
UROLOGICAL SURVEY

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STONE DISEASE

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Percutaneous nephrolithotomy for proximal ureteral calculi with severe hydronephrosis: assessment of different lithotriptors

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Purpose: We compared the efficacy and safety of percutaneous nephrolithotomy (PCNL) with different intracorporeal lithotriptors for proximal ureteral stones in patients with severe hydronephrosis.

Patients and Methods: We retrospectively analyzed the records of 192 patients with proximal ureteral calculi and severe hydronephrosis who underwent PCNL between February 2003 and December 2007. Calculi were fragmented with a pneumatic lithotripter in 44 patients (group 1), Swiss Lithoclast Master in 54 (group 2), low-power holmium:yttrium-aluminum-garnet (YAG) laser in 56 (group 3) and high-power holmium:YAG laser in 38 (group 4). Patients were assessed about 12 months postoperatively with intravenous urography and ultrasonography for late complications. Stone size, operative time, stone-free rate, and follow-up were analyzed in each group.

Results: Mean stone size for different groups were 16.2 +/- 2.8 mm, 16.6 +/- 2.1 mm, 16.0 +/- 2.7 mm, and 16.4 +/- 1.1 mm, respectively. Average operative time for different groups were 118 +/- 17 minutes, 81 +/- 10 minutes, 85 +/- 14 minutes, 110 +/- 16 minutes, respectively. Group 2 and group 3 showed superior outcomes of shorter operative time ($P = 0.000$). The overall stone-free rate was 86.5%. As stratified by lithotriptors, the stone-free rate was 81.8% in group 1, 92.9% in group 2, 88.9% in group 3, and 78.9% in group 4 ($P = 0.190$). No significant difference was found among the groups in terms of blood loss and postoperative hospital stay. Repeated PCNL or shockwave lithotripsy was necessary as an auxiliary procedure in 26 patients. The overall complication rate was 18.2%; most complications were minor and insignificant. During the follow-up, ureteral stricture developed in 10 patients and new renal stones developed in 4 patients.

Conclusions: PCNL combined with Swiss Lithoclast Master or low-power holmium:YAG laser is the preferred endourologic modality for the management of proximal ureteral calculi in patients with severe hydronephrosis.

Editorial Comment

The authors do not comment on their use of basket devices for fragment removal. They comment that one deterrent to pneumatic lithotripsy is the large fragments that are formed, requiring "time-consuming" extraction. Indeed, the absence of a nephrostomy sheath in their surgical technique suggests that active fragment extraction is not performed. As such, this may impact their findings of higher efficacy for lithotriptors that either form smaller fragments (low-energy HO:YAG) or actively extract stone fragments (ultrasonic component of the Lithoclast). The finding of a higher ureteral stricture rate with High-energy HO:YAG is an important contribution to the literature.

The authors do not report their selection of calyx for percutaneous access; one would anticipate a high percentage of upper and middle calyces to facilitate access to the proximal ureter with a rigid nephroscope. For centers selecting a lower calyceal access and the use of a flexible endoscope, the low-energy HO:YAG would come out on top.

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Fever after shockwave lithotripsy--risk factors and indications for prophylactic antimicrobial treatment

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Purpose: To identify risk factors for fever after shockwave lithotripsy (SWL) and suggest guidelines for prophylactic antimicrobial treatment.

Patients and Methods: Between 1985 and 2007, a total of 15,324 SWL procedures were performed in our institution using the Dornier HM3 lithotripter. Because stone analyses were not available in the majority of patients, management of stones larger than 2 cm in diameter were excluded from this analysis to minimize the ratio of struvite stones as a possible cause for postprocedural fever. In this analysis, 11,500 SWL treatments were included. Clinical parameters before, during, and after treatments were prospectively registered using a computerized database. Potential risk factors for fever after SWL were evaluated.

Results: Fever >38.0 degrees C developed in 161 (1.4%) patients. The risk factors for fever after SWL were: A positive urine culture ($P < 0.05$), an indwelling nephrostomy tube or stent during the procedure ($P < 0.001$), lithotripsy of kidney or upper ureteral stones ($P < 0.05$) and preoperative symptomatic urinary tract infection (UTI) ($P < 0.05$) or sepsis ($P < 0.05$). Lithotripsy of mid and lower ureteral stones, stone size, and the use of ureteral catheters during the procedures were not associated with increased risk of fever after SWL.

Conclusions: Fever (>38.0 degrees C) develops in only 1.4% of the patients undergoing SWL. Therefore, prophylactic antibiotic treatment is not indicated in all patients. Selective prophylactic treatment is recommended in patients who present with UTI, kidney or upper ureteral stones, and those for whom a nephrostomy tube or stent is necessary.

Editorial Comment

At first glance, this paper suggests that the AUA statement regarding prophylactic antibiotics at the time of shockwave lithotripsy deserves further scrutiny. However, the great majority of stones treated with SWL in the United States are renal and proximal ureteral stones; which this study confirms may benefit from preoperative antibiotic prophylaxis. As ureteroscopic approaches to ureteral stones have been demonstrated to be more efficacious and more cost-effective, the use of SWL in this subset of patients would be less common.

The AUA statement for prophylaxis is based on Level 1a evidence - a metaanalysis of eight randomized prospective controlled trials. The current study suggests that routine antibiotics need not be used for mid-ureteral and distal ureteral stones that do not have an indwelling ureteral stent or nephrostomy tube. As this select group likely represents a very small portion of patients treated with SWL, for practical purposes, routine prophylaxis remains warranted!

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ENDOUROLOGY & LAPAROSCOPY

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Initial experience with 50 laparoendoscopic single site surgeries using a homemade, single port device at a single center

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Purpose: We report our technique of and initial experience with 50 patients who underwent laparoendoscopic single site surgery using a homemade single port device at a single institution.

Materials and Methods: Between December 2008 and August 2009 we performed 50 laparoendoscopic single site surgeries using the Alexis wound retractor, which was inserted at the umbilical incision. A homemade single port device was made by fixing a size 7 1/2 surgical glove to the retractor outer ring and securing the glove fingers to the end of 3 or 4 trocars with a tie and a rubber band. A prospective study was performed in 50 patients to evaluate outcomes.

Results: Of 50 patients 34 underwent conventional laparoendoscopic single site surgery, including radical and simple nephrectomy, and cyst decortication in 8 each, nephroureterectomy in 3, partial nephrectomy and adrenalectomy in 2 each, and partial cystectomy, ureterectomy and ureterolithotomy in 1 each, while 16 underwent robotic laparoendoscopic single site surgery, including partial nephrectomy in 11, nephroureterectomy in 3, and simple and radical nephrectomy in 1 each. Mean patient age was 52 years, mean body mass index was 23.4 kg/m², mean operative time was 201 minutes and mean estimated blood loss was 201 ml. Four intraoperative complications occurred, including 2 bowel serosal tears, diaphragm partial tearing and conversion to open radical nephrectomy. One case of postoperative bleeding was managed by transfusion. Surgical margins were negative in the 13 patients who underwent partial nephrectomy. Mean hospital stay was 4.5 days (range 1 to 16).

