespread with several technical variations. A comprehensive review of the published literature on laparoscopic radical prostatectomy was performed to determine the current state of the art of this surgical innovation in terms of perioperative parameters, functional results and cancer control.

Materials and Methods: English language, peer-reviewed articles published before June 2004 concerning laparoscopic radical prostatectomy were found by MEDLINE query. All articles were analyzed and none was a priori excluded. Conclusions were drawn from series of 50 or more patients.

Results: Laparoscopic radical prostatectomy is being performed at multiple centers worldwide using various surgical approaches and technologies. Analysis of perioperative parameters, including surgical blood loss, operative time, complications and convalescence, demonstrated low morbidity and showed a clear trend toward improvement with increased experience. The reported positive surgical margin rates were lower in series that are more recent. As measured by prostate specific antigen recurrence and disease-free intervals, oncological results and cancer control rates are difficult to ascertain in the immature series published to date. Functional results in terms of postoperative urinary and sexual function appear encouraging.

Conclusions: Overall, the current operative, oncological and functional results of laparoscopic radical prostatectomy appear to approximate those of open radical retropubic prostatectomy. These results justify the considerable interest of the urological community in laparoscopy, as evidenced by its widespread application. Nevertheless, longer follow-up and more mature data are needed definitively to establish laparoscopic radical prostatectomy as an alternative to the retropubic approach.

Editorial Comment

It is clear that laparoscopic radical prostatectomy is a surgical technique that can be learned and reproduced anywhere in the globe. Long-term data is still lacking in terms of oncological safety but overall this is a technique that seems comparable to open retropubic prostatectomy.

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IMAGING

Correlation of proton MR spectroscopic imaging with Gleason score based on step-section pathologic analysis after radical prostatectomy

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Purpose: To determine whether hydrogen 1 magnetic resonance (MR) spectroscopic imaging can be used to predict aggressiveness of prostate cancer.

Materials and Methods: All patients gave informed consent according to an institutionally approved research protocol. A total of 123 patients (median age, 58 years; age range, 40-74 years) who underwent endorectal MR imaging and MR spectroscopic imaging between January 2000 and December 2002 were included. MR imaging and spectroscopy were performed by using combined pelvic phased-array and endorectal probe. Water and lipids were suppressed, and phase-encoded data were acquired with 6.2-mm resolution. Voxels in the peripheral zone were considered suspicious for cancer if (Cho + Cr)/Cit was at least two standard deviations above the normal level, where Cho represents choline-containing compounds, Cr represents creatine and phosphocreatine, and Cit represents citrate. Correlation between metabolite ratio and four Gleason score groups identified at step-section pathologic evaluation (3 + 3, 3 + 4, 4 + 3, and > or =4 + 4) was assessed with generalized estimating equations.

Results: Data from 94 patients were included. Pathologic evaluation was used to identify 239 lesions. Overall sensitivity of MR spectroscopic imaging was 56% for tumor detection, increasing from 44% in lesions with Gleason score of 3 + 3 to 89% in lesions with Gleason score greater than or equal to 4 + 4. There was a trend toward increasing (Cho + Cr)/Cit with increasing Gleason score in lesions identified correctly with MR spectroscopic imaging. Tumor volume assessed with MR spectroscopic imaging increased with increasing Gleason score.

Conclusion: MR spectroscopic imaging measurement of prostate tumor (Cho + Cr)/Cit and tumor volume correlate with pathologic Gleason score. There is overlap between MR spectroscopic imaging parameters at various Gleason score levels, which may reflect methodologic and physiologic variations. MR spectroscopic imaging has potential in noninvasive assessment of prostate cancer aggressiveness.

Editorial Comment

MR spectroscopic imaging of prostate provides metabolic data to the anatomical data obtained with conventional MR imaging. This technique has demonstrated an improvement in localizing cancer to a sextant of the prostate, estimating extracapsular extension, assessing the aggressiveness of prostate cancer and in localizing hidden suspicious areas of cancer in patients with rising PSA and negative prior biopsies. Specifically, MR spectra from regions of prostate cancer show a significant reduction or absence of citrate and polyamines, while choline is elevated relative to creatine resulting in significant changes in the (choline + creatine)/citrate ratio in regions of cancer . In this paper, the authors confirm previous study on the value of MR spectroscopic imaging as a noninvasive tool to assess prostate cancer aggressiveness. This is a very important contribution since prostate cancer aggressiveness is a key predictor of patient outcome. Several studies have shown that the biopsy results are limited in the determination of all cancer and Gleason grades. In the present study the authors' shows that when compared with radical prostatectomy results, biopsy was used to correctly predict the pathologic Gleason score in only 64% of patients, 27 % were upgraded and 9 % downgraded. Another interesting observation was that the tumor volume, as defined by the number of MR spectroscopic imaging positive voxels, was positively correlated with Gleason score. In other words, MR spectroscopic imaging measurements of prostate tumor (Cho + Cr) / Cit and tumor volume correlate with pathologic Gleason score.

In this study, they had a sub-optimal overall sensitivity of MR spectroscopic imaging for cancer Gleason 3+3. This results are very different from ours .We had a much higher sensitivity than 44% for the detection of tumor Gleason 3+3. One possible explanation is probably related to the fact that the authors used air in the endorectal coil. By switching the air to liquid perfluorocarbon, in the last 2 years, we were able to obtain much better MR spectra with superior metabolites discrimination and superior detection of tumor Gleason 3+3. Similarly to the authors we have found higher (Cho+Cr) / Cit ratios in patients with tumor with higher Gleason scores.

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Evaluation of the renal venous system on late arterial and venous phase images with MDCT angiography in potential living laparoscopic renal donors

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AJR Am J Roentgenol. 2005; 184: 539-45

Objective: The objective of our study was to assess whether both renal arteries and renal veins can be evaluated using single-phase MDCT data sets alone to eliminate the need for both arterial and venous phase data sets.

Materials and Methods: One hundred consecutive potential living renal donors who underwent 4-MDCT were evaluated. CT was performed with 120 mL of IV contrast material at an injection rate of 3 mL/sec. Both late arterial and venous phase acquisitions were obtained at 25 and 55 sec from the start of IV contrast injection, respectively. The number of the right and left renal veins and its anatomic variations were assessed by two reviewers. Late arterial phase images were evaluated initially, and then venous phase images were analyzed to assess opacification of the renal vein and to see whether venous phase data sets changed or added information about the venous anatomy as seen on late arterial phase images.

