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UROLOGICAL SURVEY

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STONE DISEASE

Effects of specific alpha-1A/1D blocker on lower urinary tract symptoms due to double-J stent: a prospectively randomized study

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The aim of our study was to evaluate the effect of tamsulosin in improving symptoms in patients with indwelling double-J ureteral stents. This prospective study lasted from April 2006 to March 2008. All the patients with symptomatic lower ureteral stones with < 15 mm diameter were enrolled, and were prospectively randomized (random numbers table) into two groups. A total of 154 patients, with insertion of a double-J ureteral stent after ureteroscopic stone removal. In group 1, 75 patients were enrolled and received placebo for 2 weeks. Group 2 included 79 patients who received 0.4 mg of tamsulosin, once daily for 2 weeks. All patients completed the validated ureteral stent symptom questionnaire (USSQ) and quality of life of international prostate symptom scale (IPSS) for evaluating the symptoms of double-J stents and quality of life after double-J stent insertion and removal, respectively. The analysis of the questionnaire at W1 revealed a significant difference in the main score index of urinary symptoms, body pain and general health between groups 1 and 2. When comparing W1 evaluation with that of W4 after double-J removal, both groups showed significant worsening of urinary symptoms, body pain, general health and work performance, except sexual performance. The mean score of quality of life in IPSS was 4.21 in group 1 and 1.6 in group 2. Tamsulosin can improve a subset of stent-related urinary symptoms and quality of life effectively and may be applied in routine clinical practice.

Editorial Comment

This is a well designed, implemented and analyzed study that lends support to prior studies suggesting the efficacy of alpha-blockers in the management of ureteral stent discomfort. Patients receiving tamsulosin had less urinary symptoms and body pain and better general health and quality of life than those on placebo. Remarkably, only 3% of patients in the tamsulosin group required narcotics, compared to 33% in the placebo group. Urinary symptoms were less in both men and women treated with tamsulosin irrespective of age. Improvement in body pain was noted primarily in patients > 50 years of age.

Alpha-blockers may alleviate stent discomfort by decreasing ureteral spasm, decreasing trigone sensitivity, decreasing voiding pressures or decreasing resting ureteral pressure and peristalsis.

Though previous studies have suggested return to normal activities at two weeks following ureteroscopy, it is possible that a small subset of patients may not have reached "baseline" by the 4-week time point following ureteroscopy. Administering this questionnaire at 2-3 months may have been a more reliable baseline, albeit logistically more challenging.

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Ureteral stone location at emergency room presentation with colic

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Purpose: It is thought that the 3 narrowest points of the ureter are the ureteropelvic junction, the point where the ureter crosses anterior to the iliac vessels and the ureterovesical junction. Textbooks describe these 3 sites as the most likely places for ureteral stones to lodge. We defined the stone position in the ureter when patients first present to the emergency department with colic.
Materials and Methods: We retrospectively reviewed the records of 94 consecutive patients who presented to the emergency department with a chief complaint of colic and computerized tomography showing a single unilateral ureteral calculus. Axial, coronal and 3-dimensional reformatted computerized tomography scans were evaluated, and stone position and size (maximal axial and coronal diameters) were recorded, as were the position of the ureteropelvic junction, the iliac vessels (where the ureter crosses anterior to the iliac vessels) and the ureterovesical junction. Patients with a history of nephrolithiasis, shock wave lithotripsy, ureteroscopy or percutaneous nephrolithotripsy were excluded from study. Statistical analysis was performed using Student's t test and Pearson's correlation coefficient.
Results: At the time of emergency department presentation for colic ureteral stone position was the ureteropelvic junction in 10.6% cases, between the ureteropelvic junction and the iliac vessels in 23.4%, where the ureter crosses anterior to the iliac vessels in 1.1%, between the iliac vessels and the ureterovesical junction in 4.3% and at the ureterovesical junction in 60.6%. Proximal calculi had a greater axial diameter than distal calculi (mean 6.1 vs. 4.0 mm) and a greater coronal diameter than distal calculi (6.8 vs. 4.1 mm, each $p < 0.001$). Axial and coronal diameters moderately correlated with stone position ($r = -0.47$ and -0.55, respectively, each $p < 0.001$).
Conclusions: Proximal ureteral stones were larger in axial and coronal diameter than distal ureteral stones. At emergency department presentation for colic most stones were at the ureterovesical junction and in the proximal ureter between the ureteropelvic junction and the iliac vessels. A few stones were at the ureteropelvic junction and only 1 lodged at the level where the ureter crosses anterior to the iliac vessels, despite the literature stating that these locations are 2 of the 3 most likely places for stones to become lodged.

Editorial Comment

The authors have identified the most common stone locations associated with significant renal colic - the ureterovesical junction and the proximal ureter. Whether this re-defines the narrowest points in the ureter remains to be determined. The authors do not report the duration of symptoms prior to presenting to the emergency room or the subsequent successful migration of the stone or need for intervention. An alternative way to define the tightest spots would be to evaluate the site of stone impaction after a trial of conservative therapy - in other words, where do stones get stuck? One could evaluate the points of resistance commonly encountered during retrograde ureteroscopy. One could obtain ureteral dimensions from contrast-enhanced images. Interestingly, the authors report no difference in ureteral length between men and women - this may be another misconception that the authors could investigate further. The authors note 2 important implications for imaging in the face of renal colic - evaluation of plain radiography should focus on the ureterovesical junction and upper ureter, while ultrasonography should be performed with a full bladder to better visualize the ureterovesical junction.

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ENDOUROLOGY & LAPAROSCOPY

Renal artery pseudoaneurysm following laparoscopic partial nephrectomy

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Urology. 2009 [Epub ahead of print]

Objectives: To present our experience with the management of renal artery pseudoaneurysms following laparoscopic partial nephrectomy (LPN).
Methods: Our bi-institutional LPN database of 259 patients from July 2001 to April 2008 was queried for patients diagnosed with a postoperative renal artery pseudoaneurysm. Demographic data, perioperative course, complications, and follow-up studies in identified subjects were analyzed. Postembolization success was defined as symptomatic relief, resolution of hematuria, and a stable hematocrit and serum creatinine.
Results: We identified 6 patients (2.3%) who were diagnosed with a renal artery pseudoaneurysm after LPN. The mean age of our cohort was 61.2 years (49-76), mean operative time was 208 minutes (140-265), and mean estimated blood loss was 408 mL (50-800). Patients presented at a mean of 12.6 days (5-23) after the initial surgery. Five patients had gross hematuria and a decreased hematocrit, with 1 patient presenting with clinical symptoms of hypovolemia. The sixth patient was incidentally diagnosed. The diagnosis of a renal artery pseudoaneurysm was confirmed in all cases by angiography. Selective angioembolization was successfully performed in all patients. At a median follow-up of 8.3 months all patients (100%) remained without any evidence of recurrence.
Conclusions: Although pseudoaneuryms are a rare postoperative complication of LPN, they are potentially life-threatening. Early identification and proper management can help reduce the potential morbidity associated with pseudoaneurysms. Our experience demonstrates the feasibility and supports the use of selective angioembolization as an excellent first-line option for patients who present with this form of delayed bleeding.