Conclusions: Our homemade single port device is cost-effective, provides adequate range of motion and is more flexible in port placement for laparoendoscopic single site surgery than the current multichannel port.

Editorial Comment

After the first laparoscopic nephrectomy performed many years ago, laparoscopic urological surgery has evolved. Recently, laparoendoscopic single site surgery has been developed allowing experienced surgeons to investigate new applications and feasibility of a new minimally invasive surgical approach. The clinical advantages are not clear yet and the platforms and instruments are not optimally developed. One of the major challenges is the entry portal that could allow the utilization of a small incision to permit all different laparoscopic maneuvers, as well as the insertion of robotic and/or laparoscopic instrumentation. The authors of this report should be congratulated for the creativity and high level of minimally surgery understanding for developing an easy access device with everyday use components (surgical gloves and laparoscopic ports). This idea may allow industry to mature this initial idea to an effective device.

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Experience with 750 consecutive laparoscopic donor nephrectomies--is it time to use a standardized classification of complications?

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Purpose: Laparoscopic living donor nephrectomy offers patients the benefits of decreased morbidity and improved cosmesis, while maintaining equivalent graft outcomes and complication rates similar to those of open donor surgery. With expressed concern for donor safety, using a standardized complication scale would allow combining data in a donor registry so potential donors could be adequately followed and counseled. We present the largest series to our knowledge of laparoscopic living donor nephrectomy by a single surgeon.

Materials and Methods: The institution's initial 750 laparoscopic living donor nephrectomies were included in the study, and a retrospective and prospective chart and database analysis was performed.

Results: Mean donor age was 40.5 years and average body mass index was 25.7 kg/m(2). There were 175 patients (23%) with 2 or more renal arteries while 161 (21.5%) had early arterial bifurcations. There were 3 open conversions (0.4%) and the overall complication rate was 5.46%. Median hospital stay was 1 day and the readmission rate was 1.2%. There were 5 reoperations (0.67%), none of which was for the control of bleeding. No patients required a blood transfusion and there were no mortalities. Using a modified Clavien classification of complications for living donor nephrectomy 65.8% were grade 1, 31.7% grade 2 (12.2% grade 2a, 14.6% grade 2b, 4.9% grade 2c) and 2.4% grade 3. There were no grade 4 complications.

Conclusions: With appropriate patient selection and operative experience, laparoscopic living donor nephrectomy is a safe procedure associated with low morbidity. The use of a standardized complication system specific for this procedure is encouraged and could aid in counseling potential donors in the future.

Editorial Comment

After the first Laparoscopic living donor nephrectomy by Kavoussi et al., many institutions have adopted this surgical technique worldwide due to the many advantages offered by it, such as, improved postoperative recovery and shorter convalescence with no effect on recipient renal function.

Live donor renal transplantation has many advantages including greater graft and patient survival, shorter waiting periods, improved HLA matching, and less cold ischemia. However, until recently disincentives from the operation such as prolonged hospitalization, postoperative pain, and significant convalescence have deterred live donor renal transplantation. The authors demonstrated a vast experience of 750 laparoscopic living donor nephrectomies with only 3 open conversions (0.4%) and the overall complication rate of 5.46%. A short hospital stay and low readmission rate. Using a modified Clavien classification of complications for living donor nephrectomy 65.8% were grade 1, 31.7% grade 2 (12.2% grade 2a, 14.6% grade 2b, 4.9% grade 2c) and 2.4% grade 3. There were no grade 4 complications. The data demonstrate the feasibility of an established technique with great outcome.

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IMAGING

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Utility of diffusion-weighted MRI in characterization of adrenal lesions

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Objective: The purpose of our study was to evaluate the utility of apparent diffusion coefficient (ADC) values for characterizing adrenal lesions and determine if diffusion-weighted imaging (DWI) can distinguish lipid-rich from lipid-poor adenomas.

Materials and Methods: We retrospectively evaluated 160 adrenal lesions in 156 patients (96 women and 60 men; mean age, 63 years). ADCs and signal intensity (SI) decrease on chemical shift imaging were measured in adrenal lesions with a wide variety of pathologies. Lipid-rich and lipid-poor adenomas were identified by unenhanced CT. The overall predictive power of ADC, SI decrease, and lesion size were determined by receiver operating characteristic (ROC) analysis. Areas under the ROC curve (AUC) were compared for equivalence using nonparametric methods. Sensitivity, specificity, and positive and negative predictive values were calculated. Correlation coefficients were used to assess ADCs versus percentage SI decrease and ADCs versus CT attenuation.

Results: ADCs of adrenal malignancies (median, 1.67×10^{-3} mm²/s; interquartile range, 1.41 - 1.84×10^{-3} mm²/s) were not different compared with those of benign lesions (1.61×10^{-3} mm²/s; 1.27 - 1.96×10^{-3} mm²/s; $p > 0.05$). Cysts (2.93×10^{-3} mm²/s; 2.70 - 3.09×10^{-3} mm²/s) showed higher ADCs than the remaining adrenal lesions ($p < 0.05$). The median ADCs of lipid-rich adenomas did not differ from those of lipid-poor ones ($p > 0.05$). The CT attenuation had no negative or positive correlation with the ADCs of adrenal adenomas ($r = -0.05$, $p = 0.97$).

Conclusion: Unlike lesion size and percentage decrease in SI, the ADCs were not useful in distinguishing benign from malignant adrenal lesions. Lipid-poor adenomas could not be distinguished from lipid-rich adenomas and all other nonfatty lesions of the adrenal gland with DWI.

Editorial Comment

Diffusion-Weighted MRI (DWI), is a technique used to detect the state of molecular translational motion of water in the tissue. In some tumors, densely packed malignant cells, causes restricted diffusion of water relative to that of normal tissue. DWI is quantified by the apparent diffusion coefficient map-ADC. Since apparent diffusion coefficient (ADC) reflects primarily diffusion coefficient of extra-cellular water, ADC values tend to be lower for tumors compared to normal tissue. Contrary to cancer, in benign lesions, extra-cellular space volume is higher, thus ADC values are higher as well. For this reason, DWI is an important complementary tool in the evaluation of pathologic conditions in the abdomen and is increasingly used in routine imaging. The authors of this study showed that lipid-poor adenomas could not be distinguished from lipid-rich adenomas and all other non-fatty lesions of the adrenal gland with DWI. They showed that ADCs were not useful in distinguishing benign from malignant adrenal lesions. Similarly recent report has been shown that this technique has also limitation in other abdominal organs since a lesion with restricted diffusion was found to be benign in about 22% of the lesions (1). Fortunately, radiological characterization of an adrenal incidentaloma can be done with high sensitivity and specificity using well established techniques such, CT attenuation without contrast enhancement, wash-out CT technique and chemical-shift MR imaging. Thus, further evaluation with diffusion-weighted MRI is not essential.