Results: The retroaortic left renal vein was found in two subjects, and the circumaortic left renal vein was detected in three subjects. The renal veins were adequately opacified on late arterial phase images in all subjects. There were six subjects who had a normal left renal vein with a small posterior branch coursing posterior to the aorta and draining into the inferior vena cava, which were difficult to differentiate from the lumbar vein or ascending lumbar vein; in three of these six subjects, the small posterior branch was opacified only on venous phase images.

Conclusion: Late arterial phase images obtained at 25 sec after the start of contrast injection can reveal the renal vein anatomy except for a small posterior branch of the left renal vein difficult to differentiate from the lumbar or ascending lumbar vein, as seen in three subjects. The data suggest that venous phase imaging is not necessary for the evaluation of renal vein anatomy.

Editorial Comment

Recently, several studies have shown that helical multidetector CT angiography has the potential to replace excretory urography and renal angiography in the evaluation of potential living renal donors. As we know this evaluation should include the assessment of renal arteries, renal parenchyma, collecting system and renal venous system. In order to obtain such complete evaluation several acquisitions should be used (pre-contrast and 25 sec, 70-80 sec, and 180 sec after the start of an intravenous injection of contrast material). It is evident that the radiation dose delivered to living donor will increase with the number of acquisition performed. The purpose of this paper was to assess whether both renal arteries and renal veins can be evaluated using single-phase helical multidetector CT angiography in an attempt to eliminate the need for both arterial and venous phases. The authors concluded the late arterial phase images obtained at 25 sec adequately demonstrated renal arteries and the right and left renal veins in all subjects, but in 7% and 16% of the patients they could not demonstrate the left adrenal vein and left gonadal vein. This can be considered a relatively limitation of this study since the adrenal vein and gonadal veins are tributary of the left renal vein in almost all individuals. For an adequate and global evaluation of the living donor who is going to be operated by a laparoscopic nephrectomy, some institutions, including ours, prefer the utilization of magnetic resonance imaging. MR-angiography presents 89.4% sensitivity, 94.1% specificity and 90.6% accuracy for the demonstration of the arterial anomalies. For demonstration of the venous anomalies MR-angiography has 98.3% sensitivity, 100% specificity and 98.4% accuracy. One of the greatest advantages of MR over CT angiography is the fact that MR does no use ionizing radiation. For these reason we can perform, as many acquisition are necessary in order to obtain a complete evaluation of the living donor. However, one of the main limitations of MR imaging is its inability to demonstrate urinary stones particularly those located in the renal parenchyma. This interesting study suggests that venous phase imaging is not necessary for the evaluation of renal vein anatomy. However, a large number of patients need to be studied using this single phase protocol in order to validate this conclusion.

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UROGENITAL TRAUMA

Selective nonoperative management in 1,856 patients with abdominal gunshot wounds: should routine laparotomy still be the standard of care?

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Ann Surg. 2001; 234: 395-402; discussion 402-3

Objective: To evaluate the safety of a policy of selective nonoperative management (SNOM) in patients with abdominal gunshot wounds.

Summary Background Data: Selective nonoperative management is practiced extensively in stab wounds and blunt abdominal trauma, but routine laparotomy is still the standard of care in abdominal gunshot wounds.

Methods: The authors reviewed the medical records of 1,856 patients with abdominal gunshot wounds (1,405 anterior, 451 posterior) admitted during an 8-year period in a busy academic level 1 trauma center and managed by SNOM. According to this policy, patients who did not have peritonitis, were hemodynamically stable, and had a reliable clinical examination were observed.

Results: Initially, 792 (42%) patients (34% of patients with anterior and 68% with posterior abdominal gunshot wounds) were selected for nonoperative management. During observation 80 (4%) patients developed symptoms and required a delayed laparotomy, which revealed organ injuries requiring repair in 57. Five (0.3%) patients suffered complications potentially related to the delay in laparotomy, which were managed successfully. Seven hundred twelve (38%) patients were successfully managed without an operation. The rate of unnecessary laparotomy was 14% among operated patients (or 9% among all patients). If patients were managed by routine laparotomy, the unnecessary laparotomy rate would have been 47% (39% for anterior and 74% for posterior abdominal gunshot wounds). Compared with patients with unnecessary laparotomy, patients managed without surgery had significantly shorter hospital stays and lower hospital charges. By maintaining a policy of SNOM instead of routine laparotomy, a total of 3,560 hospital days and US$9,555,752 in hospital charges were saved over the period of the study.

Conclusion: Selective nonoperative management is a safe method for managing patients with abdominal gunshot wounds in a level 1 trauma center with an in-house trauma team. It reduces significantly the rate of unnecessary laparotomy and hospital charges.

Editorial Comment

This is not a new article, but it is an important one. By now, everybody knows that many renal injuries can be treated nonoperatively: adult blunt injuries (1), pediatric blunt injuries (2), stab wounds (3), and even some gunshot wounds (4). Understanding some of the other ways that nonoperative (or “selective”) management of trauma patients has been applied can be very useful when managing your own patients. Here is a paper from a major US trauma center, and written by well-regarded general surgery traumatologists, regarding 1,856 patients with gunshot wound to the abdomen. At most centers, such wounds would be treated with 1,856 laparotomies. In this series, 1,046 (57%) patients that were hemodynamically stable, did not have peritonitis, and were examinable (no significant head injury, etc.) were admitted to the intensive care unit for observation. No laparotomy was performed unless the patients developed peritoneal signs or hypotension. Only 4% of patients developed these symptoms and had to undergo delayed laparotomy. The benefits of avoiding the unnecessary operations were obvious: unnecessary laparotomy rate decreased by 47% and observed patients enjoyed a speedier discharge from the hospital.

I think this study is amazing. Most of us that care for gunshot victims "know" that if you are shot in the abdomen you need a surgery. Clearly we were wrong. When you are trying to convince others or yourself to expand you own use of nonoperative therapy in those cases where it may be prudent (most hemodynamically stable renal injuries), remember this study.

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Transpelvic gunshot wounds: routine laparotomy or selective management?