Editorial Comment

The authors should be congratulated for reviewing their experience of pseudoaneurysms following laparoscopic partial nephrectomy (LPN). In contrast to case reports describing this particular complication post LPN, this manuscript reviewed the incidence of pseudoaneurysms post LPN in a series of LPN. From a total of 259 LPNs performed in 81 months the authors identified 6 patients (2.3%) who were diagnosed with a renal artery pseudoaneurysm after LPN. The majority of patients presented with gross hematuria and a decreased hematocrit, with 1 patient presenting with clinical symptoms of hypovolemia. One patient was incidentally diagnosed. Their diagnosis was confirmed in all cases by angiography. Selective angioembolization was successfully performed in all patients. At a median follow-up of 8.3 months, all patients (100%) remained without any evidence of recurrence. Their conclusion was that pseudoaneurysms are a rare postoperative complication of LPN, but they are potentially life threatening. Early identification and proper management can help reduce the potential morbidity associated with pseudoaneurysms and selective angioembolization is an excellent first-line of treatment of patients who present with this form of delayed bleeding. It would be beneficial if we could predict the patients that would develop this type of complication, i.e.; localization of the tumor, size, anatomical characteristics, etc., so we could foresee and prevent the occurrence of postoperative bleeding due to a pseudo-aneurysm.

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Laparoscopic radical prostatectomy in renal transplant recipients

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Objectives: To report our experience with 9 consecutive laparoscopic radical prostatectomy (LRP) on renal transplant recipients (RTR) and to compare it with other LRPs performed during the same period by the same surgeons. Retropubic radical prostatectomy has widely been described in RTR, whereas LRP has rarely been studied.
Methods: Between January 2007 and December 2008, all clinical data from patients undergoing radical prostatectomy were prospectively collected in a database. The database was searched to find information of LRP on RTR. We compared RTR and other patients for all relevant clinical data and for surgical complications.
Results: A total of 9 LRP on RTR (5.8%) and other 164 LRP were performed. LRP on RTR were compared with other LRP. No statistically relevant difference was observed in patient characteristics, biopsy core pathologic analysis, prostate specimen pathologic analysis, and oncologic outcomes. Surgical procedure was also achieved under the same conditions in RTR than in other patients (surgical time, blood loss, transfusion rate, bladder injury). Rectal injury rate was significantly higher in RTR than in other patients (22.2% vs 1.8%, P = .022).
Conclusions: LRP in RTR is feasible. The procedure can be managed the same way as LRP on other patients, but special care must be taken to avoid rectal injury. In our experience, the dissection of the posterior side of the prostate was more difficult on RTR than on other patients.

Editorial Comment

The authors described a difficult procedure, that is laparoscopic radical prostatectomy (LRP) in a population that has a complex medical history. Moreover, the possible anatomical challenges may cause an increase in morbidity. When cadaveric grafts are used, the immune system may alter the course of wound healing and increase not only the morbidity but also the mortality due to postoperative complications.

I congratulate the authors for sharing their experience describing a significant increase in rectal injury due to the anatomical challenges due to prior renal transplantation, the million dollar question is whether these patients can better served by other methods of therapy and ablation, such as, cryoablation of the prostate under transrectal ultrasonography.

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IMAGING

Imaging in pediatric urinary tract infection: a 9-year local experience

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Objective: Urinary tract infection (UTI) is a common disease entity in children, and a number of imaging options are offered for these patients. The purpose of our study was to retrospectively describe the (99m)Tc-labeled dimer captosuccinic acid (DMSA) renal scintigraphy, ultrasound, and micturating cystourethrography (MCU) findings over a 9-year period.
Materials and Methods: All children younger than 10 years old who presented to a local hospital in Hong Kong between July 1, 1997, and June 30, 2006, with culture-confirmed UTI and who subsequently underwent DMSA scintigraphy, ultrasound, and MCU were identified. For the purpose of this study, patients with underlying major congenital urinary tract abnormalities were excluded. DMSA scintigraphy was regarded as the gold standard for the diagnosis of renal scarring. DMSA scintigraphy, ultrasound, and MCU findings and clinical outcomes were reviewed and analyzed.
Results: A total of 583 children were included in the study. Of these, 432 children (74.1%) had normal findings on ultrasound and on MCU. Only 13 children (3%) of this group had renal scarring as shown on DMSA scintigraphy. The overall negative predictive value (NPV) for excluding renal scarring of combined ultrasound and MCU reached 97%. The NPV was 97.7% in the subgroup of patients 0 to 2 years old. Conclusion: For children younger than 2 years with UTI in the absence of underlying major congenital urinary tract abnormalities, we recommend that DMSA scintigraphy may be withheld if findings on both ultrasound and MCU examinations are normal.

Editorial Comment

The authors performed a retrospective study in order to evaluate the potential role of combined ultrasound (US) and MCU as first-line imaging tests in predicting renal scarring using DMSA scintigraphy as the gold standard. In their cohort, almost 600 children were included. The performances of US alone, MCU alone, and the techniques combined were systematically evaluated and compared with the performance of DMSA scintigraphy. If US alone was performed, the probability of missing renal scarring was as high as 7.2% compared to 3.1 % with MCU alone. If MCU and US were considered together, the probability of missing renal scarring could be further reduced to 3.0%. A normal US and normal MCU therefore would safely exclude renal scarring in most cases with a false-negative risk of 2.3% in children younger than 2 years. The authors concluded that DMSA scintigraphy may be withheld in children younger than 2 years in the absence of major congenital urinary tract abnormalities. For children with either positive US or positive MCU findings, further evaluation with DMSA scintigraphy should be performed to determine whether scarring is present.

In this study, DMSA scintigraphy was generally performed a minimum of 3 months after the onset of UTI. As we know there is on going debate in order to establish the most adequate timing to perform DMSA scintigraphy since pyelonephritis and renal scarring looks similar on DMSA scans (1). In other words, it is difficult to determine at what time point a scintigraphic defect should be considered permanent scarring rather than potentially recovering pyelonephritis. Up to now there is no consensus regarding the length of time after the initial episode of UTI that this follow-up DMSA scanning for scarring should be performed. In the literature, this length of time varies from 3 months to 12 months. As we can see, we are still distant from following accurate strict guidelines in imaging protocol in these children.

