UROLOGICAL SURVEY

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Role of adjunctive medical therapy with nifedipine and deflazacort after extracorporeal shock wave lithotripsy of ureteral stones
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Objectives: To increase the success rate of the first treatment of ureteral stones through extracorporeal shock wave lithotripsy (ESWL), we tested the efficacy of a medical therapy with nifedipine and deflazacort administered to patients who had undergone ESWL for ureteral stones.

Methods: This prospective study lasted from October 1998 to September 2000 and involved 80 patients. All the patients underwent ESWL with Sonolith 4000+. The patients were randomly divided into two groups: 40 patients (group 1) received an “adjunctive” treatment with oral medical therapy (nifedipine and deflazacort); the other 40 patients (group 2) were used as the control group.

Results: Complete fragment expulsion occurred in 30 (75%) of the 40 patients of group 1 and in 20 (50%) of the 40 patients of group 2 at the endpoint. A statistically significant difference was observed in the stone-free rate (P = 0.02). Concerning the symptomatic therapy, the average diclofenac use was 37.5 mg per patient in group 1 and 86.25 mg per patient in group 2 (P = 0.02).

Conclusions: The results of this study have shown the role that adjunctive medical therapy with nifedipine and deflazacort given after an ESWL procedure can play in increasing the success rate of ureteral stone treatment. Furthermore, these results would suggest that adjunctive medical therapy can reduce total analgesic consumption after the ESWL procedure.

Editorial Comment
Based on previous studies demonstrating facilitated spontaneous passage of ureteral stones with the use of corticosteroids and calcium channel blockers, the authors performed a prospective, randomized trial evaluating a similar medical regimen in patients with ureteral stones undergoing shock wave lithotripsy. Patients in the group receiving adjuvant medical therapy were treated with a 10-day regimen of nifedipine and deflazacort while the control group received no adjuvant therapy. The study group demonstrated improved rates of fragment discharge and reduced narcotic requirements compared with the control group (75% versus 50% stone free, respectively, and 37.5 mg versus 86.3 mg of diclofenac, respectively).

This study adds to the mounting evidence that pharmacologic manipulation of ureteral physiology can be used to facilitate the passage of ureteral stones, whether intact or fragmented. Consequently, consideration should be given to instituting a similar medical regimen in eligible patients (those in whom the use of corticosteroids or calcium channel blockers is not contraindicated) presenting to the emergency room with renal colic due to a ureteral stone or in patients undergoing shock wave lithotripsy for ureteral stones. Use of this regimen in patients undergoing shock wave lithotripsy for renal stones has yet to be studied, and therefore it is not clear if improved stone clearance rates can be expected from the kidney.

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When is medical prophylaxis cost-effective for recurrent calcium stones?
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J Urol. 2002; 168:937-40

Purpose: Medical management is generally recommended for recurrent calcium stones to prevent future episodes. However, in this era of extracorporeal shock wave lithotripsy and outpatient ureteroscopy it is not known whether medical prophylaxis is more cost-effective than treatment of recurrent stone episodes. The cost of medical prophylaxis was compared with the cost of clinically managing recurrent stone episodes, and the stone recurrence rate without prophylaxis (stone frequency) at which these 2 treatment approaches became cost equivalent was determined.

Materials and Methods: An international cost survey was conducted in 10 countries to compare costs of medical prophylaxis and managing recurrent acute stone episodes. Costs of an acute stone episode included an emergency room visit, associated radiographic imaging to confirm diagnosis of a symptomatic stone and outpatient treatment of upper urinary tract stones that did not pass spontaneously. Costs of medical management included an initial limited metabolic evaluation, drug therapy, a followup office visit every 6 months that included a 24-hour urinalysis and radiographic imaging of the kidneys, ureters and bladder once a year.

Results: Costs of medical prophylaxis and managing an acute stone episode varied significantly from country to country. The stone frequency at which costs of these management options became equivalent ranged from 0.3 to 4 stone episodes a year.

Conclusions: Medical management of a first stone episode is not cost-effective. Cost analysis should be individualized for specific health care plans to determine which practice patterns are most cost-effective for a particular patient with recurrent calcium stone formation.

Editorial Comment

Although effective diagnostic protocols and treatment regimens are available for the diagnosis and prevention of recurrent nephrolithiasis, the cost-effectiveness of stone metaphylaxis versus treatment of acute stone episodes as they arise has not been thoroughly explored. In this article, the costs of medical evaluation and management and treatment of symptomatic stone episodes were determined world-wide from an economic survey of representative individuals in selected countries. The point of cost equivalence, representing the stone recurrence rate at which the cost of medical evaluation and therapy and management of an acute stone episode were equivalent, was determined for each country and varied between 0.32 and 0.69 in the United States, depending on the estimated need of surgical intervention. Based on their findings, the authors suggest that a medical preventative program for the first stone former is not cost-effective.