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Mandatory exploration is the standard method for managing patients with gunshot wounds to the abdomen and back. This policy is associated with a high incidence of unnecessary laparotomies and significant morbidity. Reports from our center have shown that a policy of selective management, based on clinical findings, is safe in such patients. Patients with bullet trajectories that carry a high likelihood for intraabdominal organ injury may constitute a subgroup at particular risk. The need for routine or selective exploration in similar patients must be assessed. Therefore we decided to analyze patients with transpelvic gunshot wounds. The objective of the study was to examine if a policy of selective management of patients with transpelvic gunshot wounds is safe. This prospective study was conducted at an academic level I trauma center. We admitted 37 patients with transpelvic gunshot wounds over a 12-month period. All patients were managed according to a protocol that dictated laparotomy in the presence of significant clinical findings (peritoneal signs, hemodynamic instability, gross hematuria, rectal bleeding) and observation in the absence of the above. Additional diagnostic workup was performed only in appropriate cases rather than routinely. Nineteen (51.3%) patients were immediately operated on the basis of clinical findings. Sixteen of these laparotomies were therapeutic. Eighteen (48.6%) patients were initially observed. Subsequently, three of them underwent exploration for development of abdominal tenderness. All three laparotomies were nontherapeutic. The remaining 15 (40.5%) patients were successfully managed nonoperatively. There were no delays in diagnosis or missed injuries. Clinical examination had a sensitivity of 100% and specificity of 71.4% in detecting the need for laparotomy. A policy of selective management is thus safe, even for patients who suffer gunshot wounds with a high likelihood for intraabdominal organ injury. Clinical examination, supported by additional studies in appropriate cases, is the main method of selecting patients for operation or nonoperative treatment.

Editorial Comment

While the first paper deals with selective management of gunshot wounds to the back and abdomen, this paper centers on gunshot wounds to the pelvis. It is a much smaller study of only 37 patients, and as in the 2001 study cited previously, patients only had laparotomy if they had peritoneal signs, hemodynamic instability, gross hematuria or rectal bleeding. 51% got immediate operation and 49% were observed. 3/18 (17%) of those observed required exploration for peritoneal signs, but all 3 were nontherapeutic! So, once again this group turns what we know about trauma on its head. If you pick the correct physical exam signs to trigger surgery, you can avoid unnecessary laparotomy in about half of patients with gunshot to the pelvis. I must repeat, I think this is amazing. I think data such as this can give us the strength to "sin boldly" in our own world of genitourinary trauma, and determine which of our signs and symptoms predict who will not need operating.

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PATHOLOGY

Risk of prostate cancer on re-biopsy following a diagnosis of high-grade prostatic intraepithelial neoplasia (HGPIN) is related to the number of cores sampled

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Background: We aimed to determine whether the extent of needle biopsy sampling both on the initial biopsy that showed HGPIN and on re-biopsy would influence the detection rate of cancer.

Design: 4,237 patients with an initial diagnosis of only HGPIN on needle biopsy were identified; patients who in addition to HGPIN had a focus of atypical glands, suspicious for cancer were excluded. Of these, 937 patients had at least one follow up biopsy and were the subject of this study. The mean age was 67.5 (range from 39 to 87 years). The mean interval from diagnosis of HGPIN to rebiopsy was 4.8 months. In the initial biopsy resulting in a diagnosis of HGPIN, 371 men had > 8 cores (median 10; range 8-26) and 399 men had 6 core sampling.

Results: Not taking into account the number of cores on rebiopsy, in the 6 core initial sampling group, the risk of cancer on rebiopsy was 22.1% versus 15.1% in the > 8 core group (p value = 0.013). The table shows the combined influence of numbers of cores in the initial and rebiopsy sampling.

Group	N Cores 1st Biopsy	N Cores Rebiopsy	Risk of Cancer
1	6	6	29/173 (16.8%)
2	6	≥ 8	26/83 (32.4%)
2	≥ 8	≥ 8	44/285 (15.4%)

The differences between groups 1 and 3 as compared to group 2 were statistically significant ($p = 0.001$ and $p < 0.0001$, respectively).

Conclusions: Many cases of HGPIN on biopsy are associated with adjacent unsampled cancer. With relatively poor sampling (6 cores) on the initial biopsy, associated cancers are missed resulting in only HGPIN

on biopsy, and with relatively poor sampling on rebiopsy there is also a relatively low risk of finding cancer on rebiopsy. With poor sampling on the initial biopsy and better sampling on rebiopsy, some of these missed cancers are detected on rebiopsy yielding a higher detection of cancer. Sampling more extensively on the initial biopsy detects many associated cancers, such that when only HGPIN is found they often represent isolated HGPIN; rebiopsy even with good sampling does not detect many additional cancers. Our study demonstrates that the risk of cancer following a diagnosis of HGPIN (15.1%) is not that predictive of cancer on rebiopsy if good sampling (> 8 cores) is initially performed. Routine rebiopsy of men with HGPIN may not be necessary in the modern era of more extensive needle biopsy sampling.

Editorial Comment

The detection of adenocarcinoma on a re-biopsy varies from 23% to 79% (1). The study from the Johns Hopkins University shows a declining trend for this frequency. The authors clearly give the most important cause: sampling more extensively on the initial biopsy (extended biopsy) detects many associated cancers, such that when only high-grade intraprostatic neoplasia (HGPIN) is found they often represent isolated HGPIN; re-biopsy even with good sampling does not detect many additional cancers.

It is worth mentioning that HGPIN is different that ASAP; with the latter a re-biopsy is always indicated. ASAP was coined by Iczkowski, MacLennon & Bostwick (2) to refer to a condition when the pathologist is not sure with the diagnosis of adenocarcinoma. Unfortunately, many urologists equate the term ASAP with HGPIN and since the diagnosis of HGPIN has diminished relevance as a marker lesion to detect adenocarcinoma (as recent data seem to indicate), if the term ASAP is used by pathologists and misunderstood by urologists, a clinically significant suspicion for cancer may trigger a less than adequate clinical follow-up.

Considering these facts, a 2004 WHO-sponsored International Consultation Consensus held in Stockholm on prognostic and predictive factors and reporting of prostate carcinoma in prostate needle biopsy specimens, recommended to use the terms “suspicious or highly suspicious for adenocarcinoma” instead of ASAP.

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Current practice of Gleason grading among genitourinary pathologists

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There is consensus that the Gleason system should be used for grading of prostate cancer. However, a number of controversial issues remain as regards how this grading is applied. A questionnaire was sent to 91 genitourinary pathologists in countries around the world with the purpose to survey current practice of Gleason grading. The response rate was 74%, including 43 North American pathologists and 24 from other continents.

Of all participants, only 13% and 36%, respectively, ever diagnosed a Gleason score (GS) of 2 to 3 or 4 on needle biopsies (NBX), and 88% of those who did so assigned a GS 4 to < 1% of cancers. Cribriform Gleason pattern (GP) 3 was acknowledged by 88% but a majority of them would classify < or =20% of cribriform patterns as GP 3. One third only accepted cribriform or fusion patterns as GP 4, but two thirds also included incomplete or poorly defined glands. For GP 5 to be identified on NBX, 83% required clusters of individual cells, strands, or nests seen at less than x40 lens magnification. Only 26% defined GS on NBX as primary + tertiary GP, and a majority would mention a tertiary pattern separately. For NBX, global or highest GS was reported by 40% and 10%, respectively, whereas 46% only gave a separate GS for each individual NBX core. In conclusion, there is a need to standardize practical application of Gleason grading both in terms of interpretation of patterns as well as how grading is reported. Our survey data provide information to general pathologists about the most common grading practices among genitourinary pathologists.

