
UROLOGICAL SURVEY

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STONE DISEASE

Self-Retaining Ureteral Stents: Analysis of Factors Responsible For Patients' Discomfort

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J Endourol. 2006; 20: 33-7

Purpose: To determine factors affecting patients' discomfort during the period self-retaining ureteral stents are in place.

Patients and Methods: Between April 2001 and May 2003, 58 male and 42 female patients underwent temporary double-pigtail stenting. The indications were endopyelotomy in 39 patients, ureteroscopy in 32, laparoscopic pyeloplasty in 18, and endoureterotomy in 11. The stents were silicone in 56 patients and Percuflex in 44. The median stenting period was 8 weeks (range 4-16 weeks). Patient discomfort was evaluated by a questionnaire conducted by the physician before stent removal. Tested variables were patients' sex, side of the stent, urine culture, stent material, stent length and diameter, and stenting duration. The site of the upper coil (renal pelvis or calix), the site of the lower coil (in the same side or crossing the midline), and the shape of the lower coil (complete circle or not) were also tested. Univariate and multivariate analysis were carried out to determine significant independent variables, with $P < 0.05$ being significant.

Results: Of the total, 59 patients experienced discomfort consisting of dysuria, urgency, urge incontinence, loin pain, suprapubic pain, frequency, nocturia, or gross hematuria or some combination. Significant factors associated with discomfort were a positive urine culture, crossing of the lower end of the stent to the opposite side, caliceal position of the upper coil, and longer stenting duration.

Conclusion: Proper positioning of the coils of the stent, eradication of infection, and shorter stenting duration are advised to decrease patient discomfort during the period of ureteral stenting.

Editorial Comment

The authors confirm the significant impact ureteral stents have on patient comfort and quality of life, and they identify the following 3 variables that affect stent morbidity: Location! Duration! Infection! Though previous studies evaluating patient comfort have attempted to focus on stenting of a symptomatic ureteral stone or stenting after uncomplicated ureteroscopy, this study included patients undergoing a wide variety of endourological and laparoscopic procedures. Pain measurements may therefore have been confounded by urinary extravasation after endopyelotomy, port site pain, diaphragmatic irritation by carbon dioxide or other variables. In addition, the length and size of stent used was not standardized. The stent duration in this study was long - typically, we leave a ureteral stent for 4-7 days after an uncomplicated ureteroscopy and 2-3 weeks after an endopyelotomy or endoureterotomy. Noting these limitations, it is important to consider some of the simple method proposed by this study to decrease stent discomfort. Intraoperatively, one should ensure proper positioning of the stent coils such that the bladder coil does not cross midline and the renal coil is in the pelvis. Postoperatively if the patient reports discomfort it may be important to perform a urine culture and eradicate any infection. Lastly, shortening the duration of stenting should be emphasized.

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Percutaneous Nephrolithotomy in Patients Who Previously Underwent Open Nephrolithotomy

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J Endourol. 2005; 19: 1161-4

Background and Purpose: Open stone surgery nowadays is rare. However, some patients who are treated today have in the past undergone open nephrolithotomy. The aim of this study was to determine the possible impact of open nephrolithotomy on the efficacy and morbidity of subsequent percutaneous nephrolithotomy (PCNL).

Patients and Methods: We reviewed the files of all 167 patients undergoing PCNL at our institution between December 2000 and December 2003. The same surgeon performed all of the procedures. We compared 21 patients undergoing PCNL after open nephrolithotomy to the same kidney with all other patients undergoing PCNL. The groups did not differ in terms of age or stone burden (mean size, number of stones, percentage with staghorn calculi). The outcomes measured were operating time, necessity for secondary procedures, stone free rate, and intraoperative and postoperative complications.

Results: The operating time (203+/-92 v 177+/-52 minutes) and percentage of secondary procedures (29% v 12%) were significantly higher in patients who had previously undergone open stone surgery. However, the stone-free rate (95% v 93%), intraoperative complication rate (10% v 9%), and postoperative complication rate (10% v 11%) did not differ significantly.

Conclusions: A PCNL in a patient with a history of open nephrolithotomy may take longer and lead to a higher percentage of auxiliary procedures, probably because of scar tissue and anatomic changes in the kidney. However, the morbidity and efficacy of PCNL appear to remain the same in these patients.

Editorial Comment

Preoperative planning for PCNL pays off particularly in the complicated patient who has a prior open renal surgery. Though the authors conclude that efficacy is not affected, the secondary procedure rate was significantly higher if the patient has had a prior open surgery. The authors present some important technical tips to consider during complicated PCNL. Firstly, they utilize contrast-imaging to evaluate for intrarenal scarring that would necessitate a direct puncture onto the stone. Secondly, they utilize an upper pole puncture if an incisional hernia is present at the old subcostal incisional site. Thirdly, they emphasize the need for precise initial alignment of the entry needle as the ability to maneuver the needle once inserted is limited by scarring. Lastly, they employ a step-wise algorithm for dilation of the percutaneous tract - starting with a balloon dilator, using a fascia cutting needle and re-inflating if residual waist is present, proceeding to rigid Amplatz dilators if still not successful, and lastly using telescopic metal dilators if all else fails. It is important to emphasize that experience in each of these techniques is important to ensure access to the stone in these complicated patients. Unfortunately, they did not report how often they resorted to each of these techniques. One can conclude from this study that patients undergoing PCNL who have had prior open renal surgery should undergo contrast-imaging studies to delineate the collecting system anatomy. Having the availability and experience of a range of dilation systems is important for successful percutaneous access.

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ENDOUROLOGY & LAPAROSCOPY

Meta-Analysis of the Complications of Laparoscopic Renal Surgery: Comparison of Procedures and Techniques

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J Urol. 2006; 175: 1208-13

Purpose: We performed a meta-analysis of the literature to define the current expectations of complications during laparoscopic renal surgery.

Materials and Methods: References were searched in the MEDLINE database from 1995 to 2004 using the terms complications and laparoscopic nephrectomy. Inclusion criteria were any series with greater than 20 cases, patient age older than 16 years and any complications listed for certain procedures, including laparoscopic radical nephrectomy, HA laparoscopic radical nephrectomy, LPN, HALPN, laparoscopic donor nephrectomy, HA laparoscopic donor nephrectomy, laparoscopic simple nephrectomy, laparoscopic nephroureterectomy and retroperitoneal laparoscopic nephrectomy. A data extraction form was created to categorize major or minor complications. A 5 member panel adhered to the strict criteria and extracted data from articles that met inclusion criteria. Data were entered into a spreadsheet and a meta-analysis was performed.

Results: Initial review identified 73 of 405 references that were acceptable for retrieval and data extraction, of which 56 met inclusion criteria. The overall major and minor complication rates of laparoscopic renal surgery were 9.5% and 1.9%, respectively. There was a significant difference between the major complication rates of LPN and HALPN (21.0% vs 3.3%, $p < 0.05$).

Conclusions: Our results show that patients who undergo laparoscopic renal surgery may have an overall major complication rate of 9.5%. The highest major complication rate is associated with technically challenging LPN (21%). There appears to be a significantly higher wound complication rate associated with HA surgery in comparison to that of standard laparoscopy (1.9% vs 0.2%, $p < 0.05$).

Editorial Comment

Since the first laparoscopic nephrectomy was performed and documented by Clayman and colleagues, the array of procedures using the laparoscopic approach has evolved. The development of new laparoscopic instruments and technology allowed laparoscopic surgeons to apply the same surgical principles as in open surgery. The authors demonstrated that laparoscopic renal surgery is safe and reproducible. Moreover, laparoscopic partial nephrectomy remains a complex procedure including ablative and reconstructive steps but the aid of hand assist devices may decrease the rate of complications for this particular procedure. Conversely, the hand assisted surgeries compared to pure laparoscopic procedures had higher incidence of wound related complications. In conclusion, the laparoscopic approach for kidney surgery should be considered a “winner” in terms of surgical technique allowing patients to benefit from it for over a decade and half.