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Split-bolus MDCT urography: Upper tract opacification and performance for upper tract tumors in patients with hematuria

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Objective: Our purpose was to assess upper urinary tract opacification and the performance of split-bolus MDCT urography for upper tract tumors in patients with hematuria.

Materials and Methods: Between January 2004 and December 2006, we identified 200 patients (119 men, 81 women; median age, 58 years, age range, 18-89 years) who underwent MDCT urography for hematuria. MDCT urography included unenhanced and combined nephrographic and excretory phase imaging of the urinary tract. Images were independently reviewed by two radiologists blinded to the final diagnosis. The degree of upper urinary tract opacification and the diagnosis were recorded. Prospective interpretations were also reviewed. The standard of reference included all available clinical, imaging, and laboratory data for up to 12 months after MDCT urography. Sensitivity, specificity, accuracy, and positive and negative predictive values were calculated for upper tract tumors for prospective and retrospective interpretations.

Results: For reviewers 1 and 2, 85.1% and 84.5% of segments were at least 50% opacified, respectively. Final diagnoses for hematuria were no cause, 123 (61.5%); urothelial cancer, 27 (13.5%); nonmalignant, 46 (23%) and indeterminate, four patients (2%). There were nine upper tract cancers. Sensitivity, specificity, and accuracy for upper tract cancers for prospective interpretation, reviewer 1 and reviewer 2, were 100%, 99%, 99%; 100%, 99.5%, 99.5%; and 88.9%, 99.0%, 98.5%, respectively.

Conclusion: Split-bolus MDCT urography provided at least 50% opacification of the majority of upper urinary tract segments and had high sensitivity, specificity, and accuracy for the detection of upper urinary tract tumors.

Editorial Comment

Multidetector CT-urography (MDCT-urography) has been shown to be an effective single comprehensive examination in the evaluation of patients with hematuria or with risk for the development of urothelial malignancies. Since protocols for MDCT urography varies from each institution, most MDCT-urography images are obtained in the unenhanced phase (detection of calculi), nephrographic-phase (detection of renal masses) and excretory-phase (detection of urothelial lesions). The authors present their results with a protocol called split-bolus MDCT- urography where the unenhanced phase is followed only by a combined nephrographic and excretory phase. During split-bolus, CT-urography the intravenous injection of contrast material is performed in two steps. First, 40 ml is injected at 2 ml/s and after 120 second from the beginning of the first injection, the

remaining 80 ml is injected. According the authors in patients with hematuria, split-bolus MDCT- urography and oral hydration provide complete opacification of the majority of upper urinary tract segments and are accurate for the diagnosis of upper tract urothelial tumors. Since the main objective of MDCT-urography is to detect all possible causes of hematuria, this study has some limitations. The authors did not include an analysis of the capability of split-bolus technique for the detection of urinary calculi, renal parenchymal tumor and bladder cancers. As we know small bladder cancer can be missed if only excretory phase of the full bladder is obtained.

Another issue that could be addressed is how the renal parenchymal masses can be adequately characterized by the combined nephrographic /excretory phase obtained with split-bolus technique. Classically, renal masses are best characterized by the combination of findings obtained without intravenous contrast enhancement, scans obtained in nephrographic phase (70-90") and scans obtained in the excretory phase. In our opinion split bolus MDCT- urography may be useful for follow up patients with higher risk of develop upper tract urothelial cancer, particularly those already evaluated with cystoscopy. These patients should benefit with the use of this examination, which has high accuracy for the detection of urothelial cancer and uses low dose of radiation.

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PATHOLOGY

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Should pathologists continue to use the current pT2 substaging system for reporting of radical prostatectomy specimens?

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Background: During the International Society of Urological Pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens, 65.5% of the attendants answered that the current pT2 substaging system should not be used. Answering to another question, 63.4% favored to be reduced to two categories based on studies showing that pT2b does not exist. There was no consensus in regard to a minimum size for a second tumor to be considered for the whole case to be classified as pT2c as well as in regard to the definition of index tumor. We compared clinicopathologic findings and biochemical progression following surgery classifying pT2 patients into two categories.

Design: The study was based on whole-mount consecutive surgical specimens from 142 patients with organ confined cancer. Using a semiquantitative method for evaluation of tumor extent, 10 positive points corresponds roughly to a 0.5ml tumor. We considered pT2a/pT2b substage (group 1) whenever a tumor presented > 10 positive points on only one side and pT2c whenever presented > 10 positive points on each of right and left side (group 2). The variables analyzed were: age, preoperative PSA, clinical stage, Gleason score on needle biopsy, and biochemical progression following surgery defined as PSA > 0.2ng/mL. The data were analyzed using

the Mann-Whitney test, and the Kaplan-Meier product-limit analysis using the log-rank test for comparison between the groups. Results: Substage pT2a/pT2b corresponded to 84/142 (59.2%) patients and substage pT2c to 58/142 (40.8%) patients. There was no statistically significant difference between the groups in relation to: age ($p = 0.30$), preoperative PSA ($p = 0.13$), clinical stage ($p = 0.34$), and Gleason score on needle biopsy ($p = 0.27$). In 5 years of follow-up, 61% of patients pT2a/pT2b and 71% of patients pT2 were free of biochemical progression (log-rank, $p = 0.68$).

Conclusions: There was no significant difference for several clinicopathological variables and time of biochemical progression following surgery between patients with stage pT2a/pT2b and patients with stage pT3c. The results of this study favor to discontinue using the current pT2 substaging system for reporting of radical prostatectomy specimens.

Editorial Comment

In 1997, the TNM staging of T2 prostate cancers was divided into T2a (unilateral tumor) and T2b (bilateral tumor). In 2002 and now in 2010, T2 stage was substaged as in 1992, i.e., into 3 groups: T2a (unilateral tumor, less than half lobe), T2b (unilateral tumor, more than half lobe), and T2c (bilateral tumor). The clinical staging of T2 prostate cancers gives a good prognostic information. Time of biochemical (PSA) recurrence shows significant difference among the 3 groups. The clinical staging is a reflection of the detection methods employed and the substaging of clinical stage T2 prostate cancers is largely based on the extent of the abnormality palpated during a digital rectal examination (DRE) or shown during transrectal ultrasonography (TRUS) in each half of the prostate.