Editorial Comment

The questionnaire clearly disclosed controversies among pathologists regarding how to report Gleason grading. During the annual meeting of the United States and Canadian Academy of Pathology (USCAP) held in San Antonio, Texas, 2005, a consensus meeting on Gleason grading was organized by JI Epstein. Over 70 urological pathologists were invited to attend and the result of the meeting shall be published in the American Journal of Surgical Pathology. Three recommendations are particularly useful for the urologist:

a) Gleason score 4 rarely is seen on needle biopsies and almost never the lesion is seen in its totality due to the thickness of the core, therefore, a note should be added to the report stating that the Gleason score probably is underestimated;

b) in case a tertiary grade is present on needle biopsies, the consensus of the group was to report the primary pattern and the highest grade as the secondary pattern. Example: grade 3 (60% of the area), grade 4 (30% of the area), grade 5 (10% of the area) - Gleason 3 + 5 = 8;

c) each core should be graded individually; the urologist should consider the highest score.

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INVESTIGATIVE UROLOGY

The Macedo-Malone antegrade continence enema procedure: early experience

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Purpose: The successful treatment of fecal incontinence can dramatically improve the quality of life of affected children. The introduction of the Malone antegrade continence enema provides the opportunity to manage previously resistant cases. However, using the appendix to create this catheterizable channel is not always possible, and the duration of these antegrade enemas is a source of concern for the patients. We describe a new approach to create left continent colonic access to shorten the duration of these enemas, and report the experience gained from the first 9 cases managed at our institution.

Materials and Methods: During a 5-year period 9 patients underwent a Macedo-Malone antegrade continence enema at our institution. Incontinence was associated with myelomeningocele in 7 patients and anorectal malformation in 2. The antegrade continence enema procedure is begun by isolating a 2 cm flap in a tenia on the left colon (spleen flexure). A 12Fr silicone Foley catheter is placed on the mucosal surface of the flap to allow tubularization of the plate with interrupted polyglycolic acid 3-zero transverse sutures, creating an efferent tubular conduit. Antegrade colonic washouts were started 2 weeks after surgery with saline solution or tap water in all patients.

Results: Followup of our 9 cases ranged from 8 to 33 months (average 20.7). Enema volume varied from 250 to 800 ml, with administration taking from 45 to 60 minutes, and colonic evacuation occurred within 30 to 60 minutes of enema administration. Of the 9 patients 8 were completely continent and 1 was partially continent. Four patients experienced difficulty with catheterization initially because of stenosis of the stomal track. The affected stomas were dilated, which was successful in 1 case. Three patients subsequently required stomal revision.

Conclusions: The Macedo-Malone procedure is a relatively straightforward operative approach providing an effective washout technique that is acceptable to parents and children.

Editorial Comment

After extensive investigation in animals, the authors transposed to clinical setting their experience with a new approach to create left continent colonic access to shorten the duration of antegrade enemas for children who have not only urinary incontinence, but also have problems of fecal elimination. Macedo & Srougi (1) described a continent catheterizable ileum based reservoir in which a catheterizable conduit could be created in continuity with the augmented segment. The Macedo-Malone procedure incorporates some of the same principles that have proved reliable in urinary diversion. The authors initially demonstrated that this procedure in the left colon might significantly decrease the time required for enema administration and washout, thereby increasing patient satisfaction and compliance. The authors have to be congratulated on this new technique to antegrade enemas, based on a solid previous basic investigation in animals.

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Urinary glycosaminoglycan excretion during the menstrual cycle in normal young women

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J Urol. 2005; 173: 1789-92

Purpose: We investigated whether the menstrual cycle affects urinary glycosaminoglycan (GAG) excretion in normal young women.

Materials and Methods: Urine samples from 10 healthy women 19 to 21 years old were collected daily during the whole menstrual cycle. Concentration of total urinary GAG was assessed as μg hexuronic acid per mg creatinine. Proportions of sulfated GAG species were determined by agarose gel electrophoresis.

Results: Mean excretion values +/- SD for period days 4 to 13 and 15 to 28 of the cycle were significantly different (0.445 +/- 0.041 vs 0.356 +/- 0.035 microg/mg, $p < 0.001$). Correlation between values for the first and second halves of the cycle showed that this difference was consistent irrespective of individual variations in GAG excretion ($r = 0.9757$, $p < 0.001$). Proportions of urinary sulfated GAG did not change during the cycle.

Conclusions: Excretion of total urinary GAG during the normal menstrual cycle of young women has a biphasic pattern with significantly higher values occurring in the first half of the cycle. This variation implies modulation by estrogens and consequently it should be considered when comparing the GAG concentration in urine samples from women of childbearing age.

Editorial Comment

In the current study urine samples were obtained on a daily basis from a highly homogeneous group of donors. The authors isolated total GAG from these samples, thereby, eliminating other metabolites. The results showed a significant increase in total urinary GAG excretion in the first half of the cycle, which paralleled the normal increase in serum estrogen levels that occurs at this phase. In general, estrogen inhibits the synthesis of extracellular matrix molecules by many mesenchymal cell types, such as vascular smooth muscle cells. Such inhibition would shift normal proteoglycan turnover toward degradation, which could explain the increase in GAG urinary excretion that was found in the first half of the cycle.

It was not observed significant variation in the relative concentration of sulfated GAG during the different phases of the cycle. On the other hand, the results indicate that heparan sulfate was the prevailing urinary GAG during the whole cycle. Because heparan sulfate is the most abundant GAG in the glomerulus, the present findings support the hypothesis that renal structures are one of the main sources of urinary GAG.

Worth of attention, is the fact that pathogenesis of interstitial cystitis is usually related to alterations in the GAG urothelial layer, which would allow the permeation of irritant urinary components into the vesical wall. Several reports have shown abnormal urinary GAG excretion in patients with interstitial cystitis, although the results are conflicting. Accordingly, urinary GAG levels in female patients may be decreased, unaltered or significantly increased. In these reports controls usually consisted of urine samples from healthy women of childbearing age. However, the dates of the menstrual cycle in which these control samples were collected were not provided. Since the results of the present work indicate that urinary GAG excretion during the normal menstrual cycle has a significant and consistent variation, studies evaluating GAG excretion in women could lead to misleading or erroneous results if comparisons were made among samples taken from different phases of the cycle. This may be indeed the reason underlying the inconsistent results in previously published reports.