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Intermediate Results of Laparoscopic Cryoablation in 59 Patients at the Medical College of Wisconsin

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J Urol. 2006; 175: 1225-9; discussion 1229

Purpose: We report our experience with LC for small renal tumors.

Materials and Methods: Patients who underwent LC at our institution between February 2000 and September 2004 were included in the study. A retrospective chart review was done for perioperative and postoperative parameters as well as clinical outcomes.

Results: A total of 65 LCs were performed in 59 patients during the period reviewed. Overall 81 renal tumors were cryoablated. Median patient age was 62 years. Median tumor size was 2.5 cm. Median operative time was 190 minutes. Median estimated blood loss was 50 ml. Median hospital stay was 2 days. Conversion to open surgery occurred in 2 patients. Nephrectomy for bleeding occurred in 1 patient. Median followup was 26.8 months. Two recurrences were identified after LC.

Conclusions: LC is an alternative modality to laparoscopic partial nephrectomy or open partial nephrectomy for small renal tumors. Tumor recurrence rates in the studies published to date are comparable to those of partial nephrectomy, although longer followup is needed.

Editorial Comment

Laparoscopic cryoablation of small renal tumors is still in development. The new cryo probes have increased the efficiency of cytotoxic effects to treat the renal lesions and decreased the rate of complications. So far, the technology has demonstrated to be efficient to treat renal tumors. The authors concluded that laparoscopic cryoablation is a potential alternative modality to laparoscopic partial nephrectomy or open partial nephrectomy for small renal tumors but the cryoablation technique requires a basic skill set in laparoscopic surgery, which makes this technique appealing for less experienced laparoscopic surgeons. Moreover, laparoscopic cryoablation may be associated with decreased risks of bleeding and urine leakage in comparison to laparoscopic partial nephrectomy. Future comparative studies are needed to fully validate this technique but initial reports of oncological control are encouraging.

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IMAGING

Radiation Dose Associated with Unenhanced CT for Suspected Renal Colic: Impact of Repetitive Studies

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AJR Am J Roentgenol. 2006; 186: 1120-4

Objective: The purpose of our study was to assess the dose of ionizing radiation delivered through the use of unenhanced CT for suspected renal colic by determining the incidence of repeated unenhanced CT examinations and the cumulative radiation dose delivered.

Materials and Methods: All unenhanced CT examinations for suspected renal colic performed at our institution over a 6-year period were included, and patient age, sex, and multiplicity of examinations were determined. For the adult patient, this protocol prescribes a fixed tube current of 200 mA, 140 kVp, and a nominal slice width of 5 mm. The dose-length product (DLP) was estimated for 15 randomly chosen single-detector CT (SDCT) and MDCT adult flank pain examinations using manufacturer's software. The mean DLPs for SDCT and MDCT were computed and converted to effective doses. Total effective doses were calculated for patients who underwent more than three examinations, and values were compared with established standards.

Results: A total of 5,564 examinations were performed on 4,562 patients. Of these patients, 2,795 (61%) were women (mean age, 45.5 +/- 16.2 [SD] years) and 1,731 (38%) were men (mean age, 44.7 +/- 16.4 years), with 144 patients (3%) of pediatric age. The mean effective doses for a single study were 6.5 mSv for SDCT and 8.5 mSv for MDCT. A subset of 176 patients (4%) had three or more examinations, with estimated effective doses ranging from 19.5 to 153.7 mSv. All patients with multiple examinations had a known history of nephrolithiasis.

Conclusion: Patients with a history of nephrolithiasis and flank pain are at increased risk for serial CT with potentially high cumulative effective doses.

Editorial Comment

Recent studies have been shown that computed tomography (CT) contribute to 35-45% of total radiation dose to the patient population. Nowadays, radiologists' aim must be to decrease radiation dose to the patient and also check very carefully all indications and recommend alternative imaging methods. Recently several CT protocol imaging have been developed in order to decrease the total amount of radiation dose that a patient receives during abdominal CT. This is a very important study, which discusses all the issues and possibilities regarding those patients that are submitted to repetitive abdominal CT for the evaluation of acute flank pain. The authors showed that a small but significant subset of the patient population (4%) was estimated to receive from 20 to as high as 154 mSv, which is totally undesirable. In order to decrease the amount of radiation dose they suggested that sonography associated with abdominal radiography (KUB), should be used as a first imaging examination in patients known to have chronic stone formation who have a high pretest probability of nephrolithiasis and thus are less likely to have a missed alternative diagnosis. Another useful approach for these patients is to use the reduced radiation-dose technique. When using these optimized CT protocol, the tube current can be reduced to 70 mA in comparison with the higher tube current of multidetector conventional CT protocol (200 mA). By using this optimized low dose protocol, the estimated effective dose is reduced from 8.6 mSv to 1.5 mSv. This reduced radiation-dose protocol result in scans with high accuracy for detecting urinary calculi in patients evaluated for acute flank pain.

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Conventional MRI Capabilities in the Diagnosis of Prostate Cancer in the Transition Zone

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AJR Am J Roentgenol. 2006; 186: 729-42

Objectives: Our objectives were to evaluate the diagnostic capabilities of conventional MRI for the accurate detection of prostate cancer within the transition zone and to compare the results with histopathologic examination results.

Materials and Methods: One hundred sixteen prostate specimens with prostate cancer were consecutively obtained. Axial, sagittal, and coronal T2- and T1-weighted MR images with gadopentetate dimeglumine were independently reviewed by two radiologists. The diagnostic base criteria of the MR images were determined for detecting transition zone cancer as follows: lesions with A, uniform low intensity on T2-weighted images; B, homogeneous gadolinium enhancement; and C, irregular margins both on gadolinium-enhanced and T2-weighted images. Wilcoxon's rank sum and chi-square tests and receiver operating characteristic curves were used. Differences of less than 0.05 were considered significant.

Results: Eighty-six lesions in the transition zone were analyzed. Histopathologic analysis showed 53 cancers and 33 benign lesions. The diagnostic sensitivity, specificity, and accuracy for cancer were 50%, 51%, and 51%, respectively with criteria A; 68%, 75%, and 71% with criteria B; and 60%, 72%, and 65% with criteria C. When base criteria were combined into criteria A-B, A-C, and B-C and then further divided into three subgroups, accuracy was found to be highest when the lesion satisfied any two criteria from A, B, and C than those of base criteria, combination criteria, and the other two subgroups.

Conclusion: The addition of gadolinium-enhanced MRI to T2-weighted imaging provides better accuracy for detecting cancerous transition zone lesions than the use of T2-weighted imaging alone.

Editorial Comment

Radical prostatectomy studies have demonstrated that 75-85% of cancers arise in the peripheral zone, but up to 25% prostate cancer occurs within the transition zone. Endorectal MR imaging is a useful modality in the detection of the peripheral zone cancers. This technique is able to detect 67-76% of peripheral cancer demonstrated by step-section histopathologic studies but has limitations in the demonstration of cancer in the transition zone. This limitation occurs because the transition zone appears usually as a very heterogeneous region on T2-weighted images due to the presence of nodular hyperplastic changes. Previous studies have suggested some MR imaging features found in transition zone cancer: homogeneous hypointense lesion on T2-weighted images with ill-defined margins and lack of capsule. The authors of this study demonstrate that conventional MR imaging, without the use of an endorectal coil, can be useful for the detection of transition prostate cancer. They added new imaging criteria: homogeneous enhancement and presence of irregular margins. If these additional findings are used, the specificity rates for the detection of transition zone cancer could be increased from 51% to 82%. In the last 2 years, we have been using routinely, in our institution, endorectal MR imaging and spectroscopy for the detection of prostate cancer arising in the transition zone. We have found that diffusion weighted images and the evaluation of the kinetics of gadolinium enhancement by the lesion can be of further value. Thus the presence of a nodule with ill-defined margins, homogeneous hypointensity on T2 weighted images, with hypointensity on diffusion weighted images and fast contrast enhancement ("wash-in") and fast contrast de-enhancement ("wash-out"), is very suggestive of transition zone cancer. Spectroscopy shows only high levels of choline particularly in larger tumors and thus can also be of some value.