In a Consensus Meeting held during the United States and Canadian Academy of Pathology meeting in Boston 2009, 65.5% of the uropathologists present answered that the current pathologic T2 substaging should not be continued. Why the pathologic T2 substaging should be discontinued?

In contrast to clinical substaging of T2 cancers, pathological substaging does not convey prognostic information. This happens because prostate cancer is essentially a multifocal tumor. In general, there is a larger tumor (index tumor) but almost always, other foci scattered along the gland. Therefore, a large unilateral tumor palpated by the urologist (cT2b) is always bilateral in the surgical specimen (pT2c) (1-3). It has been argued that the prognostic significance of clinical substaging by DRE and TRUS of T2 cancers is a direct effect of understaging (4). The paper surveyed was a platform presentation at the 99th Annual Meeting of the United States and Canadian Academy of Pathology held in Washington DC, 2010, and is supported by several other previous studies (5-8). The conclusions included no significant difference for several clinicopathological variables and time of biochemical progression following surgery between patients with pathologic stage T2a/pT2b and patients with pathologic stage T3c. The results of the study favor to discontinue using the current pathologic T2 substaging system for reporting of radical prostatectomy specimens.

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Radical prostatectomy (RP) findings in cases with only intraductal carcinoma of the prostate (IDC-P) on needle biopsy

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Background: When IDC-P is present on biopsy, it is usually seen with infiltrating acinar adenocarcinoma. In 2006, we reported 27 cases with IDC-P only on biopsy; however, only 6 cases had available RP findings.

Design: 82 men with IDC-P only on prostate biopsy were identified from the consult files of one of the authors. Follow-up information was available in 66 cases. 20 men were treated with RP, 17 radiation therapy (RT), 8 hormone therapy (HT), 13 RT and HT, 6 active surveillance, and 2 rebiopsy. An attempt was made to retrieve the slides of all 20 RP cases.

Results: Of the 20 RP cases, 5 showed extraprostatic extension, 3 seminal vesicle invasion, 10 were organ-confined, and 2 showed extensive IDC-P only without identifiable invasive cancer. Of the 18 cases with invasive cancer, the average Gleason score (GS) was 7.8. 1 patient developed bone metastases 3 years post-RP, and 3 others were post-RP PSA failures. 13 RPs were available for our review. 9 showed extensive IDC-P (including one case of IDC-P only), defined as > 10% of the tumor volume being intraductal; 3 focal IDC-P; and 1 no IDC-P. All cases with invasive carcinoma were acinar, although 3 cases were classified as ductal by referring pathologists. We concurred with the outside GS in 5/13 cases (5 undergraded, 3 overgraded). In the 3 cases that we gave lower GS, the outside institution graded cribriform IDC-P with and without necrosis as Gleason pattern 5 or 4, respectively.

Conclusions: Our study, the largest to date with RP findings following IDC-P only on needle biopsy, confirms that aggressive therapy is appropriate for patients whose biopsies show only IDC-P. It is likely that the pathological findings are even worse than we report herein, as most RPs were only partially sampled. Most cases likely represent intraductal spread of high grade cancer, but some cases represent in situ acinar adenocarcinoma.

Editorial Comment

Intraductal carcinoma of the prostate (IDC-P) is defined as presence of atypical cells that span the entire lumen of prostatic ducts or acini while the normal architecture of ducts or acini is still maintained including presence of basal cells (1,2). With presence of IDC-P on a biopsy, the pathologist considers 4 possibilities: 1)

ductal carcinoma; 2) high-grade intraepithelial neoplasia (HGPIN); 3) intraductal carcinoma; and, 4) intraductal spread of an invasive carcinoma.

Ductal carcinoma may be ruled out because of the presence of basal cells; in cases of irregularity and distortion of the ducts, HGPIN may also be ruled out; and, in presence of an invasive carcinoma, intraductal spread is most probable and the finding adds no additional information to the report. The problem is related to cases that IDC-P is the only finding on a biopsy.

The Johns Hopkins group studied 20 radical prostatectomy specimens of patients who presented on biopsy only the diagnosis of IDC-P. Two out of twenty patients showed extensive IDC-P only, without identifiable invasive cancer. IDC-P in these 2 patients may represent: 1. an early phase of ductal or acinar carcinoma; or 2. intraductal spread of an invasive not detected tumor.

According to the authors, IDC-P as the only finding on needle biopsy corresponds to almost always to aggressive tumors and the patients may have definitive treatment. A more conservative approach would be an extended rebiopsy in order to detect a possible invasive cancer.

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BASIC AND TRANSLATIONAL UROLOGY

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Potential mechanism of action of human growth hormone on isolated human penile erectile tissue

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Urology. 2010; 75: 968-73

Objectives: To evaluate the mechanisms of growth hormone (GH) action on isolated human penile erectile tissue. Human GH (hGH) has been suggested to play a role in male reproductive function, including penile erection. Nevertheless, it still remains unclear which intracellular pathways mediate the physiological effects of GH on the human corpus cavernosum (HCC).

Methods: Using the organ bath technique, the effects of GH were investigated on electrical field stimulation (EFS)-induced relaxation of isolated HCC in the absence and presence of the guanylyl cyclase inhibitor 1H-

[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ) and nitric oxide synthase (NOS) inhibitor N(G)-nitro-L-arginine (L-NOARG, 10 microm). Effects of GH on the production of tissue cyclic guanosine monophosphate (cGMP) in the absence and presence of ODQ and L-NOARG were also elucidated using radioimmunoassay.

Results: ODQ and L-NOARG abolished the relaxation of the tissue induced by EFS, whereas amplitudes were increased by physiological concentrations of GH (1-100 nm). The attenuation of EFS-induced amplitudes by L-NOARG but not ODQ was, in part, reversed by GH. The production of cGMP (pmol cGMP/mg protein) induced by 10 nm GH was abolished in the presence of 10 microm ODQ. In contrast, the combination of GH (10 nm) and L-NOARG (10 microm) maintained cGMP production significantly greater than baseline (0.68 +/- 0.36 vs 1.07 +/- 0.48 pmol cGMP/mg protein).

Conclusions: Our data provide evidence that GH may act on human HCC by an NO-independent effect on guanylyl cyclase activity and may thus explain how growth factors, such as hGH, regulate male erectile function. Copyright 2010 Elsevier Inc. All rights reserved.

Editorial Comment

This group of investigators has been studying the effects of growth hormone for more than 10 years. They have demonstrated previously that growth hormone likely mediates penile erection through its stimulating effect on the cGMP pathway in human cavernous smooth muscle. Later, they compared the in vivo serum profiles of growth hormone in the systemic and cavernous blood samples obtained from healthy volunteers were compared to the serum profiles of patients with erectile dysfunction. In the healthy subjects, systemic growth hormone serum levels significantly increased during penile tumescence, followed by a transient decline from tumescence to rigidity and detumescence. During penile tumescence, the mean increase in the growth hormone levels in the systemic and cavernous blood of patients with organogenic dysfunction, this increase was found to be negligible.