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Three-dimensional CT pyelography for planning of percutaneous nephrostolithotomy: accuracy of stone measurement, stone depiction and pelvicalyceal reconstruction

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Retrospective evaluation of computed tomographic (CT) pyelography before percutaneous nephrostolithotomy (PCNL). Twenty patients with renal calculi underwent CT pyelography using a dedicated protocol. Calculus size, uniformity of contrast excretion and accuracy of calculus and pelvicalyceal (PC) system reconstructions were scored and compared on axial and coronal maximum intensity projections (MIP) and volume reconstructions (VRmovie loops). After contrast medium administration, the size of calculi is accurate on axial images, but underestimated on coronal studies: mean 14.7 mm vs. 14.4 mm (axial) and 17.2 mm vs. 16.1 mm (coronal) for measurements before and after enhancement, respectively ($p = 0.11$ and 0.03). Uniform contrast medium excretion (median 228 HU; 95% CI 209-266 HU) was sufficiently lower than calculus density (median 845 HU; 95% CI 457-1,193 HU) for precise calculus and pelvicalyceal reconstructions in 87% and 85%, respectively. Coronal MIP scans were rated best for calculus depiction (mean score 2.68 vs. 2.50 and 2.41 for coronal, axial and VRs, respectively; $p = 0.14$) and VR studies best for PC anatomy (mean score 4.4 vs. 3.73 and 2.89 for VR, coronal and axial studies, respectively; $p = < 0.0001$). Three-dimensional CT pyelography can accurately demonstrate calculus position and spatial relationships of the collecting system before PCNL.

Editorial Comment

Percutaneous nephrostolithotomy (PCNL) requires detailed imaging techniques to define stone burden and delineate the anatomy of the kidney and other adjacent organs and structures. Adequate safe percutaneous access can also be accomplished with preoperative imaging studies. As we know, non-contrast MDCT studies using multiplanar, curve and surface reconstruction are useful tools for the detection of renal stones but offers poor information regarding the pelvicalyceal anatomy. Coronal and sagital MIP and volume-rendered reconstructions obtained during routine CT-urography technique offers superb anatomic details of the pelvicalyceal system. However using this technique the visualization of low-density stones (pure acid uric with density ranging from 230-340 HU) is a difficult task since the contrast density within pelvicalyceal system in CT-urography ranges from 500-600 HU.

For this reason, the authors developed a tailored protocol called CT-pyelography, using both furosemide and saline bolus after contrast medium, in attempt to decrease the contrast density within pelvicalyceal system. The median contrast medium density observed with CT-pyelogram was 228 HU (range 134-1498 HU). This technique allowed the detection of 87% of significant renal calculi and 85% of all upper pelvicalyceal system details. In our opinion, however, low-density matrix and small or low-density stones may still be missed by this new approach.

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PATHOLOGY

The utility of microscopic findings and immunohistochemistry in the classification of necrotic testicular tumors: a study of 11 cases

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Necrotic testicular tumors are relatively frequent and can present a significant diagnostic challenge. Because of differing treatments for seminomas versus nonseminomas, accurate diagnosis is critical. Eleven totally (n = 9) or almost totally (n = 2) necrotic testicular tumors were retrieved from our consult files. The submitting pathologists favored benign processes in 4 cases, Leydig cell tumor in 1, and lymphoma in 1. The cases were evaluated for histologic features and, when material was available, by immunostaining with 7 antibodies: keratin (AE1/AE3), OCT4, placental alkaline phosphatase, alpha-fetoprotein (AFP), CD117, CD30, and S100. Only distinct reactivity in a cellular distribution in the necrotic zone was considered positive; nuclear reactivity alone was scored for OCT4 and membrane reactivity for CD117 and CD30. Mean patient age was 35 years (range 16-63). Mean tumor size was 19 mm (range 7-53). All patients presented with unilateral testicular masses (6 right, 5 left); 2 also had acute pain. The combination of histologic features, immunostains and, in 1 case, serum AFP permitted classification of 8 tumors (4 seminomas, 3 embryonal carcinomas, 1 yolk sac tumor). Three were not classifiable. The necrotic seminomas lacked associated coarse intratubular calcifications and were positive for OCT4 (4/4) and CD117 (3/3) but negative for keratin (0/4) and CD30 (0/4). The necrotic embryonal carcinomas had associated coarse intratubular calcifications and were positive for keratin (2/3), OCT4 (2/2), and CD30 (3/3). OCT4 stained 1 unclassifiable tumor, which lacked other specific markers. We did not find placental alkaline phosphatase, AFP, and S100 stains useful, although S100 did highlight tumor "ghost" cells in 1 case. Other features in most cases included intratubular germ cell neoplasia (6/11), tubular atrophy/hyalinization (10/11), tumor "ghost" cells (10/11), scar (9/11), and inflammation (10/11). Of the 5 patients with available follow-up, 3 were free of disease at 1, 5, and 8 years after orchiectomy (2 necrotic seminomas and 1 germ cell tumor, unclassified). One patient with yolk sac tumor (age 63 y) developed widespread metastases after 15 months and died of disease. The final case was initially misinterpreted as "testicular infarction, no malignancy" and 16 months later the patient developed a large retroperitoneal seminoma. Most totally necrotic testicular tumors can be placed into clinically important groups by assessment for coarse intratubular calcifications and staining reactions for keratin, OCT4, CD117, and CD30.

Editorial Comment

For a proper treatment, testicular tumors must be classified as seminomatous and non-seminomatous. In order to consider a tumor purely seminoma the neoplasia must be adequately processed. At least one section per centimeter of greatest diameter of the tumor is optimal. Each histological type has peculiar microscopic findings that allow a proper diagnosis. In some cases, the diagnosis is difficult. One example is the differential diagnosis in cases of solid embryonal carcinoma. Characteristically this tumor shows tubular arrangement. In cases it is solid it must be differentiated from seminoma. Some nuclear characteristics help in this distinction but immunohistochemistry is also very helpful (1).

In cases of necrotic tumors or totally necrotic the diagnosis is a challenge for the pathologist. The study by Miller et al. shows that immunohistochemistry and some other additional microscopic findings may be very helpful in the recognition of the type of tumor. As an example: necrotic seminomas lacked associated coarse intratubular calcifications and were positive for OCT4 and CD117 but negative for keratin and CD30, and necrotic embryonal carcinomas had associated coarse calcifications and were positive for keratin, OCT4,

and CD30. The study showed that in spite of necrosis, most tumors could be placed into clinically important groups for treatment.