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UROGENITAL TRAUMA

Cystogram Follow-Up in the Management of Traumatic Bladder Disruption

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J Trauma. 2006; 60: 23-8

Background: The utility of obtaining a routine cystogram after the repair of intraperitoneal bladder disruption before urethral catheter removal is unknown. This study was designed to examine whether follow-up cystogram evaluation after traumatic bladder disruption affected the clinical management of these injuries. We hypothesized that routine cystograms, after operative repair of intraperitoneal bladder disruptions, provide no clinically useful information and may be eliminated in the management of these injuries.

Methods: Our prospectively collected trauma database was retrospectively reviewed for all ICD-9 867.0 and 867.1 coded bladder injuries over a 6-year period ending in June 2004. Demographics, clinical injury data, detailed operative records, and imaging studies were reviewed for each patient. Bladder injuries were categorized as intraperitoneal (IP) or extraperitoneal (EP) bladder disruptions based on imaging results and operative exploration. Patients with IP injuries were further subdivided into those with “simple” dome disruptions or through-and-through penetrating injuries and “complex” injuries involving the trigone or ureter reimplantation. All patients sustaining isolated ureteric or urethral injury were excluded from further analysis.

Results: In all, 20,647 trauma patients were screened for bladder injury. Out of this group, there were 50 IP (47 simple, 3 complex) and 37 EP injuries available for analysis. All IP injuries underwent operative repair. Eight of the IP injuries (all simple) had no postoperative cystogram and all were doing well at 1- to 4-week follow-up. The remaining 42 patients underwent a postoperative cystogram at 15.3 +/- 7.3 days (range 7 to 36 days). All simple IP injuries had a negative postoperative cystogram. The only positive study was in one of the three complex IP injuries. In the EP group, 21.6% had positive cystograms requiring further follow-up and intervention. **Conclusions:** Patients sustaining extraperitoneal and complex intraperitoneal bladder disruptions require routine cystogram follow-up. In those patients undergoing repair of a simple intraperitoneal bladder disruption, however, routine follow-up cystograms did not affect clinical management. Further prospective evaluation to determine the optimal timing of catheter removal in this patient population is warranted.

Editorial Comment

When it comes to diagnosing bladder injuries, in the vast majority, the presenting sign is gross hematuria and pelvic fracture (1). For penetrating bladder injuries, up to 50% will only have microscopic hematuria. Accurate methods for diagnosing and staging the bladder injury are a formal cystogram with retrograde filling until at least 300 mL or bladder spasm, as well as a post-drainage film to look for another potential 10-15% of injuries, hidden behind the contrast on filling. Computed tomography (CT) cystogram is also very accurate for bladder injury, and has the advantage that it can be performed at the same time as the abdominal and pelvic imaging CT. The key is that clamping the Foley often produces inadequate bladder distention for injury diagnosis. Retrograde filling is required in order to avoid missed injuries.

This article nicely illustrates the management and evaluation methods for intraperitoneal (IP) and extraperitoneal (EP) bladder injuries. Inaba et al. divide IP bladder injuries into simple (bladder dome and wall) and complex (involve the trigone and ureteral orifice). Of 39 simple IP bladder injuries closed at the time of celiotomy, 100% were healed by 15 days. They thus effectively argue that after 2 weeks of Foley catheter rest, a cystogram is not required before Foley removal. In contrast, complex bladder injuries (which involve the trigone or ureter) typically also have significant blast injury and require prolonged Foley drainage and thus

cystography to confirm healing. For EP bladder injuries, only 10-15% of pelvic fractures have an associated bladder injury, while over 90% of bladder injuries have a pelvic fracture. Inaba et al. show that 88% of EP bladder injuries heal with Foley catheter alone, by 16 days and the remaining 12% by 47 days. This is consistent with prior reports that most EP injuries heal within 2 weeks and the remaining by 4 to 6 weeks. The only EP bladder injury cases that I have seen that not heal with bladder rest were due to bony pelvic spicules penetrating the bladder, and thus required open surgical repair. Such cases are very rare.

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Does Nephrectomy for Trauma Increase the Risk of Renal Failure?

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World J Surg. 2005; 29: 1472-5

Renal failure is a feared complication following operations for severe trauma. Injuries to the kidney may be managed by nephrectomy or nephrorrhaphy. Nephrectomy may increase the risk of renal failure in already at-risk trauma patients. Nephrectomy for trauma should be avoided to the extent possible because it is associated with renal failure. From a prospectively collected trauma database, 59 patients with nephrectomy were matched at 1:1 ratio with 59 patients with nephrorrhaphy. Matching criteria were age (+/- 5 years), Injury Severity Score (+/- 3), abdominal Abbreviated Injury Score (+/- 1), and mechanism of injury (blunt or penetrating). The rates of renal function compromise (defined as a serum creatinine level >2 mg/dl for more than 2 days) and renal replacement therapy (continuous or intermittent) were compared in the two groups. The two groups were well-matched and similar with regard to injury severity and organs injured. Between nephrectomy and nephrorrhaphy patients, there were no differences in renal function compromise (10% vs. 14%, $p = 0.57$), renal replacement therapy (5% vs. 0%, $p = 0.12$), length of hospital stay (19 +/- 26 vs. 20 +/- 21, $p = 0.8$), and mortality (15% vs. 12%, $p = 0.59$). Salvaging the injured kidney does not seem to offer an obvious clinical benefit regarding postoperative renal function. Given the increased operative complexity of nephrorrhaphy in comparison to nephrectomy and the frequent need to abbreviate the operation in patients with severe trauma, nephrectomy should not be avoided when appropriate.

Editorial Comment

Contemporary trauma management employs a damage control principle. Patients who become cold, coagulopathic, and acidotic have a very high mortality rate. In order to avoid this fatal triad, it was observed that if the trauma patient underwent an abbreviated operation to control bleeding and fecal soiling, followed by ICU resuscitation, then followed by a staged definitive repair, the patient survival rates were dramatically improved. Currently, abbreviated surgeries and staged definitive repair are standard of trauma care and have

been applied to all organ system, including genitourinary. Although as urologists, we are in the kidney preservation business, the overall survival of the patient should not be compromised in order to save the kidney. In other words, do not kill the patient trying to save the kidney. In trauma circles, the way to damage control injures organs is to quickly control bleeding and fecal and urinary soiling. To control bleeding the organ can be packed, quickly repaired or removed. To control urinary spillage, the ureter can be exteriorized, ligated or quickly repaired. The use of damage control to urology was popularized (1). To the trauma surgeons, since most trauma patients are young healthy adults with 2 normal kidneys and a normal creatinine, the kidney can be removed without too much overall kidney function compromise. Velmahos et al., puts up a good argument in the above article, but I would argue a different conclusion. The authors are trying to support the high 50-60% nephrectomy rates of yester-year. I would argue that the nephrectomy rate does not have to be higher the 20% and we can still follow a damage control method. Furthermore, palpating for a normal feeling contralateral kidney can be unreliable. I have personally seen 2 cases of trauma patients with a nonfunctioning contralateral multi-cystic dysplastic kidney and one hypertrophied psoas muscle that was thought to be palpably normal kidney by the trauma service. In the stable blunt trauma patient, all grade 1-4 renal injuries should managed conservatively if possible. In the blunt trauma patient who is explored, a stable, nonpulsatile, nonexpanding, contained perinephric hematoma should be left alone. In the penetrating trauma patient who is explored and the kidney does not have much blast injury and not really bleeding, I would just cover the gunshot holes with a surgi-cell and place a drain. The kidney can also be packed. Once resuscitated on a staged celiotomy, the kidney can be reexamined and a more definitive repair can be performed.