This important paper attempts to identify select subgroups of stone formers in whom a medical treatment program is cost-effective. In doing so, the assumptions used in the model are of critical importance. Unfortunately, the rate of surgical intervention varies widely in the literature and the distribution of surgical procedures for symptomatic stones is not well known. Furthermore, charges and not costs were used to determine the points of cost equivalence in several countries, despite the inherent problems involved in using the more arbitrary charge data. Nonetheless, for well-defined patient populations (i.e., recurrent stone formers at an institution where intervention rates and surgical distribution is known), this model can be used to identify patients in whom a medical treatment program is cost-effective.

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Ronald postoperative imaging is important after ureteroscopic stone manipulation
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Purpose: Improved fiber optics and advanced intracorporeal lithotripsy devices have significantly
decreased the incidence of complications during ureteroscopic procedures. Despite recent reports suggesting
that radiographic imaging may not be necessary in all individuals after routine ureteroscopy silent obstruction
may develop in some, ultimately resulting in renal damage. We determined the incidence of postoperative silent
obstruction at our institution and assessed the need for routine functional radiographic studies after ureteroscopy.

Materials and Methods: We retrospectively reviewed the charts of 320 patients who underwent a total
of 459 ureteroscopic procedures for renal or ureteral calculi in a 3-year period. Complete followup with imaging
was available for 241 patients (75%). Average patient age was 47.2 years. The variables of interest reviewed
included preoperative pain, preoperative obstruction, targeted calculus site, stone-free rate, postoperative pain
and postoperative obstruction. Mean followup was 5.4 months (range 2 to 43).

Results: A total of 241 patients with complete followup were identified in this analysis. Preoperative
pain was present in 202 patients (84%) and 168 (70%) had preoperative obstruction. Overall targeted calculus
clearance was successful in 73% of the patients and an additional 15.8% had residual fragments less than 4 mm.
The renal, proximal or mid and distal ureteral stone-free rate was 32.1%, 81.9% and 90.5%, while in an additional
46.4%, 6.3% and 6.7% of cases, respectively, residual fragments were less than 4 mm. Of the 241 patients 30
(12.3%) had obstruction postoperatively due to residual stone in 25 (83.3%), stricture in 3 (10%), edema of the
ureteral orifice in 1 (3.3%) and a retained encrusted stent in 1 (3.3%). Postoperatively obstruction correlated
with postoperative pain in 23 of the 30 patients (76.7%). Pain was present postoperatively in 30 of the 211
patients (70%) without evidence of ureteral obstruction postoperatively. However, silent obstruction developed
in 7 patients (23.3%) or 2.9% of the total cohort. All 7 patients underwent secondary ureteroscopy to alleviate
obstruction. A single patient ultimately received chronic hemodialysis for renal failure, 1 was lost to followup
and in 5 there was documented successful resolution of the cause of obstruction.

Conclusions: Our analysis suggests that silent obstruction remains a potentially significant complication
after stone management. Relying on postoperative pain to determine the necessity of postoperative imaging
places patients at risk for progressive renal failure due to unrecognized obstruction. Therefore, we recommend
that imaging of the collecting system should be performed by excretory urography, spiral computerized
tomography or ultrasound within 3 months after routine ureteroscopic stone treatment to avoid the potential
complications of unrecognized ureteral obstruction.

Editorial Comment
This article raises some disturbing issues for those of us who may have been lulled into security by the
usual high success and lower complication rates of modern ureteroscopy. Among 241 ureteroscopic patients
with complete follow-up, 30 were documented to have postoperative obstruction, usually due to residual calculi.
Of these 30, there was no pain in 7 (23%), representing 2.9% of the total patient population. Earlier studies had
suggested that in patients without postoperative pain, imaging to detect obstruction was not necessary. The
authors of this paper contend that although the incidence of silent obstruction (obstruction without postoperative
pain) is low, that the clinical significance of missing obstruction in these patients is considerable and that
therefore routine imaging of all patients following ureteroscopy with a modality that would detect potential obstruction (IVP, CT scan, renal scan, or ultrasonography) is indicated. Of the 7 patients with silent obstruction, 2 did not have obstruction pre-operatively. Moreover, stone location or size did not consistently suggest patients at increased risk for obstruction. Of note, however, the obstruction was due to calculi in 6 of 7 patients. The article did not provide data as to how many of these calculi were visible on plain radiography. I would like to think that most of these patients would have been detected to have residual calculi with plain radiography; such patients whom would be followed up with additional imaging that would have detected the obstruction. I would also like to think that very few patients without adverse risk factors (significant preoperative obstruction, postoperative pain, difficult or multiple stone procedures, residual calculi) would suffer silent obstruction. Nonetheless, the results of this study suggest that perhaps a more liberal application of postoperative imaging for obstruction should be applied to patients following ureteroscopy.