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RECONSTRUCTIVE UROLOGY

A randomized controlled trial of duloxetine alone, pelvic floor muscle training alone, combined treatment and no active treatment in women with stress urinary incontinence

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J Urol. 2005; 173: 1647-53

Purpose: We primarily compared the effectiveness of combined pelvic floor muscle training (PFMT) and duloxetine with imitation PFMT and placebo for 12 weeks in women with stress urinary incontinence (SUI). In addition, we compared the effectiveness of combined treatment with single treatments, single treatments with each other and single treatments with no treatment.

Materials and Methods: This blinded, doubly controlled, randomized trial enrolled 201 women 18 to 75 years old with SUI at 17 incontinence centers in the Netherlands, United Kingdom and United States. Women averaged 2 or more incontinence episodes daily and were randomized to 1 of 4 combinations of 80 mg duloxetine daily, placebo, PFMT and imitation PFMT, including combined treatment (in 52), no active treatment (in 47), PFMT only (in 50) and duloxetine only (in 52). The primary efficacy measure was incontinence episode frequency. Other efficacy variables included the number of continence pads used and the Incontinence Quality of Life questionnaire score.

Results: The intent to treat population incontinence episode frequency analysis demonstrated the superiority of duloxetine with or without PFMT compared with no treatment or with PFMT alone. However, pad and Incontinence Quality of Life analyses suggested greater improvement with combined treatment than single treatment. A complete population analysis demonstrated the efficacy of duloxetine with or without PFMT and suggested combined treatment was more effective than either treatment alone.

Conclusions: The data support significant efficacy of combined PFMT and duloxetine in the treatment of women with SUI. We hypothesize that complementary modes of action of duloxetine and PFMT may result in an additive effect of combined treatment.

[Drug therapy of female urinary incontinence]

[Article in German]

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Urologe A. 2005; 44: 244-55

Drug treatment for female urinary incontinence requires a thorough knowledge of the differential diagnosis and pathophysiology of incontinence as well as of the pharmacological agents employed. Pharmacotherapy has to be tailored to suit the incontinence subtype and should be carefully balanced according to efficacy and side effects of the drug. Women with urge incontinence require treatment that relaxes or desensitizes the bladder (antimuscarinics, estrogens, alpha-blockers, beta-mimetics, botulinum toxin A, resiniferatoxin, vinpocetine), whereas patients with stress incontinence need stimulation and strengthening of the pelvic floor and external sphincter (alpha-mimetics, estrogens, duloxetine).Females with overflow incontinence need reduction of outflow resistance (baclofen, alpha-blockers, intrasphincteric botulinum toxin A) and/or improvement of bladder contractility (parasympathomimetics). If nocturia or nocturnal incontinence are the major complaints, control of diuresis is obtained by administration of the ADH analogue desmopressin. Future developments will help to further optimize the pharmacological therapy for female urinary incontinence.

Editorial Comment

Almost a year after the introduction of duloxetine.

In the past the possibilities to treat female urinary stress incontinence with drugs was almost impossible. A drug treatment requires knowledge of differential diagnosis and pathophysiology beside the pharmacologic influence of the used drug.

Women with urinary stress incontinence need stimulation and strengthening of the external sphincter and the pelvic floor, which can be aimed by the one or the other drug (duloxetine, estrogen, alpha-mimetics).

Although duloxetine is so fare only approved in Europe the recommendation of the third international Consultation of Incontinence (2004) concluded, “there is level 1B evidence to suggest that women with stress incontinence should have pelvic floor muscle training (PFMT) alone or in combination with a serotonin-norepinephrine reuptake inhibitor before they are forwarded to an other special treatment (surgery)”.

In the recent published study of Ghoneim et al. the influence of the last year introduced duloxetine in combination with pelvic floor exercise vs. each approach alone was evaluated against no treatment at all.

The presented data concludes that the combined treatment of PFMT and the oral drug duloxetine is the most efficient of all groups. The individual approach with the one or the other was better than no treatment at all, but any of the two did demonstrate a significant better outcome in comparison to the other.

The most mentioned side effect of duloxetine was nausea with 44%, which is higher than prior published in the initiative studies. Although it is already recommended by the pharmaceutics to decrease the drug in steps before stopped, it should be recommended in addition that duloxetine should be introduced by twice 20 mg before the daily dose of twice 40 mg is taken. By titrating the drug the side effect of nausea can be reduced significantly.

The medication probably gives a fast relive of the major symptom of incontinence whereas the PFMT gives a further support with the strengthening of the muscle structure. The fast improvement might help to motivate the patient to continue the PFMT, which will insure the lasting efficiency to delay the surgical approach.

Both the recommendation of the International Consultation of Incontinence 2004 and the published data suggest and might even request in the future to treat female urinary stress incontinence first with a serotonin-norepinephrine reuptake inhibitor to stimulate the pudendal nerve in combination with PFMT. Both approaches have an impact but only the combination demonstrated in the presented study a significant improvement of female urinary stress incontinence.

In the moment the serotonin-norepinephrine reuptake inhibitor duloxetine is not approved for male patients with urinary stress incontinence. With the small experience we have we see the two major results. First male seem not to have the high percentage of nausea, Second, in two groups of patients the following improvement are noticed; those who look for a fast relive right after radical prostatectomy and those where the surgery is “long” ago and still face urinary incontinence. These are only small case numbers but trials will be done in the near future to prove and hopefully verify these findings.

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Primary urethral reconstruction: the cost minimized approach to the bulbous urethral stricture

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J Urol. 2005; 173: 1206-10

Purpose: Treatment for urethral stricture disease often requires a choice between readily available direct vision internal urethrotomy (DVIU) and highly efficacious but more technically complex open urethral reconstruction. Using the short segment bulbous urethral stricture as a model, we determined which strategy is less costly.

Materials and Methods: The costs of DVIU and open urethral reconstruction with stricture excision and primary anastomosis for a 2 cm bulbous urethral stricture were compared using a cost minimization decision analysis model. Clinical probability estimates for the DVIU treatment arm were the risk of bleeding, urinary tract infection and the risk of stricture recurrence. Estimates for the primary urethral reconstruction strategy were the risk of wound complications, complications of exaggerated lithotomy and the risk of treatment failure. Direct third party payer costs were determined in 2002 United States dollars.

Results: The model predicted that treatment with DVIU was more costly (17,747 dollars per patient) than immediate open urethral reconstruction (16,444 dollars per patient). This yielded an incremental cost savings of $1,304 per patient, favoring urethral reconstruction. Sensitivity analysis revealed that primary treatment with urethroplasty was economically advantageous within the range of clinically relevant events. Treatment with DVIU became more favorable when the long-term risk of stricture recurrence after DVIU was less than 60%.