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PATHOLOGY

Update on the Gleason Grading System for Prostate Cancer: Results of an International Consensus Conference of Urologic Pathologists

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Adv Anat Pathol. 2006; 13: 57-9

The Gleason system for prostate cancer was based on a study of 270 patients from the Minneapolis Veterans Administration Hospital in 1966-1967. In 1974, Gleason and the Veterans Administrative Cooperative Urological Research Group expanded this study to 1032 men. These studies formed the basis of the Gleason grading system, which is now endorsed as the primary grading system for prostate cancer by the World Health Organization, the Armed Forces Institute of Pathology Fascicle on prostate cancer, the Association of Directors of Anatomic and Surgical Pathology, and the College of American Pathologists. In the nearly 40 years since its

inception, several aspects about prostate cancer and its management have changed, most notably serum prostate-specific antigen, transrectal ultrasonography, 18-gauge needle biopsy sampling, immunohistochemistry for the diagnosis of cancer, and radical prostatectomy and radiation therapy as primary treatment modalities. Several aspects of the disease, and consequently the reporting needs, have changed such as reporting cancer on multiple cases in needle biopsies, multiple nodules in prostatectomy, tertiary patterns, variants and variations in prostate cancer. The application of the Gleason system, therefore, has varied considerably in contemporary surgical pathology practice. An International Consensus Conference attended by 80 urologic pathologists from 20 countries was convened to discuss clarifications and modifications to the Gleason system. This article serves as a brief overview and summary of the proceedings that have been published in detail in recent literature.

Editorial Comment

In 2005 during the USCAP (United States and Canadian Academy of Pathology) meeting in San Antonio, Texas, there was a Consensus Conference on Gleason grading system sponsored by the International Society of Urological Pathology (ISUP). The results were published in the November issue of the *American Journal of Surgical Pathology* (1). There are several arguments favoring a need for a consensus on Gleason grading: 1) In the 1960s, there was no screening for prostate cancer other than by digital rectal examination; 2) The use of 18-gauge thin biopsy needles and the concept of sextant needle biopsies to more extensively sample the prostate were not developed until the 1980s; 3) Tertiary patterns were not addressed within the original Gleason system; 4) The Gleason system predated the use of immunohistochemistry (it is likely that many of Gleason's original 1 + 1 = 2 adenocarcinomas would today be regarded as adenosis); 5) The original Gleason grading system was not applied to newly described variants of adenocarcinoma of the prostate; and, 6) The Gleason system varies considerably in contemporary surgical pathology practice and has led to several recent attempts to achieve consensus on Gleason grading.

Some of the recommendations of the consensus conference are the following: 1) Cribriform pattern 3 should only be diagnosed for well circumscribed glands of the same size of normal glands; 2) Ill-defined glands with poorly formed glandular lumina also warrant the diagnosis of Gleason pattern 4; 3) In high-grade cancer, lower grade patterns should be ignored if they occupy less than 5% of the area of the tumor; and 4) For tertiary Gleason patterns, both the primary and the highest grade are recorded.

A recent study described the impact of the consensus recommendations on a series of 172 consecutive needle prostatic biopsies of patients subsequently submitted to radical prostatectomy previously graded according to the standard Gleason system (2). There was a grading concordance in 83.14%, 63.37%, and 68.02% biopsies for Gleason primary pattern, Gleason secondary pattern, and Gleason score, respectively. There was a change of prognostic Gleason grading groups in 2.33% and 26.74% biopsies toward a lower group and toward a higher group, respectively. There was a change in 15.7%, 9.88%, 0.58% and 0.58% biopsies from group 5-6 toward group 7, 7 toward 8-10, 5-6 toward 8-10, and 2-4 toward 5-6, respectively. The conclusion was that the highest impact of the consensus recommendations was seen on the secondary pattern that had the lowest percentage of concordance. It reflected in a change toward a higher Gleason grading group in 46/172 (26.74%) of the cases. A further study is warranted to show how different are these 46 cases according to several clinicopathologic variables: preoperative PSA, positive surgical margins, tumor extent, pathologic staging and biochemical progression following radical prostatectomy.

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Prostate Needle Biopsies Containing Prostatic Intraepithelial Neoplasia or Atypical Foci Suspicious For Carcinoma: Implications for Patient Care

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J Urol. 2006; 175 (3 Pt 1): 820-34

Purpose: We identified information critical for patient treatment on prostate needle biopsies diagnosed with prostatic intraepithelial neoplasia or atypical foci suspicious for carcinoma.

Materials and Methods: A search was performed using the MEDLINE database and referenced lists of relevant studies to obtain articles addressing the significance of finding PIN or atypical foci suspicious for carcinoma on needle biopsy.

Results: There were certain results concerning PIN. 1) Low grade PIN should not be documented in pathology reports due to poor interobserver reproducibility and a relatively low risk of cancer following re-biopsy. 2) The expected incidence of HGPIN on needle biopsy is between 5% and 8%. 3) Although the diagnosis of HGPIN is subjective, interobserver reproducibility for its diagnosis is fairly high among urological pathologists, and yet only moderate among pathologists without special expertise in prostate pathology. 4) The median risk recorded in the literature for cancer following the diagnosis of HGPIN on needle biopsy is 24.1%, which is not much higher than the risk reported in the literature for repeat biopsy following a benign diagnosis. 5) The majority of publications that compared the risk of cancer in the same study following a needle biopsy diagnosis of HGPIN to the risk of cancer following a benign diagnosis on needle biopsy show no differences between the 2 groups. 6) Clinical and pathological parameters do not help stratify which men with HGPIN are at increased risk for a cancer diagnosis. 7) A major factor contributing to the decreased incidence of cancer following a diagnosis of HGPIN on needle biopsy in the contemporary era is related to increased needle biopsy core sampling, which detects many associated cancers on initial biopsy, such that re-biopsy, even with good sampling, does not detect many additional cancers. 8) It is recommended that men do not need routine repeat needle biopsy within the first year following the diagnosis of HGPIN, while further studies are needed to confirm whether routine repeat biopsies should be performed several years following a HGPIN diagnosis on needle biopsy. There were certain results concerning atypical glands suspicious for carcinoma. 1) An average of 5% of needle biopsy pathology reports are diagnosed as atypical glands suspicious for carcinoma. 2) Cases diagnosed as atypical have the highest likelihood of being changed upon expert review and urologists should consider sending such cases for consultation in an attempt to resolve the diagnosis as definitively benign or malignant before subjecting the patient to repeat biopsy. 3) Ancillary techniques using basal cell markers and AMACR (alpha-methyl-acyl-coenzyme A racemase) can decrease the number of atypical diagnoses, and yet one must use these techniques with caution since there are numerous false-positive and false-negative results. 4) The average risk of cancer following an atypical diagnosis is approximately 40%. 5) Clinical and pathological parameters do not help

predict which men with an atypical diagnosis have cancer on repeat biopsy. 6) Repeat biopsy should include increased sampling of the initial atypical site, and adjacent ipsilateral and contralateral sites with routine sampling of all sextant sites. Therefore, it is critical for urologists to submit needle biopsy specimens in a manner in which the sextant location of each core can be determined. 7) All men with an atypical diagnosis need re-biopsy within 3 to 6 months.

Conclusions: It is critical for urologists to distinguish between a diagnosis of HGPIN and that of atypical foci suspicious for cancer on needle biopsy. These 2 entities indicate different risks of carcinoma on re-biopsy and different recommendations for followup.

Editorial Comment

This is an excellent review of two important diagnoses on needle prostatic biopsies. Urologists should clearly distinguish these two pathologic conditions. High-grade prostatic intraepithelial neoplasia (high-grade PIN) is diagnosed whenever acinar cells show nucleomegaly and conspicuous nucleoli. This finding is indistinguishable from prostate cancer, however, in high-grade PIN, there is no acinar architectural disarrangement and, very important, basal cells are present. High-grade PIN corresponds to grade 2 or 3 prostatic intraepithelial neoplasia. Low-grade PIN corresponds to grade 1 and should not be reported by the pathologist due to poor interobserver reproducibility and a relatively low risk of cancer following re-biopsy. On the other hand, high-grade PIN is associated with a moderate risk of cancer following re-biopsy, however, due to an increased needle biopsy core sampling, which detects many associated cancers on initial biopsy, there is a decreased incidence of cancer following a diagnosis of high-grade PIN. Due to these facts, it is recommended that men do not need routine repeat needle biopsy within the first year following the diagnosis of high-grade PIN.