In the present study they found evidence that growth hormone may act on human corpus cavernosum by an effect independent of nitric oxide on guanylyl cyclase activity. The group has to be commended for the important contribution they have been providing during the last years to elucidation of growth hormone activity in human erection

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Atorvastatin protects renal function in the rat with acute unilateral ureteral obstruction

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Urology. 2010; 75: 853-7

Objectives: To examine the effects of atorvastatin on renal hemodynamics and urinary microalbumin levels in rats with acute unilateral ureteral obstruction (UUO). Previous studies have demonstrated that treatment with statins attenuated renal structural damages in rodents with chronic UUO. However, it is not known whether statins afford protection of renal function.

Methods: UUO was created by ligation of the left ureter in rats maintained on a regular diet or the same diet but supplemented with atorvastatin (50 mg/kg/d) for 2 weeks. Renal clearance experiments were performed after release of UUO at 1 hour, 6 hours, or 12 hours.

Results: Atorvastatin treatment lowered plasma triglyceride but not cholesterol levels. Both glomerular filtration rate and effective renal plasma flow were significantly greater in atorvastatin-treated rats after release of UUO at 1 hour, 6 hours, and 12 hours. Significant reduction of urinary microalbumin to creatinine ratios occurred in the atorvastatin-treated group at 12 hours but not earlier.

Conclusions: Atorvastatin treatment affords protection of renal function in acute UUO and reduces urinary microalbumin levels without lowering cholesterol levels. This pleiotropic action of atorvastatin on preservation of renal hemodynamics may be important in attenuating subsequent renal structural injury in chronic UUO.

Editorial Comment

Previous studies examined molecular markers of fibrosis and histologic changes in chronically obstructed kidney. This is the first research that analyzed the effects of statins (atorvastatin) on renal hemodynamics of kidneys with ureter acutely obstructed unilaterally. The present investigation showed by the first time that treatment with atorvastatin in rats with acute unilateral ureteral obstruction resulted in improvement in renal perfusion and filtration function.

The authors emphasized that these findings raise the possibility that some of the benefits of statins in the clinical trials may originate from the pleiotropic effects of statins and not specifically from the lipid-lowering effect alone. Also, it is worth to note that the dose of statin used in the present study is proportionally much higher than the doses currently used in clinical practice. The authors also remembered that other studies also used supra-pharmacological doses of statins to demonstrate attenuation of tubulo-interstitial inflammation and fibrosis in rats with unilateral ureteral obstruction. Therefore, the dosage of statins required to exert their pleiotropic actions is still unknown and remains to be determined. Anyway, the present study shown that treatment with a statin in rats with acute unilateral ureteral obstruction, resulted in improvement in renal perfusion and filtration function. This open new avenue for renal protective agents.

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RECONSTRUCTIVE UROLOGY

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Management of radiotherapy induced rectourethral fistula

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J Urol. 2006; 175: 1382-7; discussion 1387-8

Purpose: An increasing number of men are being treated with BT or a combination of external beam radiation therapy and BT for localized prostate cancer. Although uncommon, the most severe complication following

these procedures is RUF. We reviewed our recent experience with RUF following radiotherapy for prostate cancer to clarify treatment in these patients.

Materials and Methods: We recently treated 22 men with RUF following primary radiotherapy for adenocarcinoma of the prostate in 21 and adjuvant external beam radiation therapy following radical prostatectomy in 1. Time from the last radiation treatment to fistula presentation was 6 months to 20 years.

Results: Four patients underwent proctectomy with permanent fecal and urinary diversion. RUF repair in 5 patients was performed with preservation of fecal or urinary function. Six patients were candidates for reconstruction with preservation of urinary and rectal function, including 5 who underwent proctectomy, staged colo-anal pull-through and BMG repair of the urethral defect. The additional patient underwent primary closure of the rectum, BMG repair of the urethra and gracilis muscle interposition. Successful fistula closure was achieved in the 9 patients who underwent urethral reconstruction. All 8 candidates for rectal reconstruction showed radiological and clinical bowel integrity postoperatively with 2 awaiting final diverting stoma closure.

Conclusions: With the increasing use of prostate BT the number of patients with severe rectal injury will likely continue to increase. Radiotherapy induced RUF carries significant morbidity and most patients are treated initially with fecal and urinary diversion. In properly selected patients good outcomes can be expected following repair using BMG for the urethral defect along with colo-anal pull-through or primary rectal repair and gracilis muscle interposition.

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Incidence, clinical symptoms and management of rectourethral fistulas after radical prostatectomy

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J Urol. 2010; 183: 608-12

Purpose: Rectourethral fistula is a rare but severe complication after radical prostatectomy and there is no standardized treatment. We retrospectively evaluated the incidence, symptoms and management of rectourethral fistulas based on our experience. **Materials and Methods:** From 1999 to 2008 we performed 2,447 radical prostatectomies. Patients in whom postoperative rectourethral fistulas developed were identified. Based on the therapeutic approach patients were categorized into group 1-conservative treatment, group 2-colostomy with or without surgical closure and group 3-immediate surgical closure without colostomy.

Results: Rectourethral fistulas developed in 13 of 2,447 patients (0.53%) after radical prostatectomy. The risk of rectourethral fistulas was 3.06-fold higher ($p = 0.074$) for perineal (7 of 675, 1.04%) than for retropubic prostatectomy (6 of 1,772, 0.34%). In 7 of 13 patients (54%) a rectal lesion was primarily closed at radical prostatectomy. Median followup was 59 months. In all patients in group 1 (3) the fistula closed spontaneously with conservative treatment. None of these patients had fecaluria. In group 2 of the 9 patients 3 (33%) experienced spontaneous fistula closure after temporary colostomy and transurethral catheterization. In this group 6 patients (67%) required additional surgical fistula closure, which was successful in all. Surgical fistula closure (1) without colostomy in presence of fecaluria failed (group 3).

Conclusions: The therapeutic concept for rectourethral fistulas should be guided by clinical symptoms. Rectal injury during radical prostatectomy is a major risk factor. In cases with fecaluria colostomy is required for control of infection and may allow spontaneous fistula closure in approximately a third of cases. In the remainder of cases surgical fistula closure was successful in all after protective colostomy.

Editorial Comment

These two single institution case series review management and outcome of rectourethral fistula repair in two vastly different patient groups: surgery vs. radiation. It is well accepted that rectourethral fistula repair

is made more difficult by prior radiotherapy. Another difference between the two groups is that the post-radical prostatectomy patients were primarily managed by the authors whereas in post-radiation patients were referred for management after a failed period of conservative management.