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Focal prostatic atrophy: mimicry of prostatic cancer on TRUS and 3D-MRSI studies

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Prostatic atrophy which represents a form of adaptive response to injury most commonly to inflammation and/or chronic ischemia is a histological abnormality frequently found in prostate biopsies and autopsies. Although commonly found, this lesion is rarely reported in the prostatic biopsy reports. It is well known that histologically focal prostatic atrophy (FPA) is one of the most frequent mimics of prostatic adenocarcinoma. On conventional and color Doppler transrectal ultrasound and on magnetic resonance spectroscopic imaging studies (MRSI), FPA may also simulate prostate cancer. Thus, this entity should be considered together with prostatitis as an important cause of false-positive results in MRSI of the prostate. It has been shown that there is a positive and significant association between extent of FPA in biopsies and serum total or free PSA elevation. For this reason, pathologists should include the presence of FPA in the pathology report of a prostatic biopsy, particularly in those patients with absence of cancer. When extensive FPA is the only finding in patients with several negative prostatic biopsies, this lesion may be the source for PSA elevation.

Editorial Comment

Prostatic atrophy is one of the most frequent microscopic mimics of prostatic adenocarcinoma (1). In the study reviewed, the lesion is also an important mimicker of adenocarcinoma on conventional and color Doppler transrectal ultrasound and on magnetic resonance spectroscopic imaging studies MRSI). It occurs most frequently in the peripheral zone and gained importance with the increasing use of needle biopsies for the detection of prostatic carcinoma. The frequency of the lesion in autopsies is 85% and increases with age. Inflammation, radiation, antiandrogens and chronic ischemia due to local arteriosclerosis are all considered causes of the lesion although many examples of atrophy are still considered idiopathic in nature. The histological subtypes of prostatic atrophy do not represent distinct entities but a morphologic continuum of acinar atrophy and most of the times are seen concomitantly. The most common subtype that causes difficulty for pathologists is partial atrophy due to the pale cytoplasm lateral to the nuclei giving rise to pale staining glands that more closely mimic cancer.

Some reports suggest that focal atrophy may be causally linked to prostate cancer and to other pre-neoplastic lesions (2). However, other studies do not support this hypothesis (3). An intriguing finding is the association of extent of atrophy to serum PSA elevation (4). What would be a possible pathogenesis for the serum PSA elevation associated to focal prostatic atrophy? It is intriguing that cells of the secretory compartment of

atrophic acini may produce higher levels of PSA. It is speculated that injurious stimuli causing focal prostatic atrophy may interfere in the physiologic barrier that prevents the escape of any significant amounts of PSA to the general circulation.

Prostate-specific antigen is a single chain glycoprotein with proteolytic enzyme activity mainly directed against the major gel-forming protein of the ejaculate (semenogelin). PSA induces liquefaction of semen with release of progressively motile spermatozoa. There are several efficient physiologic barriers to prevent the escape of any significant amounts of PSA from the prostatic ductal system: basement membrane of the acini, basal cells lining the acini, prostatic stroma, basement membrane of capillary endothelial cells, and endothelial cells. These barriers normally prevent PSA from entering the general circulation at concentrations of more than 3 ng/mL.

Focal prostatic atrophy represents a form of adaptive response to injury most commonly to inflammation and/or local ischemia. Inflammation and/or ischemia are injurious stimuli resulting in diminished oxidative phosphorilation, membrane damage, influx of intracellular calcium, and accumulation of oxygen-derived free radicals (oxidative stress). Studies showing elevated levels of glutathione S-transferase P1, glutathione S-transferase A1, and Cox-2 in prostatic atrophic epithelial cells suggest a stress-induced response (5,6). We do not know which mechanisms are involved in the physiologic barrier that prevents the escape of any significant amounts of PSA to the general circulation, however, all these stress-induced responses may affect this barrier. Inflammation and particularly ischemia may have also a field effect affecting the physiologic barrier of normal acini close to atrophic acini.

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BASIC AND TRANSLATIONAL UROLOGY

Stereological and biochemical analysis of muscular and connective tissue components in the penile corpus cavernosum adjacent to the fibrous plaque of Peyronie's disease

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Objective: To investigate the structural organization of the connective tissue in the corpus cavernosum (CC) adjacent to the fibrous plaque in Peyronie's disease (PD) using stereological and biochemical techniques, as most studies on PD have focused on the analysis of the fibrous plaque that forms in the tunica albuginea (TA). Because this fibrotic reaction is mediated by various inflammatory soluble factors, adjacent connective tissues might also be affected and this secondary effect might explain, for example, the erectile dysfunction that occurs in PD.
Patients and Methods: During surgery biopsies were taken from the CC adjacent to the fibrous plaque and from the plaque itself in seven patients with PD (mean age 48.3 years). All the patients had normal erections. Control samples were similarly located samples from 'normal' penises obtained during autopsy of five men (mean age 52.3 years). Tissue samples were stained with Weigert's stain (elastic fibres), Van Gieson's stain (connective tissue), and Sirius red (collagen). Stereological analysis was done using a 42-point grid to determine volumetric densities (Vv). Total collagen content was estimated as micrograms of hydroxyproline per milligram dry CC.
Results: The Vv of elastic fibres was significantly reduced in PD by 17.3% compared with controls, at a mean (sd) of 19.49 (3.27)% vs 23.56 (1.87)% ($P < 0.05$). While in PD the Vv of smooth muscle at 34.46 (2.06)% and connective tissue at 35.39 (6.15)% were not significantly different from those of controls at 38.38 (3.17)% and 38.02 (5.03)%, respectively. The Vv of elastic fibres in the fibrous plaque was decreased by 38.3% compared with the normal TA, at 20.25 (5.49)% vs 32.81 (4.75)% ($P < 0.02$). The mean (sd) collagen concentration in the CC from controls was 77.94 (24.26) microg/mg and in the patients with PD was 66.57 (19.39) microg/mg, which did not differ significantly. Sirius red-stained sections under polarized light showed that, in the normal CC, collagen-associated colours were homogeneously distributed. However, in the PD samples, stained collagen had a disrupted orientation and had a more heterogeneous birefringence, implying looser collagen bundles.
Conclusions: The quantitative analyses indicated that collagen in the CC close to the fibrous plaque was not affected, although its organization was noticeably altered. The CC elastic fibres were reduced though, and there was a similar change in the fibrous plaque of the TA. These results suggest that, although occurring primarily in the TA, the PD fibrous plaque may induce changes in the adjacent CC.

Editorial Comment

The authors have carried out a study, which may provide new insights regarding the pathogenesis associated with Peyronie's disease (PD). It was studied men with preserved potency but with curvature changes of the penis for some select morphological endpoints. The main finding is that elastic fibers are decreased and collagen is disorganized but not decreased in cavernosal tissue adjacent to the plaque.

In the present study, the authors focused the analysis on smooth muscle cells and the extracellular matrix of the corpora cavernosa (CC), which are important components involved in normal erection and in erectile dysfunction. The results showed that these components are modified in the CC close to the fibrous plaque, which therefore supports an association between PD and erectile dysfunction.