Atypical foci suspicious for carcinoma are a completely different condition that urologists should not interpret as high-grade PIN, adenosis, or any other pathologic entity. It refers to a condition in which the pathologist is not able to make a diagnosis of adenocarcinoma with confidence. This happens in 3 main conditions: 1. the suspicious focus is very small; 2. the focus disappears in further sectioning of the paraffin block; and, 3. absence of cytologic criteria for the diagnosis of adenocarcinoma (1). Atypical focus suspicious for carcinoma was formerly known as ASAP (atypical small acinar proliferation). This term should not be used because may be erroneously interpreted by the urologist as a pathologic entity such as high-grade PIN, adenosis or any other one (2). Furthermore, not all suspicious foci for carcinoma show small acini; large acini may also be suspicious.

Differently from high-grade PIN, atypical foci suspicious for carcinoma have a high risk of cancer on a repeat biopsy. All men with a pathology report “suspicious but not diagnostic for adenocarcinoma” need re-biopsy within 3 to 6 months. Repeat biopsy should include increasing sampling from the suspicious site. This is very important and emphasizes the need for properly identifying the cores from the different regions biopsied, which must be sent in separate containers to the pathology laboratory.

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INVESTIGATIVE UROLOGY

Prevalence of Peyronie's Disease among Patients with Erectile Dysfunction

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Eur Urol. 2006; 49: 564-9

Purpose: To assess the prevalence of Peyronie's disease (PD) among patients with erectile dysfunction (ED).

Materials and Methods: A total of 1,440 male patients with ED were enrolled in this study. Patients were interviewed for ED using the International Index of Erectile Function (IIEF). All patients were also screened for socio-demographic data and risk factors for ED that included age, smoking, diabetes, hypertension, dyslipidemia, Ischemic Heart Disease (IHD), and psychological disorders. The diagnosis of PD was based on a palpable penile plaque or acquired penile curvature. Patients underwent routine laboratory investigation in addition to testosterone and prolactin assessment.

Results: Mean ages \pm SD were 54.1 \pm 6.9 (range 42-71) and 52.5 \pm 11.9 (range 20-84) years for patients with and without PD respectively. Of the patients, 11.8% had mild, 38.3% had moderate and 49.9% had severe ED. 7.9% of the patients had PD. Significant associations between PD and both the longer duration and the increased severity of ED were detected. There were also significant associations between PD and the following socio-demographic risk factors of ED: age, obesity, smoking, duration and number of cigarettes smoked per day. Concomitant diseases and medical comorbidities such as diabetes, dyslipidemia, psychological disorders and the presence of at least one risk factor were significantly associated with PD in patients with ED.

Conclusions: Peyronie's disease was not rare among the study population. There were significant associations between ED risk factors and PD. Further studies are needed to investigate how much ED and PD influence each other.

Editorial Comment

This is an interesting paper studying the incidence of Peyronie's disease (PD) and erectile dysfunction (ED). Peyronie's disease affects up to 9% of male adult population (1) and the present findings are not so much different from the general data.

Other recent study (2) investigated the erectile function status of men presenting with Peyronie's disease. Demographics of patients regarding age, duration of PD, nature of deformity and comorbidities were compared between the patients with PD, with and without erectile dysfunction. 35% of the patients had had ED. The mean age of patients with PD and ED was 52 \pm 22 years old. Hypertension (71.5%), hyperlipidemia (60.4%) and smoking (49.2%) were the leading comorbidities, which are also similar to those found by El-Sakka.

An interesting recent study using penile ultrasound color Doppler (USCD) for assessing ED, detected in 8.7% of the patients, with no clinical symptoms or any clinical findings, minimal lesions suggestive of Peyronie's disease (3).

In spite of further studies to investigate how much ED and PD influence each other, the association is clear, and, therefore, treatment algorithms for men with combined Peyronie's disease and erectile dysfunction must be defined based on functional and satisfaction outcomes (4).

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Long-Term Effect of Experimental Hypercholesterolemia on Cavernosal Tissues

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Objectives: To determine the effect of long-term experimental hypercholesterolemia on cavernosal tissues and to evaluate whether these alterations are reversible after improvement of hypercholesterolemia.

Methods: Thirty-seven New Zealand male rabbits with a mean age of 5 to 6 months and a weight of 2 to 2.5 kg were included in this study. The control group (group 1, n = 7) was fed with normal standard rabbit chow for 24 weeks, the hypercholesterolemia group (group 2, n = 17) was fed with a 1% pure cholesterol diet for 24 weeks, and the reversibility group (group 3, n = 13) was fed first with the 1% pure cholesterol diet for 24 weeks and then with normal standard rabbit chow for 12 weeks. The basal and 24-week serum lipid profiles of all groups and the 36-week serum lipid profiles of group 3 were measured. Core tissue samples 4 mm in diameter taken from formalin-fixed, paraffin-embedded tissue blocks of rabbit corpus cavernosum were examined for Masson trichrome histochemically and desmin and smooth muscle actin by the tissue array method using immunohistochemistry.

Results: Hypercholesterolemia was observed in groups 2 and 3 at 24 weeks compared with group 1. In group 3, at 36 weeks, the cholesterol levels were decreased. A statistically significant ($P < 0.05$) irreversible decrease was observed in smooth muscle actin level in group 3 (reversibility group) by immunohistochemical analysis. The decrease in desmin was reversible, and no significant difference was observed in collagen among the three groups.

Conclusions: Long-term chronic effects of experimental hypercholesterolemia on cavernosal smooth muscles might be irreversible and this might alter erectile function.

Editorial Comment

Conditions associated with altered function of nerves and endothelium, such as hypertension, smoking, hypercholesterolemia, diabetes, etc. may cause circulatory and structural changes in the penile erectile tissue and can result in arterial insufficiency and impaired smooth muscle relaxation (1). Hypercholesterolemia is considered one of the main risk factors of cardiovascular diseases and also for vasculogenic erectile dysfunction. It was demonstrated more than 5 years ago that hypercholesterolemia may cause impairment of endothelium-dependent relaxation and that oxidized LDL is the major causative cholesterol of the impaired

relaxation response (2). The vascular endothelial growth factor (VEGF), which is an angiogenic growth factor and an endothelial cell-specific mitogen, and whose actions are coupled to nitric oxide, is probably involved in this kind of injury, because it was found that intracavernosal injections of VEGF appear to protect corporal endothelium from hypercholesterolemia induced injury, preserving endothelial dependent corporal smooth muscle relaxation in hypercholesterolaemic rabbit (3). Recently, it was found a significantly lower in vivo and in vitro erectile response to phosphodiesterase-5 inhibition in hypercholesterolaemic rabbits than in controls (4).

The effect of experimental hypercholesterolemia on the ultrastructure of cavernosal smooth muscle cells, endothelial cells, elastic fibers, and collagen, which are the key structures for erection, were morphologically analyzed in hypercholesterolaemic rabbits, 5 years ago, by the same research group of the present paper (5). The findings shown that hypercholesterolemia in this animal model affect the percentage of staining for smooth muscle actin, endothelial cells, elastin, and collagen III and IV. However, the authors stated that this effect is temporary depending on the blood cholesterol levels, and, therefore, might not alter the erectile function.

The present study, by Karaboga et al., is very much important because demonstrates by the first time, in our knowledge, that the long-term chronic effects of experimental hypercholesterolemia on cavernosal smooth muscles might be irreversible and therefore might alter erectile function.

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RECONSTRUCTIVE UROLOGY

The Anatomy and Embryology of Posterior Urethral Valves

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Purpose: We reviewed the literature to better elucidate the history behind our understanding of the anatomy, classification and embryology of posterior urethral valves.