Conclusions: Treatment for short segment bulbous urethral strictures with primary reconstruction is less costly than treatment with DVIU. From a fiscal standpoint urethral reconstruction should be considered over DVIU in the majority of clinical circumstances.

Editorial Comment

The decision how to treat today a bulbar urethral stricture is not only influenced the best long-term outcome but although the cost effectiveness.

Patient, who are diagnosed with a urethral stricture, want to know what the best treatment might be. The urologist, who is the specialist in this field, will explain the patient where and how long this stricture is. In addition the surgeon will inform the patient about treatment options. An bulbous urethral stricture, first diagnosed, with a length of 2 cm offers two ways to be treated; through direct vision internal urethromy (DVIU) or excision and primary anastomosis (EPA). Probably the patient will prefer the DVIU because of the endoscopic approach, but the long-term data gives a different argument to prefer the open procedure. In a Medline literature research several articles about the long-term outcome of both treatment options were reviewed by Rourke et al. For each approach they reviewed 7- 8 articles, which demonstrated with a comparable follow-up of more than 58 months that the EPA does have a success rate of 93 - 100% (mean 96%) whereas the DVIU succeeded in 18 – 49% (mean 28%) for the treatment of urethral strictures of 2 cm.

It is almost impossible to predict the outcome of an individual case especially by knowing only the length of the stricture. Regarding to the literature, which was reviewed, the long-term can be predicted by the results of the single mentioned publication. The decision to treat a stricture should be related to the published data and the state of health of the patient. The authors helped to give a further argument for strictures of 2 cm to be treated by the open procedure, which is superior and even less expensive in the long term because of success rate over 95%. We suggest to proceed those urethral strictures by DVIU, which are short and uncomplicated without dens, deep spongiofibroses or in those patients who are not suitable for the open procedure because of their co-morbidities and refuse a suprapubic catheter although the risk of recurrence is high, as recommended in the Campbell's Urology (1). Hinman (2) pined it down to the following: "The internal uretherotomy in anticipation of urethral regeneration is simple to perform, but the recurrence is high. The most straightforward method is the excision and reanastomosis method, which has the greatest success".

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UROLOGICAL ONCOLOGY

A surveillance schedule for G1Ta bladder cancer allowing efficient use of check cystoscopy and safe discharge at 5 years based on a 25-year prospective database

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J Urol. 2005; 173: 1108-11

Purpose: In the absence of clear evidence, surveillance of low-grade superficial bladder cancer by regular check cystoscopy may continue unnecessarily, or discharge from follow-up may occur empirically. We review the follow-up during a prospective 25-year period of patients presenting with G1Ta bladder cancer, and it is this analysis on which we base a safe schedule for discharge.

Materials and Methods: A prospectively kept, computerized record of bladder cancers diagnosed between 1978 and 1985 and subsequently followed up at the Western General Hospital, Edinburgh was reviewed.

Results: A total of 115 patients with G1Ta disease were followed for a mean of 19.4 years. Tumor status at 3 months was the strongest prognostic factor for recurrence. Although the absence of tumor at 1 year was also a favorable prognostic sign, it was not for 5 years that the situation entirely stabilized (recurrence developed in 8 of 66 such patients between 1 and 5 years). Of those who did not have recurrence in 5 years, 98.3% patients remained tumor-free for 20 years. In contrast in those with recurrence at 3 months the recurrence rate was much higher. Overall 12% of patients experienced progression, mostly in year 1. None of the 8 who had their first recurrence after year 1 had disease progression.

Conclusions: Patients with G1Ta disease who are free of recurrence for 5 years after presentation can be safely discharged. We propose to alter the regime for patients with no recurrence in year 1 and discharge them at 5 years.

Editorial Comment

The surveillance schedule of superficial bladder cancer is empirical and based upon convenience rather than biological data. In recent times, attention has been focused on modifying the strict schedule of 3-monthly cystoscopies in certain risk groups. This paper focuses on pTa G1 cancer and bears some very interesting data. First, multiple and/or large tumors have a significantly higher risk for recurrence. Second, the first 5five years after TUR are important, with overall recurrence rates dropping from 29.1% to 14.1% ($p = 0.009$). Third, recurrence at 3three months is a bad prognostic sign. Patients who had recurrence at 3 months had further recurrences at 1 year compared with those who were tumor-free at 3 months (55.5% vs. 17.8%, $p = 0.007$). Progression occurs even in these tumors. 12.2 % had progression, which is an unexpected high figure to my opinion. 50% progressed within the first 5 years, and 35.7% within 3 months. All these patients had multiple primaries. 85.7 % of these patients had recurrence at 3 months.

Two consequences can be drawn from this important contribution. First, without recurrence, follow-up can be terminated at 5 years. Second, even TaG1 tumors sometimes recur aggressively and may progress.

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The extent of lymphadenectomy for pTXNO prostate cancer does not affect prostate cancer outcome in the prostate specific antigen era

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Purpose: Recent data suggest that extended lymph node dissection in prostate cancer may be necessary for accurate staging. With limited lymph node dissection apparently node negative cases might be under staged. We determined the impact that the number of lymph nodes removed at radical retropubic prostatectomy (RRP) has on cancer progression and cause specific survival in pTXNO cases.

Materials and Methods: We reviewed the RRP prostate cancer database on 7,036 patients with clinical T1 to T3 disease, no adjuvant therapy and node negative disease in the prostate specific antigen (PSA) era from 1987 to 2000. Factors evaluated were the number of lymph nodes obtained at RRP, preoperative PSA, clinical and pathological stage and grade, margin status, year of surgery and specific surgeon for 5 surgeons who operated throughout the period and performed more than 500 RRPs. Cox analysis was done to determine the RR of progression (PSA or systemic) and prostate cancer death for the number of lymph nodes excised.

Results: Median patient age was 65 years and median preoperative PSA was 6.6 ng/ml. At pathological evaluation 5,379 tumors (77%) were organ confined, 4,491 (65%) were Gleason score 5 to 6 and 2,027 (29%) were Gleason score 7 to 10. The median number of nodes obtained significantly decreased from 14 in 1987 to 1989 to 5 in 1999 to 2000 ($p < 0.001$). Ten years after RRP Kaplan-Meier estimates were 63% of cases free of PSA progression, 95% free of systemic progression and 98% free of prostate cancer related death. Median follow-up was 5.9 years. After adjusting for pathological factors (PSA, grade, stage, margin status and surgical date) the number of lymph nodes obtained at lymphadenectomy was not significantly associated with PSA progression (for each additional node (RR 0.99, 95% CI 0.98 to 1.02, $p = 0.90$), systemic progression (RR 0.99, 95% CI 0.96 to 1.03, $p = 0.68$) or cause specific survival (RR 1.01, 95% CI 0.96 to 1.06, $p = 0.75$).