In its earlier stages, PD does not affect sexual function, and the present findings were indeed obtained from PD patients that had normal erection. The results suggest, however, that these individuals may eventually develop erectile dysfunction as the CC already showed significant alterations. The results of the present research imply that PD is not restricted to the tunica albuginea, as it somehow affects the underlying erectile tissue. Our

results also indicate that, of the extracellular matrix components, elastic system fibers are one of the first to undergo modifications. Thus, it may be concluded that the high incidence of erectile dysfunction among PD patients is due to simultaneous and progressive alterations in the CC. Although our results refer only to the CC adjacent to the fibrous plaque, it is possible that the factors that induced this supposedly early alteration will eventually affect deeper regions of the tissue, thereby leading to erectile dysfunction.

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Nerve growth factor modulation of the cavernous nerve response to injury

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J Sex Med. 2009;Suppl 3: 347-52

Introduction: Surgical therapies for prostate cancer and other pelvic malignancies often result in neuronal damage and debilitating loss of sexual function due to cavernous nerve (CN) trauma. Advances in the neurobiology of growth factors have heightened clinical interest in the development of protective and regenerative neuromodulatory strategies targeting CN recovery following injury.
Aim: The aim of this review was to offer an examination of current and future nerve growth factor (NGF) modulation of the CN response to injury with a focus on brain-derived nerve growth factor (BDNF), growth differentiation factor-5 (GDF-5), and neurturin (NTN).
Methods: Information for this presentation was derived from a current literature search using the National Library of Medicine PubMed Services producing publications relevant to this topic. Search terms included neuroprotection, nerve regeneration, NGFs, neurotrophic factors, BDNF, GDF-5, NTN, and CNs.
Main Outcome Measures: Basic science studies satisfying the search inclusion criteria were reviewed.
Results: In this session, BDNF, atypical growth factors GDF-5 and NTN, and their potential influence upon CN recovery after injury are reviewed, as are the molecular pathways by which their influence is exerted.
Conclusions: Compromised CN function is a significant cause of erectile dysfunction development following prostatectomy and serves as the primary target for potential neuroprotective or regenerative strategies utilizing NGFs such as BDNF, GDF-5, and NTN, and/or targeted novel therapeutics modulating signaling pathways.

Editorial Comment

Impairment of cavernous nerve function is a major cause of the development of erectile dysfunction after radical pelvic surgery. This is target for potential neuroprotective or regenerative strategies utilizing nerve growth factors such as BDNF, GDF-5, and NTN, and/or targeted novel therapeutics modulating downstream signaling pathways. I recommend this well written article for all those scientists involved with this subject.

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RECONSTRUCTIVE UROLGY

Biodegradable urethral stents seeded with autologous urethral epithelial cells in the treatment of post-traumatic urethral stricture: a feasibility study in a rabbit model

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BJU Int. 2009; 104: 263-8

Objective: To evaluate the adhesion and growth of rabbit urethral epithelial cells (UECs) on a biodegradable unbraided mesh urethral stent, and to assess the feasibility and effect of the cell-seeded urethral stent for treating post-traumatic urethral stricture (PTUS) in a rabbit model.
Materials and Methods: Rabbit UECs were collected by biopsy from adult rabbit urethra and seeded onto the outer layer of a mesh biodegradable urethral stent. The growth of UECs in cell-scaffolds was assessed by scanning electron microscopy, immunohistochemical and fluorescence staining. In all, 32 male New Zealand rabbits were used, with either PTUS or uninjured, as a control group. Cell-seeded stents were implanted into the rabbits strictured urethra. The histological and immunohistochemical findings were assessed after death at 1, 2, 8, 12 and 24 weeks, respectively. The reconstruction and function were evaluated by urethroscopy and retrograde urethrography.
Results: The cultured UECs adhered to the stent and grew well. Immunohistochemistry showed that the cells were stained positively for cytokeratin. At 4 weeks, vs. 2 weeks, the thickness of the papillary projections of the epithelium decreased and inflammatory cell infiltration diminished. At 24 weeks the injured urethra was completely covered by integrated regeneration of three to five layers of urothelium. There was no evidence of voiding difficulty, stricture recurrence or other complications.
Conclusions: The unbraided mesh biodegradable urethral stent with autologous UECs seemed to be feasible for treating PTUS in the rabbit urethra, and provides a hopeful avenue for clinical application allowing reconstruction of PTUS.

Urethral replacement using cell seeded tubularized collagen matrices

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Purpose: Acellular collagen matrices derived from bladder submucosa have been used successfully as an off-the-shelf biomaterial for urethral replacement, experimentally and clinically in an onlay fashion. We investigated whether collagen matrices, either alone or with autologous cells, could be used for tubularized urethral replacement.
Materials and Methods: Acellular collagen matrices were processed and tubularized. Ten rabbits underwent an open bladder biopsy with subsequent cell expansion. Autologous bladder cells were grown and seeded onto the pre-configured tubular matrices. A 1 cm. long urethral segment was excised in 24 male rabbits. Urethroplasty was performed with the tubularized collagen matrices seeded with cells in 12 animals and without cells in 12. Serial urethrography was performed preoperatively and at 1, 2, 3 and 6 months postoperatively. Retrieved urethras were analyzed grossly, histologically, immunocytochemically and with Western blots. Contractility and the presence of neurotransmitter receptors were confirmed with organ bath studies.
Results: Serial urethrography confirmed the maintenance of a wide urethral caliber without any signs of strictures in animals implanted with the cell seeded matrices. The urethral segments replaced with the collagen

scaffolds without cells demonstrated strictures and graft collapse at all time points. The implanted cell seeded matrices had a normal urethral architecture by 1 month, consisting of a transitional cell layer surrounded by muscle cell fiber bundles with increasing cellular organization with time. Epithelial and smooth muscle phenotypes were confirmed immunocytochemically and with Western blot analyses using pancytokeratins AE1/AE3 and smooth muscle specific alpha-actin antibodies. Formation of a transitional cell layer was confirmed in the matrices implanted without cells but only scant unorganized muscle fiber bundles were present, mostly at the anastomotic sites. Organ bath studies demonstrated the capacity for contractility along with cholinergic and adrenergic specific receptors in the tissue engineered scaffolds compared to controls.
Conclusions: These results show that collagen matrices seeded with cells form normal urethral tissue can be used for tubularized replacement, whereas tubularized collagen matrices alone without cells lead to poor tissue formation and strictures. The collagen matrices seeded with cells may offer a useful alternative in the future for patients requiring a tubularized urethral segment replacement.

Tubularized urethral replacement with unseeded matrices: what is the maximum distance for normal tissue regeneration?