Materials and Methods: A directed MEDLINE literature review of the anatomy, classification and embryology of posterior urethral valves was performed. An effort was made to focus on the most frequently cited historical articles as well as those including detailed anatomical analyses of fetal specimens. Also included was the analysis of a specimen obtained at our institution in a novel manner that to our knowledge has not been previously described in the literature with respect to the anatomy of posterior urethral valves.

Results: The precise origins regarding the anatomy and embryology of posterior urethral valves remain undefined. However, the literature is abundant in theories regarding the origin of posterior urethral valves, based primarily on small uncontrolled series or case reports. There are a limited number of reports of the anatomy of posterior urethral valves in methodical fashion using reproducible scientific techniques such as histopathology. These reports are invaluable for providing a foundation of how to properly study and define the origins of posterior urethral valves.

Conclusions: Elucidating this most fundamental feature of a congenital condition central to the practice of pediatric urology is essential. More well designed studies specifically with this goal in mind are necessary. Incorporating new reconstructive imaging modalities may assist us in pinpointing the elusive origins of the embryology and anatomy of posterior urethral valves.

Editorial Comment

Although posterior urethral valves have a recognized incidence of 1/5000 to 8000 in male newborns, it is not known how common it might cause fetal demise (1).

Almost 2 centuries after its first description, the posterior urethral valves is newly investigated by Krishnan et al. with modern computer imaging in combination with histopathology in one of the few virgin cases of an untreated malformation known as a posterior urethral valve which helped to clarify its origin.

Until week 9, male and female urethral development is identical; whereas by week 14, the male urethra completes its development (2). Many of the former anatomical descriptions were misleading because of prior manipulations to the histological investigations with the result of several different described types first recognized by Dewan & Goh (3).

Krishnan et al. investigated the rare case of an untreated posterior urethral valve histologically by cross sectioning and reconstructed by three-dimensionally using computer imaging from the histology of the infant's urethra. With this investigation they revealed, as several times prior (4,5), the results of anatomical development in normal and malformed urethras. They demonstrated, with their outstanding work after an all-around literature analysis that the theory of Dewan et al. (6), seems to be the most likely with the single congenital obstructing posterior urethral membrane (COPUM).

Works similar to Krishnan et al. need our recognition/attention because they complete the understanding of the embryological development. This combination of histology and three-dimensional reconstruction helps to recognize and understand the embryonic development and will help to improve early treatment.

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Facilitatory Neuromodulative Effect of Duloxetine on Pudendal Motor Neurons Controlling the Urethral Pressure: A Functional Urodynamic Study in Healthy Women

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Objective: The aim of this functional urodynamic experiment in healthy women was to study the effect of duloxetine, which is a combined serotonin and norepinephrine (5-HT/NE) reuptake inhibitor, on urethral resting pressure, excitability of pudendal motor neurons, and urethral sphincter contractility.

Methods: In 11 healthy female subjects three baseline urethral pressure profiles (UPPs) were obtained to study resting pressure. Afterward the individual motor threshold (MT) for external urethral sphincter (EUS) contraction in response to transcranial magnetic stimulation (TMS) was determined to study the excitability of pudendal motor neurons. Another three UPPs were recorded while sacral root magnetic stimulation (SMS) was performed to evoke reproducible urethral contractions to study urethral sphincter contractility. Then the women received 40 mg duloxetine and the protocol was repeated 4h after drug administration. The resting pressure values, MT values following TMS, and the EUS pressure amplitudes in response to SMS obtained at baseline were statistically compared to the corresponding values at follow-up after duloxetine.

Results: Oral administration of duloxetine significantly lowered MT for EUS contraction in response to TMS ($p = 0.013$). In addition, duloxetine significantly increased EUS pressure amplitudes in response to SMS ($p = 0.0007$, 5 of 11 subjects evaluated) but did not change urethral resting pressures.

Conclusions: This is the first functional, urodynamic controlled study to show that the combined 5-HT/NE reuptake inhibitor duloxetine has a significant effect on the excitability of pudendal motor neurons and on urethral sphincter contractility in healthy women in vivo but no significant effect on urethral resting tone. Our data confirm a facilitatory neuromodulative effect of duloxetine on sphincter motor neurons in humans.

Editorial Comment

The first investigation regarding the norepinephrine-serotonin (NE/5-HT) reuptake inhibitor duloxetine was performed in the cat model with induced cystitis causing the symptom of overactive bladder and stress urinary incontinence. The authors reported relaxing the bladder and increasing the outlet resistance (1). The paper presented here is the first dealing with the influence of the NE/5-HT reuptake inhibitor to the pelvic floor muscles in females. The authors recorded responses of transcranial and spinal cord magnetic stimulation thereby

demonstrating individual increases in the urethral sphincter pressure with duloxetine. Although it is an elegant way to demonstrate the effect of the NE/5-HT reuptake inhibitor, the magnetic stimulation field is not very selective and stimulates all (efferent as well as afferent) nerve fibers in the field of the coil. Efferent motor neurons stimulated by these methods supply the striated muscles of the pelvis but cannot be subdivided to the urethral sphincter only. Vodusek & Zidar suggested using a needle to record from the sphincter to identify specific urethral muscle functions from a general “mass contraction” (2).

The authors reported a decreased threshold for significant urethral pressure spikes in the mid urethra after sacral root magnetic stimulation through the influence of the NE/5-HT reuptake inhibitor in 45% of the subjects. This is in line with reports of decreased incontinence episode frequency of 50 – 100% in 51.4% of the trial group (n = 344) receiving duloxetine (3). An additional double-blind trial with a more representative sample of subjects should validate the drug effect on urethral pressure after magnetic stimulation.

In addition, the outcome of the single intake of the NE/5-HT reuptake inhibitor causes under normal physiological conditions does not lead to significant stimulation of postsynaptic 5-HT receptors.

After the administration of a NE/5-HT reuptake inhibitor all 5-HT transporters at the pre-synaptic membrane are blocked, leading to higher 5-HT levels in the synaptic cleft. At the same time, these increased 5-HT levels activate 5-HT_{1A} and 5-HT_{1B} auto-receptors, located at the pre-synaptic membrane. These pre-synaptic auto-receptors inhibit as negative feedback regulators the release of 5-HT (4-6). The simulated on-demand use causes only a mild or no increase of 5-HT neurotransmission, which might be an explanation of the experimental outcome.

Still this elegant approach might serve as a single dose-screening test to predict patients with beneficial treatment responses to the duloxetine effect in a potential patient avoiding possible side effects. The blood pressure rises induced by the magnetic coil stimulation might ask for other tests than the magnet coil stimulation to underline the outcome of this approach and demonstrate the effect to motor thresholds resulting in increased urethral pressure amplitude even in a higher proportion of subjects.

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UROLOGICAL ONCOLOGY

Risk of Prostate Cancer-Specific Mortality Following Biochemical Recurrence after Radical Prostatectomy

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JAMA. 2005; 294: 433-9; Comment in: JAMA. 2005; 294: 2969; author reply 2969-70, and Comment in: JAMA. 2005; 294: 493-4

Context: The natural history of biochemical recurrence after radical prostatectomy can be long but variable. Better risk assessment models are needed to identify men who are at high risk for prostate cancer death early and who may benefit from aggressive salvage treatment and to identify men who are at low risk for prostate cancer death and can be safely observed.

Objectives: To define risk factors for prostate cancer death following radical prostatectomy and to develop tables to risk stratify for prostate cancer-specific survival.

Design, Setting, and Patients: Retrospective cohort study of 379 men who had undergone radical prostatectomy at an urban tertiary care hospital between 1982 and 2000 and who had a biochemical recurrence and after biochemical failure had at least 2 prostate-specific antigen (PSA) values at least 3 months apart in order to calculate PSA doubling time (PSADT). The mean (SD) follow-up after surgery was 10.3 (4.7) years and median follow-up was 10 years (range, 1-20 years).

Main Outcome Measure: Prostate cancer-specific mortality.