In the radical prostatectomy series by Thomas et al., nearly half of the fistulas closed spontaneously, a few even without a colostomy. Importantly, the authors note that the absence of fecaluria was a good indicator of a fistula that would close spontaneously: 4 of 8 closed spontaneously in the absence of fecaluria (3 without a colostomy) but only 1 of 5 with fecaluria. Spontaneous closure occurred after 1-3 months of urethral catheterization. All fistula repairs were accomplished transperineally.

The radiation series is quite different. No fistulas closed spontaneously. Fistulas were much larger, ranging in size up to 7 cm. Patients presented with severe problems secondary to the fistula such as sepsis and Fournier's gangrene. Only 6/22 could be repaired with preserved orthotopic fecal and urinary function; the remainder had one or both streams diverted with an ostomy. Perioperative morbidity was likewise much higher in those undergoing fistula repair after radiation.

Rectourethral or rectovesical fistula is a rare but morbid complication of surgery or radiation for prostate cancer. These series highlight the fact that with appropriate expertise good outcomes can be achieved in those who have not been previously radiated however

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UROLOGICAL ONCOLOGY

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Characteristics and outcomes of patients with clinical T1 grade 3 urothelial carcinoma treated with radical cystectomy: results from an international cohort

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Eur Urol. 2010; 57: 300-9

Background: Management of T1 grade 3 (T1G3) urothelial carcinoma of the bladder (UCB), with its variable behaviour, represents one of the most difficult challenges for urologists and patients alike.

Objective: To evaluate the characteristics and long-term outcome of patients with clinical T1G3 UCB treated with radical cystectomy (RC).

Design, Setting, and Participants: Data from 1136 patients treated with RC for clinical T1G3 UCB without neoadjuvant chemotherapy were collected at 12 centres located in Europe, the United States, and Canada. Median age was 67 yr (range: 29-94), with a male-to-female ratio of 4:1.

Measurements: Patients' characteristics and outcome are evaluated.

Results and Limitations: Of the 1136 patients, 33.4% had non-organ-confined stage at cystectomy, and 16.2% had lymph node (LN) metastasis; 49.7% were upstaged after RC to muscle-invasive disease, while 21.4% were

downstaged to lower than T1G3. Within a median follow-up of 48 mo, 35.5% of patients died of metastatic UCB.

Conclusions: Approximately half of the patients treated with RC without neoadjuvant chemotherapy for clinical T1G3 UCB are upstaged to muscle-invasive UCB. These rates support the inadequacy of clinical decision making based on current treatment paradigms and staging tools. Therefore, identification of patients with clinical T1G3 disease at high risk of disease progression is of the utmost importance, as these patients are likely to benefit from early RC.

Editorial Comment

The optimal primary treatment of stage and grade T1G3 bladder cancer, radical or conservative, is a matter of debate since years. Here, 12 international centers with a large experience in radical cystectomies present their data on this aggressive “borderline” tumor. They found a high rate of nearly 50% of tumor upstaging to muscle invasive disease.

Alas, this study suffers from several drawbacks. No indication on previous intravesical therapy, or on the time between first diagnosis of bladder cancer and cystectomy are given. These data would have made it much easier to judge on the delay as reason for the high rate of upstaging and to get information on the proportion of “true aggressive” T1G3 tumors which would indeed need immediate cystectomy without an initial trial of TUR, re-TUR and BCG.

All in all, these data reflect the aggressive nature of T1G3 bladder cancer and the need for stringent management, be it conservative or radical.

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Should all patients with non-muscle-invasive bladder cancer receive early intravesical chemotherapy after transurethral resection? The results of a prospective randomised multicentre study

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Eur Urol. 2009; 55: 773-80

Background: To decrease recurrences in non-muscle-invasive bladder cancer (NMIBC), the European Association of Urology (EAU) guidelines recommend immediate, intravesical chemotherapy after transurethral resection (TUR) for all patients with Ta/T1 tumours.

Objective: To study the benefits of a single, early, intravesical instillation of epirubicin after TUR in patients with low- to intermediate-risk NMIBC.

Design, Setting, and Participants: In this prospective randomised multicentre trial, 305 patients with primary as well as recurrent low- to intermediate-risk (Ta/T1, G1/G2) tumours were enrolled between 1997 and 2004. Patients were randomly allocated to receive 80 mg of epirubicin in 50 ml of saline intravesically within 24 h of TUR or no further treatment after TUR.

Measurements: The primary end point was time to first recurrence.

Results and Limitations: A total of 219 patients remained for analysis after exclusions. The median follow-up time was 3.9 yr. During the study period, 62% (63 of 102) of the patients in the epirubicin group and 77% (90 of 117) in the control group experienced recurrence ($p=0.016$). In a multivariate model, the hazard ratio (HR) for recurrence was 0.56 ($p=0.002$) for early instillation of epirubicin versus no treatment. In a subgroup analysis, the treatment had a profound recurrence-reducing effect on patients with primary, solitary tumours, whereas it provided no benefits in patients with recurrent or multiple tumours. Furthermore, patients with a modified European Organisation for Research and Treatment of Cancer (EORTC) risk score of 0-2 with and without single instillation had recurrence rates of 41% and 69%, respectively ($p=0.003$), whereas the corresponding rates for those with a risk score of ≥ 3 were 81% and 85%, respectively ($p=0.35$).

Conclusions: A single, early instillation of epirubicin after TUR for NMIBC reduces the likelihood of tumour recurrence; however, the benefit seems to be minimal in patients at intermediate or high risk of recurrence. Future trials will determine the value of early instillation in addition to serial instillations in NMIBC.

Editorial Comment

Bladder cancer has a high rate of recurrence. Two pathways are considered responsible for this behavior, namely genetically instable urothelium resulting in truly new tumor formation, and re-implantation (seeding) of tumor cells resulting in new occurrences from the previous tumor. The best way to date to interfere with the second pathway, seeding of tumor cells, is immediate post-TUR single shot instillation of cytotoxic drugs. However, is this sufficient therapy for all tumors? The authors answer this important question in their randomized study. First, they show that single-shot instillation (in this study given within 24 hours, but best within 6 hours after TUR) indeed is highly effective, resulting in a significant overall reduction of recurrences. This effect was pronounced in the low risk group with single primary tumors, whereas barely evident in the intermediate risk group or that with multiple tumors. The numbers needed to treat (NNT) was 3.5, which supports similar figures from previous calculations.

The authors state correctly that single-shot treatment has little or no impact on genetically instable urothelium. Therefore, next to single – shot instillation therapy, all intermediate to high-risk group patients with bladder cancer deserve more instillation therapy, be it regular courses of cytostatics or BCG.