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World J Urol. 2008; 26: 323-6

Purpose: Complete urethral replacement using unseeded matrices has been proposed as a possible therapy in cases of congenital or acquired anomalies producing significant defects. Tissue regeneration involves fibrin deposition, re-epithelialization, and remodeling that are limited by the size of the defect. Scar formation occurs because of an inability of native cells to regenerate over the defect before fibrosis takes place. We investigated the maximum potential distance of normal native tissue regeneration over a range of distances using acellular matrices for tubular grafts as an experimental model.
Materials and Methods: Tubularized urethroplasties were performed in 12 male rabbits using acellular matrices of bladder submucosa at varying lengths (0.5, 1, 2, and 3 cm). Serial urethrography was performed at 1, 3, and 4 weeks. Animals were sacrificed at 1, 3, and 4 weeks and the grafts harvested. Urothelial and smooth muscle cell regeneration was documented histologically with HE and Masson's trichrome stains.
Results: Urethrograms demonstrated normal urethral calibers in the 0.5 cm group at all time points. The evolution of a stricture was demonstrated in the 1, 2, and 3 cm grafts by 4 weeks. Histologically all grafts demonstrated ingrowth of urothelial cells from the anastomotic sites at 1 week. By 4 weeks, the 0.5 cm grafts had a normal transitional layer of epithelium surrounded by a layer of muscle within the wall of the urethral lumen. The 1, 2, and 3 cm grafts showed ingrowth and normal cellular regeneration only at the anastomotic edges with increased collagen deposition and fibrosis toward the center by 2 weeks, and dense fibrin deposition throughout the grafts by 4 weeks.
Conclusions: The maximum defect distance suitable for normal tissue formation using acellular grafts that rely on the native cells for tissue regeneration appears to be 0.5 cm. The indications for the use of acellular matrices in tubularized grafts may therefore be limited by the size of the defect to be repaired.

Editorial Comment

When no autologous tissue is available for reconstruction of the urethra from hypospadias or urethral stricture disease, tissue engineering provides an alternative. These 3 articles summarize the current state of tissue engineering in the urethra.

There are two basic components to tissue engineering: the acellular matrix and the cellular epithelium. To avoid rejection it is important that the cells populating the engineered tissue are the patient's own (autolo-

gous). In the case of urethral replacement, these are commonly derived from culturing transitional epithelial cells obtained from a bladder biopsy. Still, these cells cannot simply be injected into the diseased urethra with any hope of successful implantation and generation of a normal appearing urethra. Instead, their growth and differentiation must be supported by a tissue matrix. The extracellular matrix comes in two varieties: an acellular heterologous collagen matrix or a biodegradable synthetic polymer matrix. Examples of collagen matrices include small intestinal submucosa (SIS) and bladder collagen matrix. The synthetic matrices are composed of polymers such as polylactic acid that can be degraded by enzymatic hydrolysis into non-toxic byproducts: carbon dioxide and water. The purpose of the extracellular matrix (whether collagen or polymer) is to provide mechanical and architectural support for native cellular ingrowth. These matrices are biodegradable so that as the patient generates his new urethra, the foreign material is resorbed.

These 3 articles tell the story of the principles that have been discovered to govern urethral engineering thus far. First, acellular matrices have been successfully used in an onlay fashion by themselves (without seeding them with transitional cells). It appears that as long as there is normal urethral epithelium along the edges of the onlay matrix graft, these cells can grow in from the edges and populate the graft. However, when matrix grafts have been used as a tubular graft (i.e. complete urethral replacement) only very short graft have been successful (0.5 cm in animal models). The utility of such short tube grafts is questionable as short defects can be bridged generally with primary anastomosis of the native urethra. Tubular grafts will likely serve their role in complete replacement of longer segments of severe urethral disease when onlay options are not available or feasible due to a lack of a dorsal plate. In such cases, it is clear that whether a biodegradable synthetic mesh or an acellular heterologous matrix graft is used it will be necessary to seed these grafts with epithelial cells.

Continued investigation in animal models and human trials will expand the role of tissue engineering for salvaging the devastated urethra.

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UROLOGICAL ONCOLOGY

High frequency of intracerebral hemorrhage in metastatic renal carcinoma patients with brain metastases treated with tyrosine kinase inhibitors targeting the vascular endothelial growth factor receptor

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Objectives: To report the high incidence of intracerebral hemorrhage (ICH) in patients with metastatic renal cell carcinoma (RCC) treated with the tyrosine kinase inhibitors targeting the vascular endothelial growth factor receptor (VEGFR).
Methods and Results: Between October 2005 and December 2006, 67 patients with metastatic RCC were treated with sorafenib or sunitinib at the Montpellier Cancer Center in compassionate access programs. The

medical records of five (7%) patients who died of ICH during therapy were reviewed retrospectively. Four of them had known brain metastases. Previous radiation therapy had been indicated in two patients. Two patients had a history of hypertension. Death from ICH occurred in the first 2 wk following the onset of treatment. Three other patients with brain metastases who received sorafenib or sunitinib during the same period did not experience ICH.
Conclusions: The frequency of fatal ICH in RCC patients with brain metastases treated with tyrosine kinase inhibitors targeting the VEGFR seems high. Prospective clinical trials will be necessary for assessing the true incidence and predictive factors related to this toxicity.

Editorial Comment

Modern treatment of metastatic renal cancer involves tyrosine kinase inhibitors (TKI). This is an early report on possible lethal complications associated with this therapy in patients with brain metastases. Five cases with lethal brain hemorrhage while under TKI are reported and compared to 3 patients with brain metastases who did had not (yet) experienced any complications. No risk factors could be identified so far. Importantly, brain hemorrhage occurred within 2 – 14 days after onset of TKI medication. Urologists involved in the medical therapy of patients with renal cancer and brain metastases should be aware of immediate the risk of such complications and should report them to the community.

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Predictive factors for progression in patients with clinical stage T1a prostate cancer in the PSA era

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Objective: In the literature, most data regarding the outcome of patients with clinical stage T1a prostate cancer were established before the prostate-specific antigen (PSA) era. The aim of our study was to determine the predictive factors of progression in patients with T1a prostate cancer diagnosed in the PSA era.
Methods: Consecutive patients (n=144) with newly diagnosed T1a prostate cancer (tumor involving < or =5% of the resected prostatic tissue) were included. None of them was treated before evidence of tumor progression confirmed by prostate needle biopsies. The associations between tumor characteristics and time to cancer progression were assessed using Cox regression analysis.
Results: With a mean follow-up of 5.1 yr, 30 patients (21%) experienced cancer progression. Five adverse parameters were significantly associated with cancer progression: preoperative PSA> or =10 ng/ml, postoperative PSA> or =2 ng/ml, prostate weight > or =60 g, weight of resected tissue > or =40 g, and Gleason score> or =6. The 5-yr progression rate was 12% if fewer than two of these parameters were present, whereas it was 47% if two or more parameters were present ($p<0.001$).
Conclusion: In the PSA era the risk of progression associated with T1a prostate cancer can be predicted using five criteria, and two groups of patients can be defined. The patients at low risk of progression may be good candidates for surveillance. In those with a high risk of progression, a more aggressive treatment should be discussed.