Conclusions: The extent of lymphadenectomy does not appear to affect prostate cancer outcome in lymph node negative cases. This includes patients with high preoperative PSA, high pathological grade and extracapsular disease. These results suggest that under staging is not present in apparently node negative cases with limited lymphadenectomy and, even if present, its impact on outcome is likely to be negligible.

Editorial Comment

The extent of lymphadenectomy at radical retropubic prostatectomy (RRP) is controversial. The authors analyze their results in 7,036 patients. Ten years after RRP 63% of patients remain free of progression according to Kaplan-Meier estimates. Briefly, this paper shows clearly that in N0 patients no progression or survival

advantage exists with an increased number of nodes excised, including a group with high-risk cancer. Controversial data from European centers may be due to more advanced disease.

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FEMALE UROLOGY

Increased warning time with darifenacin: a new concept in the management of urinary urgency

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J Urol. 2005; 173: 1214-8

Purpose: We assessed the effect of darifenacin, an M3 selective receptor antagonist, on the warning time associated with urinary urgency.

Materials and Methods: In this multicenter, double-blind study subjects with urinary urgency for 6 months or greater and episodes of urgency 4 times or greater daily were randomized to darifenacin controlled release tablets (30 mg once daily) or placebo. Warning time was defined as the time from the first sensation of urgency to voluntary micturition or incontinence. Data were collected using electronic event recorders during 6-hour clinic visits or 3 urge-void cycles, if shorter, at baseline and at treatment end.

Results: A total of 72 subjects entered the study and 67 were included in the primary efficacy analysis (darifenacin in 32 and placebo in 35). Darifenacin treatment resulted in a significant increase in mean warning time with a median increase of 4.3 minutes compared with placebo ($p = 0.003$). Overall 47% of darifenacin treated subjects compared with 20% receiving placebo achieved a 30% increase or greater in mean warning time (OR 5.6, $p = 0.009$). Median and minimum warning times were also significantly increased following darifenacin treatment vs. placebo ($p = 0.004$ and 0.017, respectively). The median difference in minimum warning time was 1.9 minutes in favor of darifenacin vs. placebo.

Conclusions: To our knowledge this is the first study to evaluate change in warning time, which is potentially important to individuals with symptoms associated with overactive bladder. Darifenacin increases mean, median and minimum warning time compared with placebo, allowing subjects more time to reach a toilet and potentially avoiding the embarrassing experience of incontinence.

Editorial Comment

The authors analyze the efficacy of darifenacin, a selective M3 receptor antagonist, with regard to the parameter of micturitional warning time. Warning time was defined as the point from first sensation of urinary urgency to the patient voluntarily voiding or experiencing episode of urinary urge incontinence. The authors found that darifenacin affected a significant increase in warning time over those patients treated with placebo.

This is an excellent paper from one of the world's top urogynecologists. The analysis of warning time may produce a new benchmark of efficacy for OAB medications. This parameter, as it finds its way in use in more and more studies, will evolve. Currently, it is judged as the time between first sensation of urgency to the point of voluntary micturition or incontinence. Since voluntary micturition is a volitional act and urinary

incontinence is not, this may be an area of further refinement. In reviewing the study groups, the differences in median baseline warning times between the darifenacin and placebo groups does present a potential "possible imbalance" as suggested by the authors.

In addition, darifenacin is a M3 selective receptor antagonist. The potential changes in M2 receptor density as opposed to M3 in the denervated bladder has been discussed previously in the literature (1). Consequently, some have postulated that M3 specific antagonists may be at a potential therapeutic disadvantage secondary to the M2 up regulation in the diseased bladder (2).

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Incidence of urinary incontinence in postmenopausal women treated with raloxifene or estrogen

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Menopause. 2005; 12: 160-164

Objective: Determine the effect of raloxifene or estrogen, as compared with placebo, on the reporting of urinary incontinence in postmenopausal women participating in an osteoporosis prevention trial.

Design: The current analysis is based on adverse event data that were collected as part of a double-blind, randomized, placebo-controlled trial designed to assess the efficacy and safety of raloxifene for osteoporosis prevention in postmenopausal women. Women were 40 to 60 years of age at study entry and had a prior hysterectomy. A total of 619 women were randomized to placebo, raloxifene 60 or 150 mg/d, or conjugated equine estrogen 0.625 mg/d and followed for up to 3 years. Urinary incontinence was self-reported and rated by participants as "mild", "moderate" or "severe".

Results: The prevalence of urinary incontinence as reported by patients at baseline was similar across treatment groups (3% to 6%, P = 0.46). During 3 years of follow-up, new or worsening urinary incontinence was reported with the following frequency: placebo (1.3%), raloxifene 60 mg/d (0.7%), raloxifene 150 mg/d (0.6%), and conjugated equine estrogen (7.0%). The percentage of estrogen subjects reporting urinary incontinence was significantly greater than that for placebo and both doses of raloxifene ($P \leq 0.02$).

Conclusions: During 3 years of follow-up, conjugated equine estrogen was associated with an increased incidence of reports of urinary incontinence in women with a prior hysterectomy and this was significantly greater than both placebo and raloxifene.

Editorial Comment

The authors analyze the effect of raloxifene, estrogen and placebo on the incidence of urinary incontinence in postmenopausal women that were participating in an osteoporosis prevention trial. Urinary incontinence was self reported and self rated by the patients during the study as mild, moderate or severe. There was no clear differentiation between symptoms of urinary urge incontinence, stress urinary incontinence, or mixed urinary incontinence. After three years of follow-up, the authors noted that estrogen was found to be associated with a statistically greater increase of urinary incontinence in women with prior hysterectomy than that found with either placebo or raloxifene.

This paper raises interesting issues regarding the potential use of medical therapy as a prophylaxis against urinary incontinence. In addition, an interesting sidebar is made in the article about the potential effects of raloxifene on the incidence of female pelvic prolapse. The biological actions of raloxifene are mainly through the binding of estrogen receptors with secondary effect on estrogenic pathways. This result will potentially decrease the resorption of bone to that noted in the premenopausal state. The use of raloxifene has been noted to increase the risk of venous thromboembolism and thus the medication should be discontinued at least 3 days prior to any potential surgery, which would result in prolonged patient immobilization.

Of specific note is that the incidence of incontinence in this patient population through self reporting was vastly lower than that previously reported in the United States (1). In addition, potential points of contention in this paper are self noted by the authors and do include that the screening for incontinence was not completed through a validated questionnaire and there was no differentiation between urge or stress incontinence. This article does bring up some fascinating points in the discussion section about the use of estrogen therapy and its effect on collagen content and architecture in the paraurethral tissues and vaginal epithelium.