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NEUROLOGY & FEMALE UROLOGY

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Regular moderate intake of red wine is linked to a better women's sexual health

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J Sex Med. 2009; 6: 2772-7

Introduction: While some evidence does exist for a positive correlation between moderate wine intake and men's sexual health, there is no study addressing the potential correlation between red wine intake and women's sexual function.

Aim: The aim of our study was to assess whether there is a tie between daily red wine intake and sexual function in a sample of healthy Italian women, living in the Chianti area (Tuscany) not complaining of any sexual disorders.

Methods: We recruited 798 women (age 18-50), living in the Chianti area (Tuscany), not complaining of any sexual disorders. We divided the participants into three groups: daily moderate (one to two glasses) red wine intake (group 1); teetotallers (group 2); and daily intake of more than two glasses of red wine and/or other types of alcoholic drinks (including white wine), as well as of those reporting occasional drinking (group 3).

Main outcome measures: All participants completed anonymously the Female Sexual Function Index (FSFI) questionnaire and were asked to report on their amount and type of alcohol consumption.

Results: Group 1 had significantly higher total ($P = 0.001$), as well as desire and lubrication domain ($P = 0.001$ and $P = 0.001$, respectively) FSFI scores than participants in groups 2 and 3. No significant differences between the groups were observed concerning sexual arousal, satisfaction, pain, and orgasm. Univariate analysis showed a significant correlation between age, alcohol consumption ($P = 0.009$), and a better score at questionnaire examination. During multivariate analysis, alcohol consumption was identified as an independent prognostic parameter ($P = 0.002$) in predicting the better score at questionnaire examination.

Conclusions: The finding that regular moderate intake of red wine is associated with higher FSFI scores for both sexual desire, lubrication, and overall sexual function as compared to the teetotaller status is intriguing. While this finding needs to be interpreted with some caution, because of the small sample size, self-reported data, and the lack of support from laboratory exams, it nevertheless suggests a potential relationship between red wine consumption and better sexuality.

Editorial Comment

A fascinating paper that examines the effect of wine on women's sexual health. The authors reviewed a population of females that was subdivided into three groups with the first group being women who drank 1-2 glasses of wine daily; the second group that did not intake alcohol; and the third group being occasional drinkers, reporting less than 1 glass per day. Women who drank more than 2 glasses of red wine or 2 glasses or more of other types of alcoholic drinks including white wine were excluded from the study. The authors limited their population to women who were very sexually normal based on responding affirmative to "are you happy with your sexuality?" and responding no to the question "have you ever had a sexual problem?". Any woman who was pregnant, lactating, used supplemental hormones as well as had any kind of previous genitourinary surgery or substance abuse were excluded from the study. The primary metric of the assessment was the Female Sexual Function Index (FSFI). The authors found that the moderate alcohol drinkers of red wine (2 glasses a day) had an overall higher score on the FSFI as well as increased responses in the desire and lubrication domain. There was no difference between the groups with regards to arousal, satisfaction, pain or orgasm.

Though the authors freely admit that their data is mildly handicapped secondary to the low study numbers and the use of self-reported data they present a wonderful discussion on the potential pathways of efficacy that moderate wine intake may have on female sexual health. The discussion alone makes reading this paper worthwhile in view of the ideas presented. As with many excellent reports, this study engenders much scientific thought after the content has been appropriately digested.

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A multicenter, prospective, randomized clinical trial comparing tension-free vaginal tape surgery and no treatment for the management of stress urinary incontinence in elderly women

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Neurourol Urodyn. 2007; 26: 990-4

Aims: The aim of our study was to test the hypothesis that elderly women undergoing tension-free vaginal tape surgery (TVT) will have a better quality of life (QOL) and satisfaction compared to non-treated women despite age- and technique-related potential morbidity.

Methods: This multicenter, prospective, randomized, controlled trial enrolled a total of 69 women aged over 70 years who initially consented to be randomized to either undergo immediate TVT surgery or to wait for 6 months before submitting to the same surgery (control group). The main outcomes measured at every visit (pre-randomization, 8-12 weeks and 6 months) consisted of the Incontinence-Quality of Life (I-QOL) Questionnaire, the Patient Satisfaction Questionnaire and the Urinary Problems Self-assessment Questionnaire, among others.

Results: The analysis included 31 patients in the immediate surgery group and 27 subjects in the control group. Peri-operative complications in the immediate surgery group were bladder perforation (22.6%), urinary retention (12.9%), urinary tract infection (3.2%) and de novo urgency (3.2%). At 6 months, the mean I-QOL scores for the TVT and control groups were respectively 96.5 +/- 15.5 and 61.6 +/- 19.8 ($P < 0.0001$); mean Patient Satisfaction scores were respectively 8.0 +/- 2.7 and 2.0 +/- 2.4 ($P < 0.0001$); and mean Urinary Problems scores were respectively 4.5 +/- 4.3 and 11.6 +/- 3.5 ($P < 0.0001$).

Conclusion: At 6 months post-randomization, the group of elderly women who underwent immediate TVT surgery showed a significant improvement in QOL, patient satisfaction and less urinary problems compared to the group of women waiting for the same surgery

Editorial Comment

The authors provide a study with the primary goal of deciding whether elderly women who underwent surgery with its attendant risks would have an improved quality of life and satisfaction than those patients who deferred surgery and merely continued on in their state of incontinence or in simpler terms: should an elderly woman have surgery or just live with her symptoms. The population studied included patients that either refused or failed conservative therapy and were on no medication for bladder dysfunction (including overactive bladder or urinary tract infection). The patients had no evidence of detrusor overactivity and had normal compliance on cystometrogram. The patient population was randomized to either having surgery immediately or waiting six months and being reevaluated and then having their surgery at that time. The metrics for both groups were quantified at baseline and again at 6 months and then compared. The tools that were utilized to assess the patient's quality of life included the IQOL Questionnaire; Patient Satisfaction scores; in addition to a Urinary Problems quantification. The authors found that patients who had the surgery had improvement in the measured parameters over those practicing watchful waiting thus supporting their hypothesis that surgery was worthwhile over watchful waiting in the elderly population.

This is an excellent paper to review when pondering whether to offer surgery to an elderly woman versus telling her to live with her problem. Many times, the surgeon must make the simple but really complex assessment of whether the treatment will outweigh the cure; this report emboldens one to choose intervention.

The study begs the authors to take the next step of determining if the same promise of therapy can be applied to the super elderly population such as those of 80, 85 or 90 years of age.