Results: Median survival had not been reached after 16 years of follow-up after biochemical recurrence. Prostate-specific doubling time (< 3.0 vs 3.0-8.9 vs 9.0-14.9 vs > or =15.0 months), pathological Gleason score (< or =7 vs 8-10), and time from surgery to biochemical recurrence (< or =3 vs > 3 years) were all significant risk factors for time to prostate-specific mortality. Using these 3 variables, tables were constructed to estimate the risk of prostate cancer-specific survival at year 15 after biochemical recurrence.

Conclusion: Clinical parameters (PSADT, pathological Gleason score, and time from surgery to biochemical recurrence) can help risk stratify patients for prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. These preliminary findings may serve as useful guides to patients and their physicians to identify patients at high risk for prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy to enroll them in early aggressive treatment trials. In addition, these preliminary findings highlight that survival in low-risk patients can be quite prolonged.

Editorial Comment

How long does a patient live with a PSA recurrence after radical prostatectomy? The authors address this important issue in a rather small retrospective analysis of 379 men. Median time to biochemical progression after radical prostatectomy was 2 years. 17% of patients died within the median follow-up of 10 years.

The 10 and 15 years cause-specific survival from the time of PSA recurrence was 73% and 55%, respectively. Gleason score and PSA doubling time were predictors of death from prostate cancer.

The problem of a correct indication for surgical intervention and correct counseling of patient is again underlined by these data.

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Postoperative Radiotherapy After Radical Prostatectomy: A Randomised Controlled Trial
(EORTC trial 22911)

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Lancet. 2005; 366 (9485): 572-8; Comment in: Lancet. 2005; 366 (9485): 524-5.

Background: Local failure after prostatectomy can arise in patients with cancer extending beyond the capsule. We did a randomised controlled trial to compare radical prostatectomy followed by immediate external irradiation with prostatectomy alone for patients with positive surgical margin or pT3 prostate cancer.

Methods: After undergoing radical retropubic prostatectomy, 503 patients were randomly assigned to a wait-and-see policy, and 502 to immediate postoperative radiotherapy (60 Gy conventional irradiation delivered over 6 weeks). Eligible patients had pN0M0 tumours and one or more pathological risk factors: capsule perforation, positive surgical margins, invasion of seminal vesicles. Our revised primary endpoint was biochemical progression-free survival. Analysis was by intention to treat.

Findings: The median age was 65 years (IQR 61-69). After a median follow-up of 5 years, biochemical progression-free survival was significantly improved in the irradiated group (74.0%, 98% CI 68.7-79.3 vs 52.6%, 46.6-58.5; $p < 0.0001$). Clinical progression-free survival was also significantly improved ($p = 0.0009$). The cumulative rate of locoregional failure was significantly lower in the irradiated group ($p < 0.0001$). Grade 2 or 3 late effects were significantly more frequent in the postoperative irradiation group ($p = 0.0005$), but severe toxic toxicity (grade 3 or higher) were rare, with a 5-year rate of 2.6% in the wait-and-see group and 4.2% in the postoperative irradiation group ($p = 0.0726$).

Interpretation: Immediate external irradiation after radical prostatectomy improves biochemical progression-free survival and local control in patients with positive surgical margins or pT3 prostate cancer who are at high risk of progression. Further follow-up is needed to assess the effect on overall survival.

Editorial Comment

The problem of positive surgical margins after radical prostatectomy is common. The question is the best adjuvant treatment in this scenario, immediate or deferred radiotherapy? This important paper gives a definite answer.

Time to failure was significantly longer in the immediate radiotherapy group, with 21.4% of patients failing after 5 years in this group vs 44.2% in the deferred treatment group. Data on survival differences are not mature yet.

Immediate adjuvant radiation should be considered in margin-positive patients after radical therapy.

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NEUROUROLOGY & FEMALE UROLOGY

What Are the Supportive Structures of the Female Urethra?

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Aims: Female stress urinary incontinence is thought to result from impairment of the connective tissue “ligaments” of the urethra. Surgical repair of female incontinence mainly involves fixation of the urethra to the pubic bone or other surrounding structures. In the present anatomical-radiological study, the anatomy of the connective tissue structures around the female urethra was investigated to determine the anatomical structures that support the urethra and the rhabdosphincter.

Materials and Methods: The topography of the anterior compartment of the female pelvis was studied in serial sections and one anatomical preparation of 30 female fetuses and of six adult females. The pelves of 29 female fetuses were processed according to plastination histology technique. The pelves of the six adult specimens were processed according to sheet plastination technique. In addition, the anatomical findings were compared with MR images of 41 adult female volunteers.

Results: The ventro-lateral aspect of the urethra remains free of fixating ligaments throughout its pelvic course. Ventro-laterally the urethra is enclosed by the ventral parts of the levator ani, its fasciae and a ventral urethral connective tissue bridge connecting both sides. Dorsally, the urethra is intimately connected to the wall of the vagina.

Conclusions: The female urethra has no direct ligamentous fixation to the pubic bone. Urethral continence after pregnancy and childbirth may be explained by a widening of the hiatus of the levator ani or the anterior vaginal wall, resulting in overstretching of the ventral urethral connective tissue bridge or the disruption of the fixation between urethra and vagina.

Editorial Comment

The authors analyze the anatomy of the female urethra with regards to the support of the urethra and rhabdosphincter. This was accomplished through analysis of the pelves of 30 female fetuses and 6 female adults. The authors find that there is no pubourethral ligament attaching the urethra to the pubic bone; instead the tissues attaching the pubic bone to the bladder neck are mostly tissue containing smooth muscle cells. In addition, the dorsal end of the rhabdosphincter is connected at its dorsal end through a strong connective tissue fixation to the ventral wall of the vagina. The neurovascular bundles are identified in the dorsal lateral pelvic wall in the ventral lateral aspects of the urethra.

This excellent article is extremely well written with beautiful anatomical pictures. That the investigators were not able to find the existence of any true pubourethral ligaments helps explain the ability of a patient to continue with urinary continence after a transvaginal urethrolisis, especially one utilizing the suprameatal transvaginal technique (1). That the authors found that the neurovascular bundles ran in the dorsal lateral pelvic wall on the lateral and ventral aspects of the urethra may explain a potentiality for sexual dysfunction after formal urethrolisis. There is an excellent discussion with regards to 3 supportive structures of the urethra and rhabdosphincter, which were identified, and the pathologic effects on same, which may lead to voiding dysfunction.

Reference

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How do the Prevalences of Urogenital Symptoms Change During Pregnancy?

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Neurourol Urodyn. 2006; 25: 135-9

Aim: The aim of this study was to report the changes in prevalences of urogenital symptoms during pregnancy and to evaluate the amount of bother nulliparous pregnant women experience from these symptoms.

Methods: We have used a prospective longitudinal cohort study design. Five hundred fifteen nulliparous women with a singleton pregnancy were recruited from 10 midwifery practices between January 2002 and July 2003. The women received postal questionnaires. Urogenital symptoms were assessed with the Dutch version of the standardized and validated Urogenital Distress Inventory (UDI). We analyzed our data on item level and on the clustering of items.

Results: The prevalences of the frequency and urgency symptoms are high at 12 weeks (74% and 63%) and remain stable during pregnancy. The prevalences of urinary incontinence and voiding difficulties increase with gestational age. Frequency disappears in 12% in late pregnancy, urgency in 22%, and stress incontinence in 23%. The prevalence of bothersome frequency symptoms is much higher than of urinary incontinence (21% compared to 6%). All UDI subscales increase significantly during pregnancy.

Conclusions: Urogenital symptoms occur in almost all women during pregnancy. Whereas the prevalence of overactive bladder symptoms is high and remains stable from early pregnancy on, the prevalences of urinary incontinence symptoms increase with gestational age. Despite the high prevalences of symptoms, the majority of women report not to be bothered by it.

Editorial Comment

The authors study a large number of women during their first pregnancy and quantify both the prevalence and level of bother of the voiding symptoms that developed during this period. The investigation found that by twelve weeks of pregnancy, urgency and frequency had been identified and this symptom remained stable during pregnancy. In contrast, the incidence of urinary incontinence increased as the pregnancy matured. The authors concluded that though almost all women in pregnancy have some voiding dysfunction and the prevalence of overactive bladder symptoms is quite high from early on, the majority of women are not bothered by these symptoms.