Editorial Comment

Therapeutic options in pT1a prostate cancer vary from watchful waiting to immediate radical therapy. Because of (sometimes falsely) pathologically confirmed small tumor volume, conservative follow-up is not uncommon. These autors report on the clinical course of 144 patients with pT1a prostate cancer. This cohort is impressively low-risk with 71% Gleason score smaller or equal to 5. Still, a 25% 5 year progression rate was observed. The relative risk (RR) was increased in patients with initial PSA > 10 (RR 3.3, 40 % 5-year progression rate), Gleason score 6 or more (RR 2, 54 % 5-year progression rate) or postoperative PSA > 2 (RR 3.2, 44 % 5-year progression rate).

These figures caution anyone to recommend watchful waiting if more than 1 risk factor is involved.

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NEUROLOGY & FEMALE UROLOGY

Recurrent pseudodiverticula of female urethra: five-year experience

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Urology. 2009; 73: 1218-22

Objectives: To report our experience of transvaginal diverticulectomy with pubovaginal sling placement in a series of 32 women with recurrent urethral pseudodiverticula.
Methods: A total of 32 women underwent surgical repair from January 2000 to June 2007. Of the 32 women, 12 had undergone other concomitant previous urethral surgery, predominantly for stress urinary incontinence. Transvaginal excision of the diverticulum and concomitant pubovaginal sling placement were performed routinely. The women were evaluated postoperatively for symptom relief, anatomic result, and postoperative continence status at 1, 6, and 12 months and annually thereafter. Pelvic magnetic resonance imaging was repeated after 1 year.
Results: The mean follow-up was 4.3 years. In all cases, the voiding urethrogram after catheter removal showed a good urethral shape with an absence of urinary leaks. At the postoperative urodynamic investigation, 27 patients had an unobstructed and 5 an equivocal Blaivas-Groutz nomogram. Three patients (20%) reported a persistent degree of stress urinary incontinence, including 2 with grade 1 stress urinary incontinence and 1 with mixed incontinence. Two patients presented with clinically evident diverticulum recurrence, and in 1 patient, an intraurethral diverticulum, was found at the 1-year magnetic resonance imaging examination.
Conclusions: A pubovaginal sling added routinely to all diverticulectomy procedures offers significant support to the urethral repair and/or prevention of urinary incontinence, including in recurrent cases, and does not increase the risk of erosion into the urethra or fistula formation.

Editorial Comment

The authors review a very large series of recurrent urethro-diverticula (32 women). Of note is that aside from performing the actual diverticulectomy all patients underwent a concomitant suburethral sling. With a good

length of follow-up (mean = 4.3 years) they found that 80% of the patients were dry with 3 patients reporting persistent stress urinary incontinence. There was no notation that the synchronous suburethral sling increased the risk of erosion or fistula formation. In addition, the surgeons felt that the pubovaginal sling well buttressed the urethral repair and helped limit stress urinary incontinence.

This manuscript is very impressive with regards to the number of patients treated with recurrent urethral diverticula. The patients all underwent an autologous fascial sling but still had a 20% persistent degree of stress urinary incontinence. Almost half the patients (n = 15) had stress urinary incontinence preoperatively. Their patient population suffered no de novo incidence of stress urinary incontinence with patients reporting stress incontinence being from the population sub group that had the malady preoperatively. That they had a 0% de novo incidence of stress urinary incontinence is worth noting in view that other authors report 10 - 20% new onset incidence of stress urinary incontinence after a urethral diverticulectomy (1). It is worthwhile reviewing the paper by Kobi, et al. secondary to their discussion of prediction of new onset stress urinary incontinence before and after urethral diverticulectomy and their comments on a prophylactic operation and comparing it to this work. The authors only used a Martius flap four times in their operation. Some surgeons would be more inclined to use a Martius flap to a greater degree on this impressive re-do population. I think it is worthwhile to note than when using the Martius flap, most surgeons may place the Martius flap between the urethral proper and the pubovaginal sling. It has been noted previously that the use of the Martius flap will not impact the long-term cosmetic appearance of the external vagina (2).

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Urethral sphincter morphology and function with and without stress incontinence

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J Urol. 2009; 182: 203-9

Purpose: Using magnetic resonance images we analyzed the relationship between urethral sphincter anatomy, urethral function and pelvic floor function.
Materials and Methods: A total of 103 women with stress incontinence and 108 asymptomatic continent controls underwent urethral profilometry, urethral axis measurement with a cotton swab, vaginal closure force measurement with an instrumented speculum and magnetic resonance imaging. Striated urogenital sphincter length was determined and its thickness was measured in the proximal sphincter, where its circular shape enables estimation of striated urogenital sphincter area. A length-area index was calculated as a proxy for volume.
Results: The striated urogenital sphincter in women with stress incontinence was 12.5% smaller than that in asymptomatic continent women (mean +/- SD length-area index 766.4 +/- 294.3 vs. 876.2 +/- 407.3 mm(3), p = 0.04). The groups did not differ significantly in striated urogenital sphincter length (13.2 +/- 3.4 vs. 13.7

+/- 3.9 mm, p = 0.40), thickness (2.83 +/- 0.8 vs. 3.11 +/- 1.4 mm, p = 0.09) or area (59.1 +/- 18.4 vs. 62.9 +/- 24.7 mm(2), p = 0.24). Striated urogenital sphincter length and area, and the length-area index were associated during voluntary pelvic muscle contraction with more urethral axis elevation and increased vaginal closure force augmentation.
Conclusions: A smaller striated urogenital sphincter is associated with stress incontinence and poorer pelvic floor muscle function.

Editorial Comment

The authors reviewed two populations of women, one with stress incontinence and one without stress incontinence and had the two groups undergo urodynamic testing, physical examination as well as magnetic resonance imaging. Parameters evaluated included striated urethral sphincter length, thickness, area, and volume estimates as well as the relation of the sphincter size determined and pelvic floor metrics.

Conclusions noted included the smaller the striated urethral sphincter, the greater association with female stress incontinence and lesser pelvic floor muscle function.