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PEDIATRIC UROLOGY

Subureteral injection of Deflux for correction of reflux: analysis of factors predicting success

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Objective: To review, prospectively, our experience with endoscopic Deflux injection and evaluate the volume injected, grade, endoscopic appearance after injection, and presence or absence of voiding dysfunction as predictors of success. Subureteral injection of dextranomer/hyaluronic acid copolymer (Deflux) has become an effective treatment of vesicoureteral reflux.

Methods: A total of 52 patients (50 females and 2 males; 80 ureters) were treated with a single subureteral injection of Deflux. The mean patient age was 7.6 years (range 14 months to 22 years). The presence or absence of voiding dysfunction was evaluated with a preoperative questionnaire and patient history. The volume of

Deflux injected in each ureter was recorded. The endoscopic appearance after injection was recorded as “volcano” or “other.” Success was defined as no reflux on postoperative voiding cystourethrography.

Results: The success rate by grade of reflux in individual ureters was 82%, 84%, 78%, and 73% for grade 1, 2, 3, and 4 vesicoureteral reflux, respectively. No statistically significant difference was found in the cure rate by grade (P = 0.76). The overall cure rate by ureter was 80% and by patient was 71%. New contralateral reflux developed in 12.5% of patients. No statistically significant difference was found in the cure rate with respect to the volume injected or the presence or absence of voiding dysfunction. The ureteral cure rate with volcano and alternate morphology was 87% and 53%, respectively (P = 0.004).

Conclusions: Mound morphology was the only statistically significant predictor of a successful outcome, with an associated cure rate of 87%. Concomitant voiding dysfunction did not have an adverse effect on the cure rate. In our experience, no statistically significant difference was found in the cure rate for grades 1 through 4 vesicoureteral reflux after a single injection of Deflux.

Editorial Comment

This paper reviews a relatively small experience with using subureteral injection of Deflux for the treatment of reflux. In the sense that this is a report that is representative of a typical pediatric urologist, it is quite interesting. The authors report good results in that they were able to cure (no reflux at 3 months) about 80% of ureters and 70% of patients using this minimally invasive technique.

Several other findings were interesting in their study. First the grade of reflux had no relationship to the degree of success (Grade V patients were excluded). Second, there was a 12.5% rate of new contralateral reflux. Third, a history of voiding dysfunction had no influence on the results. Finally, and perhaps most important, the configuration of the ureter immediately after injection had the most to do with ultimate success.

There are several important caveats to this study. The average age of the patients was over 7 and the study included primarily girls. Older patients and girls may be easier to inject, partially skewing the results. Most important though s the question of how to judge success. One measure of success is whether the reflux is gone. However, is a 3 month VCUG adequate? Some of the Deflux is absorbed with time. Would less Deflux mean a recurrence of the reflux over time? How about the effect of voiding dysfunction? This would likely increase over time. Although voiding dysfunction had no effect on the 3 month VCUG, would it have a stronger effect if a VCUG were done at 12 or 24 months? Furthermore, we have pretty good evidence that open surgery prevents reflux for many years. What about Deflux? Clearly, there are no data on VCUGs 5-10 years after Deflux. Finally, is the resolution of reflux really the correct end-point? We really are trying to prevent recurrent pyelonephritis. Reflux resolution is in some ways a “proxy endpoint.” We really need a study of the rate of pyelonephritis with and without Deflux treatment. Hopefully one will be forthcoming soon.

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Dysfunctional voiding and incontinence scoring system: quantitative evaluation of incontinence symptoms in pediatric population

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Purpose: Functional voiding problems in children are common. Although pathophysiology and presentation of this clinical entity are well described, there is not yet a generally accepted method of quantitative and standard evaluation of clinical symptoms, and there are few studies addressing the issue of symptom scoring in children. We investigated use of a symptom scoring system in children with functional voiding problems and the normal population, and validated it using a scientific tool.

Materials and Methods: A symptom scoring system was designed empirically. The questionnaire was composed of items regarding daytime symptoms, nighttime symptoms, voiding habits, bowel habits and quality of life. There were 2 groups whose symptoms were evaluated using this scoring system. Group 1 consisted of 86 patients who were admitted to our clinic with various wetting and daytime voiding problems. Group 2 consisted of 265 controls with no urological complaints. Parents of all children were asked to fill out a questionnaire that included the symptom scoring system. Boys with lower urinary tract abnormalities, and patients with spina bifida occulta and neurogenic bladder were excluded from the study. Odds ratios of answers to each item in the questionnaire were used to define strength of the questions to differentiate patients from healthy controls. According to the value of odds ratios, questions were modified and a score for each question was given. Receiver operating characteristic plots were used to define detection cutoff or threshold score, and Youden's index was used to detect best reflecting optimal sensitivity and specificity.

Results: The total score was determined to range from 0 to 35, and items were modified to 13 questions and 1 quality of life question at the end of the study. Among the 86 patients in group 1 (female-to-male ratio 1.5:1) mean score was 18.56. Among the 265 controls in group 2 (female-to-male ratio 1.5:1) mean score was 2.88. Statistical analysis revealed that within a confidence interval of 96.2% patients with a score of 8.5 or greater had voiding abnormalities, with 90% sensitivity and 90% specificity. There were no statistically significant differences between the 2 genders and 2 age groups of 4 to 7 and 8 to 10 years.

Conclusions: This statistically validated functional voiding problems symptom score may provide accurate, objective and scientific bases to grade the symptoms in comparative research, diagnosis, treatment and followup of patients with wetting and functional voiding disorders

Editorial Comment

Dysfunctional voiding is common, but can be extremely difficult to identify with certainty and even harder to grade. Furthermore, it is very difficult to objectively monitor progress in the treatment of dysfunctional voiding. This is concerning, considering that dysfunctional voiding has considerable importance because of its role in the pathophysiology of urinary tract infections, vesicoureteral reflux and incontinence. In that sense, this paper, describing a new, and indeed the first, validated questionnaire for identifying and grading dysfunctional voiding is of considerable value.

Although this questionnaire is a major advance, there are some questions that remain to be answered. For example, are all voiding dysfunctions alike? In other words, how well will this scoring system separate children with frequency/urgency from those with infrequent voiding? Also, we know that in many children, bowel and bladder dysfunction co-exist. Moreover, in some children treatment of constipation will help resolve the voiding dysfunction. Unfortunately, this questionnaire only has one question about bowel function and that one only adds 1 point to the scoring system.

Despite these concerns, this paper is an important contribution. The authors are to be congratulated.

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