That nulliparous women have a known rate of voiding dysfunction is well known and quoted by the authors of this manuscript. Perhaps the pregnant women of this study felt almost no bother from their urinary symptoms secondary due to the understanding that this was a self limited phenomena that would cease because of: it was the miracle of childbirth; or, the life changes and challenges associated with a maturing pregnancy reduced voiding dysfunction to a lower priority on the list of physical, mental and situational events that may affect and bother the pregnant female. A clear message from this article is that almost all women who are pregnant will have some kind of voiding dysfunction with urge and frequency starting early and urinary

incontinence continuing to worsen as the pregnancy continues; nevertheless, the physician probably will not be challenged to find a solution to this problem for the pregnant woman does not view it as a significant bother.

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PEDIATRIC UROLOGY

Antegrade Scrotal Sclerotherapy for Treating Primary Varicocele in Children

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BJU Int. 2006; 97: 809-12

Objective: To evaluate the effectiveness and limitations of antegrade sclerotherapy (AS) for the treatment of primary varicocele in childhood.

Patients and Methods: From December 1996 to December 2004, 88 patients (mean age 13.3 years, range 9-18) with primary varicocele underwent AS (91 varicocele ablations in all). The indications for surgery were testicular pain (16 boys, 18%), a large varicocele with cosmetic implications, testicular hypotrophy (one) and in 71 (81%) the varicocele was detected incidentally during a routine physical examination; all were left-sided. According to the classification used by Tauber, 46 (52%) varicoceles were grade II and 42 (48%) grade III. The clinical and ultrasonography (US) results were evaluated over a median (range) follow-up of 11 (3-60) months, and the operative duration, X-ray exposure time, persistence rate of varicoceles and complications were compared with those using other techniques. **RESULTS:** In 11 patients there was a palpable difference in size between the testicles, but in only five (6%) was testicular hypotrophy (testicular volume (< 75% testicular volume vs the normal side) confirmed by US. The mean (SEM) operative duration for AS was 33.2 (2.14) min. In 16 (18%) patients it was necessary to expose a second or third vein because the first vein chosen was unsuitable for sclerotherapy. The mean operative radiation exposure was 2.18 (0.21) s. One patient (1%) was treated with a high ligation of the testicular vein (Palomo procedure) after initial unsuccessful AS, and was excluded from the analysis. Eighty-four (97%) patients were eligible for follow-up: six (7%) had a persistent varicocele (four grade II, two grade III), four of whom had repeat sclerotherapy successfully (no recurrence at follow-up). Fourteen (15%) patients had enlarged testicular veins only on US (varicocele grade 0). No patient developed a hydrocele after AS. There were complications after surgery in three (3%) patients (two superficial wound infections, one scrotal haematoma together with focal testicular necrosis).

Conclusions: AS is an efficient minimally invasive surgical method for correcting varicoceles in older children, although the operative duration is sometimes longer than in adults, and surgery can be more difficult because of the smaller veins. Partial testicular necrosis, despite correct AS, is a very rare but serious complication.

Editorial Comment

This paper provides more data on a new, innovative and “minimally invasive” treatment for varicocele. The technique, which uses a short time of fluoroscopy to assess venous drainage and a venous injection of a sclerosing agent, should be associated with minimal postoperative morbidity.

The authors used the technique in 88 patients over 6 years. Mean fluoroscopy time was 2 seconds and mean operative time was 33 minutes. In recent years, the procedure has been done as a “day surgery”. The authors report that there was a persistent varicocele in only 6 patients and no postoperative hydroceles. There was a postoperative increase in relative volume of the affected testis in 4 of 5 evaluable cases. One patient had an ischemic necrosis of the upper pole of the testis, presumably due to the sclerosing agent entering the testicular circulation.

The series is a bit unusual in that very few of the patients had testicular hypertrophy/atrophy. In our experience, a small left testis is the primary reason for operative intervention. If there is only a limited benefit to the procedure, then the risk of the procedure may be more than the benefit. Concerning also is a 7% recurrence rate (and this seems to exclude one patient who underwent a Palomo repair for a failure!). This is higher than anticipated, as is the wound infection rate of 2% and the incident of testicular ischemia.

Overall, this is an interesting contribution on a minimally invasive treatment of varicocele in adolescents. It is a technique worth exploring, but is clearly not without complications. In my opinion it should be reserved for patients with stronger indications.

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Clinical Significance of Primary Vesicoureteral Reflux and Urinary Antibiotic Prophylaxis after Acute Pyelonephritis: A Multicenter, Randomized, Controlled Study

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Pediatrics. 2006; 117: 626-32; Comment in: Pediatrics. 2006; 117: 919-22

Objectives: To evaluate the role of primary vesicoureteral reflux (VUR) in increasing the frequency and severity of urinary tract infections (UTIs) and renal parenchymal damage among patients with acute pyelonephritis and to determine whether urinary antibiotic prophylaxis reduces the frequency and/or severity of UTIs and/or prevents renal parenchymal damage among patients with mild/moderate VUR.

Methods: Patients 3 months to 18 years of age with acute pyelonephritis, with or without VUR, were assigned randomly to receive urinary antibiotic prophylaxis or not. Patients were monitored every 3 months for 1 year. Dimercaptosuccinic acid renal scans were repeated at 6 months or if there was a recurrence of febrile UTI. Urinalysis and urine culture were performed at each clinic visit. Renal ultrasound scans and voiding cystourethrograms were repeated at the end of 1 year of follow-up monitoring.

Results: Of the 236 patients enrolled in the study, 218 completed the 1-year follow-up monitoring. Groups were similar with respect to age, gender, and reflux grade distribution for those with VUR. No statistically significant differences were found among the groups with respect to rate of recurrent UTI, type of recurrence, rate of subsequent pyelonephritis, and development of renal parenchymal scars. **Conclusions:** After 1 year of follow-up monitoring, mild/moderate VUR does not increase the incidence of UTI, pyelonephritis, or renal scarring after acute pyelonephritis. Moreover, a role for urinary antibiotic prophylaxis in preventing the recurrence of infection and the development of renal scars is not supported by this study.

Editorial Comment

The authors present a very important study of the effects of reflux on the outcome of patient with UTIs and the benefits of prophylactic antimicrobials. Their findings suggest: 1) that reflux is not a cause of UTIs (many studies would support this notion, as an abnormality of host resistance is more likely); 2) that reflux is not associated with a statistically significant increase in pyelonephritis or renal scarring (the former tends to disagree with the previous literature and the latter is in agreement with the literature); 3) and strikingly, that antibiotic prophylaxis was associated with more UTIs and pyelonephritis than those on no therapy (a very controversial finding).

The findings, especially that prophylaxis was of no benefit (and might have been harmful), are important and suggest a change in clinical management. On the other hand, there are some significant weaknesses in this study. First, the study was not blinded. The control group was not on any medications (vs. being treated with placebo). Hence these patients may have been evaluated differently. Indeed, some of them must have been treated with antibiotics for other illnesses during the study (e.g. ear infections). There is no mention of this. Second, the statistical analysis excluded patients who were non-compliant. A more appropriate analysis would have been an "intention to treat" analysis. Furthermore, the authors state that they needed 60 patients in each group for appropriate recruitment, hence the study was underpowered. Third, clinicians have been aware that abnormalities of host resistance are the main cause of UTIs, but the authors make no mention of voiding dysfunction or constipation. Fourth, the study only lasted 1 year and during that time, only 20% of the patients resolved their reflux. To answer the question that the authors attempt to deal with, a much longer follow-up period is needed.

Despite these misgivings, the authors did find a much higher rate of pyelonephritis in those getting prophylaxis than in those on no medications (12.9% vs 1.7%). This finding is very provocative and warrants further scientific study. If substantiated, this could lead to a paradigm shift in the management of children with reflux.

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