The authors, upon review, also found that their population of stress incontinent women had a higher body mass index than those that were continent. In addition, other pertinent findings included that aging was correlated with a shorter striated urethral sphincter and a longer vesical neck and those plagued with incontinence had a smaller striated urethral sphincter. The authors have a very interesting discussion section, including their observation that the increase in the actual area of the sphincter associated with maturational process is most likely secondary to an increase in connective tissue and a decrease in the striated muscle cells. Though larger in diameter, its' shortness of length may be one of the factors towards an increase in incontinence. Numerous authors have also noted the role of striated urethral sphincter and its effect on voiding function. Reviews on the use of terazosin on females with voiding dysfunction have noted that perhaps when the medication fails; it may be secondary to the striated urethral sphincter as opposed to the bladder neck area (1). Perhaps this may explain the anecdotal observation of women with voiding dysfunction from a pelvic floor spasms or failure of relaxation being usually younger in age. In addition, when one reviews the actual physics of work being defined as work equals force times length it may make intuitive sense that the shorter striated sphincter zone, though bulkier, may allow the bladder to expel urine much easier in a stress situation in view that it requires less actual work to overcome the sphincteric resistance secondary to the lesser length.

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PEDIATRIC UROLOGY

Neoadjuvant gonadotropin-releasing hormone therapy before surgery and effect on fertility index in unilateral undescended testes: a prospective randomized trial

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Objectives: To investigate, in a prospectively randomized trial, whether preoperative gonadotropin-releasing hormone (GnRH) therapy improves the fertility index in primary cryptorchidism. Cryptorchidism is a common condition with a high risk of infertility. Treatment with GnRH appears to improve fertility later in life by inducing germ cell maturation.
Methods: A total of 24 boys, 12-123 months old (median 34.5), with 24 undescended testes were prospectively assigned to 2 groups during a 24-month period. The patients were randomized to receive either orchiopexy alone (n = 12) or orchiopexy combined with neoadjuvant GnRH therapy (n = 12) as a nasal spray for 4 weeks at 1.2 mg/d. In both groups, testicular biopsies were performed at orchiopexy, and the histopathologic fertility index was determined.
Results: The mean fertility index in the group treated with GnRH before surgery was significantly greater (0.88 +/- 0.31) than in the group without hormonal stimulation (0.49 +/- 0.52; P = .02). No significant correlation was found between the fertility index in the GnRH group and the patient's age.
Conclusions: The results of our study have shown that neoadjuvant GnRH treatment improves the fertility index in prepubertal cryptorchidism and, consequently, should improve fertility in adulthood.

Editorial Comment

Twenty-four boys were prospectively randomized to either undergo unilateral orchiopexy alone versus 1.2 mg of intranasal GnRH daily for 4 weeks prior to orchiopexy. Patients ranged from 12-123 months and biopsies were done during the orchiopexy procedure to evaluate the outcome of the hormone pretreatment. Their results showed an increased fertility index with more Ad spermatogonia per tubule in the hormone-treated group than the orchiopexy alone group. The statistically significant fertility index could only be observed in patients over three years of age.

Infertility in cryptorchid patients has long been a concern, which has led to surgery in younger age groups and consideration of hormone treatments. The major issue with all fertility studies in pediatric patients is that it takes 20-30 years follow up to evaluate the true outcome. Histology does not necessarily predict semen quality or fertility and this study has the same concern. It is interesting in this study that the older patients seem to have better outcomes with their pretreatment than younger patients, which is not intuitive. One of the other problems hampering the adoption of this pretreatment is that the GnRH analogs are not available in all countries (United States). I expect the best advice is to keep an eye on studies such as this for their impact in the future but it is likely to take a very long time before outcomes can be documented and a unified treatment plan adopted.

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Importance of methodology on (99m)technetium dimercapto-succinic acid scintigraphic image quality: imaging pilot study for RIVUR (Randomized Intervention for Children With Vesicoureteral Reflux) multicenter investigation

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J Urol. 2009; 182: 272-9

Purpose: We reviewed our experience with (99m)technetium dimercapto-succinic acid scintigraphy obtained during an imaging pilot study for a multicenter investigation (Randomized Intervention for Children With Vesicoureteral Reflux) of the effectiveness of daily antimicrobial prophylaxis for preventing recurrent urinary tract infection and renal scarring. We analyzed imaging methodology and its relation to diagnostic image quality.
Materials and Methods: (99m)Technetium dimercapto-succinic acid imaging guidelines were provided to participating sites. High-resolution planar imaging with parallel hole or pinhole collimation was required. Two core reviewers evaluated all submitted images. Analysis included appropriate views, presence or lack of patient motion, adequate magnification, sufficient counts and diagnostic image quality. Inter-reader agreement was evaluated.
Results: We evaluated 70, (99m)technetium dimercapto-succinic acid studies from 14 institutions. Variability was noted in methodology and image quality. Correlation (r value) between dose administered and patient age was 0.780. For parallel hole collimator imaging good correlation was noted between activity administered and counts (r = 0.800). For pinhole imaging the correlation was poor (r = 0.110). A total of 10 studies (17%) were rejected for quality issues of motion, kidney overlap, inadequate magnification, inadequate counts and poor quality images. The submitting institution was informed and provided with recommendations for improving quality, and resubmission of another study was required. Only 4 studies (6%) were judged differently by the 2 reviewers, and the differences were minor.
Conclusions: Methodology and image quality for (99m)technetium dimercapto-succinic acid scintigraphy varied more than expected between institutions. The most common reason for poor image quality was inadequate count acquisition with insufficient attention to the tradeoff between administered dose, length of image acquisition, start time of imaging and resulting image quality. Inter-observer core reader agreement was high. The pilot study ensured good diagnostic quality standardized images for the Randomized Intervention for Children With Vesicoureteral Reflux investigation.

Editorial Comment

A pilot study of the Randomized Intervention for Children With Vesicoureteral Reflux participating institutions submitting DMSA scans was undertaken to evaluate quality. Written technique guidelines were given and the images were submitted to the two authors for review of image quality. The pilot study lasted for six months. Seventy studies were submitted, 10 of which were resubmissions because of unacceptable quality in the past. Fourteen institutions submitted cases. The studies compared radiopharmaceutical dose, time of imaging, overlap of kidney images and adequate counts in the region of interest with an overall quality evaluation by the referee nuclear medicine physicians. Sixty studies eventually went through the complete process and 10 of these were rejected for quality issues (17%). Sixteen of the studies had disagreement between the two nuclear medicine experts, most with minor discrepancies such as left right inversions, however one study was thought to be adequate by one and poor quality by another.

When details of routine clinical imaging studies are scrutinized in this fashion it makes one wonder about the clinical judgments that are made and the quality of imaging at one's own institution. These 14 institutions were chosen because of their interest and abilities and still significant problems in following a written

protocol, monitoring of the study while the patient is in the imaging department and processing the study were discovered. In short, there is still plenty of room for error.

Of the 70 patients studied in reality there should be 80, since 10 of them are resubmissions, which should make the statistics 14% worse. It should be noted in nuclear medicine that there has been a great effort in trying to standardize kidney imaging and yet it is still an ongoing process that has not filtered down to each and every institution.

The authors should be commended for publishing not only positive, but their negative results and letting clinicians recognize that a good deal of clinical judgment should be used in interpreting and relying upon imaging studies.

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