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PEDIATRIC UROLOGY

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Improvement in vesicoureteral reflux grade on serial imaging predicts resolution

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J Urol. 2010; 183: 709-13

Purpose: When children are initially diagnosed with vesicoureteral reflux most undergo a period of antibiotic prophylaxis followed by serial imaging. Although improvement in reflux grade through time presumably predicts eventual resolution, the significance of changing grade through time is unknown. We examined whether improvement in reflux on serial imaging predicts resolution.

Materials and Methods: We retrospectively reviewed 1,761 children diagnosed with vesicoureteral reflux, of which 965 had a minimum of 2 years of follow-up. We examined initial reflux grade and grade on serial imaging up to 5 years after the original diagnosis. For each child it was determined whether reflux was resolved, eventually resolved or never resolved. Groups were further stratified by clinical characteristics.

Results: Multivariate analysis revealed that male gender (HR 1.33, $p = 0.05$), age younger than 1 year at diagnosis (HR 1.35, $p = 0.004$), lower grade at presentation (grade I HR 2.2, grade II HR 1.96, grade III HR 1.33; $p < 0.001$) and unilateral reflux (HR 1.39, $p = 0.001$) were all independent predictors of reflux resolution. Multivariate analysis also showed that reflux improvement on imaging 1 year after diagnosis (HR 3.14, $p < 0.0001$) and improvement from the previous year at any point during follow-up (HR 1.8, $p = 0.009$) were independent predictors of reflux resolution.

Conclusions: Consistent with previous findings, male gender, lower reflux grade at presentation, age less than 1 year at presentation and unilateral reflux were all predictive of reflux resolution. Our analysis also demonstrated that improvement in reflux grade on imaging study 1 year after diagnosis was predictive of resolution, and that reflux improvement from the previous year at any point during follow-up was an independent predictor of resolution. This information will prove valuable in clinical counseling and therapeutic decision making.

Editorial Comment

The authors utilized their database of over 1,700 children with vesicoureteral reflux to determine whether improvement in reflux grade on serial imaging would predict resolution of reflux. They were able to identify 965 patients who had 2-5 years of follow-up for the study and then performed a multivariate analysis to identify predictors of resolution. Nuclear cystograms were performed routinely for follow-up studies in these children, therefore they considered Grade I reflux on a nuclear cystogram to be equivalent to a grade 1 on VCUG study. A nuclear cystogram with Grade II reflux was equivalent to a VCUG with Grade II and III on VCUG and Grade III reflux on nuclear cystogram was equivalent to Grade IV and V reflux on VCUG. Their

results demonstrated that male gender, age less than one year at diagnosis, lower grade of reflux at presentation and unilateral reflux were all predictors of spontaneous resolution, which is consistent with previous studies. In addition, they were able to demonstrate that reflux improvement on imaging one year after diagnosis, as well as improvement in reflux grade from the previous year at any point during follow-up, were both independent predictors of resolution.

This study has important clinical implications when counseling with parents over the decision to continue waiting for spontaneous resolution versus pursuing surgical correction of reflux. Though many of us have assumed that improvement in the grade of reflux is a positive indicator of a greater likelihood for spontaneous resolution, we now have data to back up our assumptions.

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Incidence of new onset metabolic acidosis following enteroplasty for myelomeningocele

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J Urol. 2010; 183: 302-5

Purpose: Extant literature is mixed regarding risk of metabolic acidosis after enteroplasty for myelomeningocele. This study is the first known attempt to describe the pattern of developing metabolic acidosis in a group of children who underwent enteroplasty and served as their own controls. Multiple preoperative and postoperative laboratory measures for each child were obtained for comparison.

Materials and Methods: This retrospective cohort study allowed participants to serve as their own controls for pre-intervention and post-intervention analysis. The setting was a tertiary, university affiliated, interdisciplinary spina bifida program. All patients followed in the spina bifida program who had undergone ileal or colonic enteroplasty were included for review (total 113). Strict exclusion criteria were preoperatively diagnosed renal insufficiency, preexisting metabolic acidosis consistent with renal tubular acidosis (pH less than 7.35, bicarbonate 20 mmol/l or less) and history of augmentation using gastric or ureteral tissue. Final analysis included 71 children who met inclusion criteria. Children in our spina bifida program periodically undergo routine laboratory evaluation of electrolytes, blood urea nitrogen, creatinine, blood count, and venous blood gases including pH, bicarbonate and partial pressure of carbon dioxide. Primary outcome measures were comparative shifts in blood gases and electrolytes that would confirm the new onset of metabolic acidosis after enteroplasty. Changes in electrolytes and serum creatinine were secondary outcome measures to identify potential markers for postoperative effects. With each child as his/her own control, analysis included paired t tests.

Results: No statistically significant differences ($p < 0.05$) were found when comparing laboratory values before and after bladder augmentation, including pH, bicarbonate, partial pressure of carbon dioxide and electrolytes. No child had metabolic acidosis based on the aforementioned criteria. Followup ranged from 1 to 138 months after enteroplasty (mean 46.8). Respiratory compensation was considered in the analysis, and no difference in partial pressure of carbon dioxide following surgery was noted ($p = 0.65$).

Conclusions: To our knowledge no previous study has examined the matched paired results of before and after development of metabolic acidosis among children (serving as their own controls) with myelomeningocele

undergoing ileal or colonic enteroplasty. The negative statistical results in this controlled cohort are clinically significant. If a child with myelomeningocele has metabolic acidosis after enteroplasty, other clinical reasons beyond the effects of surgery warrant careful consideration.

Editorial Comment

The development of metabolic acidosis following enterocystoplasty is a common concern particularly in the pediatric population where such a procedure is intended to last a lifetime. The authors reviewed data from their spina bifida program that had undergone bladder augmentation using either ileum or colon. They excluded patients with preoperative renal insufficiency or metabolic acidosis. Patients in their spina bifida program routinely undergo serum evaluation of electrolytes, BUN, creatinine blood count, and venous blood gases giving them a unique opportunity to look at changes in serum values both before and after enterocystoplasty. They identified 71 children who met the inclusion criteria and had both preoperative and postoperative laboratory values. Their primary outcome was a shift in blood gases and electrolytes consistent with new onset of metabolic acidosis following bladder augmentations. Secondary outcomes included changes in electrolytes and serum creatinine. They found no evidence of new onset of metabolic acidosis following surgery for a mean follow-up period of almost four years.

Although concern for metabolic changes following enterocystoplasty in the pediatric population must be considered over extremely long time periods, it is interesting to note that these authors found no significant changes even after following their patients for a mean of four years. They also wisely point out that the spina bifida patient population is at risk for metabolic acidosis for other reasons including nutritional issues, chronic infection, pulmonary insufficiency, and/or renal insufficiency. As the authors point out in their conclusion, it may be just as important to consider other sources of metabolic acidosis (some of which may be correctable) rather than assuming the enterocystoplasty is to blame.

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