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Ureteroscopic treatment of lower pole calculi: comparison of lithotripsy in situ and after displacement

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Purpose: Ureteroscopic management is a viable option for lower pole calculi less than 2 cm. Recently a technique was described to displace the calculus into a more accessible calix using a nitinol basket or grasper before lithotripsy. We compared the efficacy and safety of this technique with in situ treatment of small and intermediate lower pole calculi.

Materials and Methods: We retrospectively reviewed the records of 95 ureteroscopy cases performed at our institution from January 1997 through August 2001 for renal calculi located only in the lower pole. Preoperative patient characteristics, stone size, operative details, complications and outcomes were compared for calculi treated in situ and those displaced before treatment.

Results: Adequate followup was available on 78 patients. Patients in the displacement group were statistically older, more often had a preoperative indwelling ureteral stent and had a mean operative time that was 16 minutes longer (p=0.04). Average stone diameter in the in situ and displacement groups was 8 and 10.3mm., respectively (p=0.04). In patients with radiographic followup greater than 1 month complete success was obtained for 77% of stones 1 cm. or less treated in situ versus 89% treated with displacement first (p=0.43). For calculi greater than 1 cm. complete success was obtained for 2 of the 7 (29%) treated in situ versus all 7 (100%) treated with displacement (p=0.005).

Conclusions: When treating lower pole calculi 1 to 2 cm. via ureteroscopy, a higher success rate can be obtained with displacement into a more accessible calyx before treatment.

Editorial Comment

Although retrospective and non-randomized, this study suggests a great utility for the displacement techniques in the management of lower pole renal calculi. The extremely flexible nitinol basket or grasper, which limits flexion of a flexible ureteroscope minimally, can often be placed into lower pole or eccentric calyces that are inaccessible to a ureteroscope through which has been placed a laser fiber or electrohydraulic
lithotripsy probe. The nitinol instruments, of which I prefer the basket, can be used to relocate the calculus into a more accessible calyx (usually an upper pole calyx). Once in this location, lithotripsy with a laser fiber or electrohydraulic lithotripsy probe can proceed much more easily and effectively. The results indicated a trend towards greater success for small calculi with the displacement compared to the in situ technique, and a significant difference in favor of displacement for stone 1 – 2 cm in diameter. With technically adequate fragmentation in most patients, the finding of a greater stone free rate in the displacement group also suggests that fragments may pass more easily from an upper pole location. Even lower pole stones that are accessible with a laser fiber or electrohydraulic lithotripsy probe, which could be treated in situ, may be more effectively treated when displaced to the upper pole. Although the mean operative time was 16 minutes longer in the displacement group, the mean stone diameter was somewhat larger in the displacement group and in a few cases displacement was performed only after technical failure of lithotripsy in situ. It was the general impression that displacement adds only a few minutes to the operative time, and that subsequent lithotripsy is performed more easily and rapidly than if the calculus had been left in situ. I recommend displacement of calculi to a more accessible calyx during ureteroscopic management of lower pole renal calculi.

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**PATOLOGY**

**Needle core length in sextant biopsy influences prostate cancer detection rate**  
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Objectives: Prostate cancer detection in biopsies increases with the number of sites and total tissue sampled. Its dependence on needle core fragment length is uncertain.

Methods: Two consecutive series of sextant needle biopsies were surveyed from two practices in 1998 to 2000: 251 patients from Pennsylvania (group P) and 1596 from Virginia (group V). The gross needle core lengths per sextant site were tabulated and the diagnoses classified as benign or nonbenign. Logistic regression analysis was used to correlate cancer with the total length (sum of six sites), with the length per single core, and the anatomic site of origin (apex, mid-gland and base).

Results: The mean total tissue length sampled was 108 ± 27mm (range 30 to 275) in group P and 81 ± 22mm (range 30 to 228) in group V. Considering single cores the mean was 12.8 ± 3.5mm tissue. Group V core lengths at the apex averaged 11.8mm, shorter (p=0.0001) than mid (13.3mm) or base (12.7mm). A predictive value of longer length for a nonbenign diagnosis was noted in four of six sextants (p=0.04), with trend strongest at the apex, for which detection was influenced by abnormal digital rectal examination (p=0.02) or ultrasound (p=0.04) findings.
Conclusions: Significant trends were noted for more detection of cancer and nonbenign findings in sextant prostate biopsies as longer single cores were sampled, particularly at the apex. Biopsy tissue length is at least as influential as the number of sites sampled and should be examined before submission for quality assurance.

Editorial Comment

This paper called my attention at the American Congress of Pathology held this year in Chicago. Sample is of utmost importance for the pathology report. The absence of carcinoma in a case that all fragments of the biopsy have less than 10mm of length certainly subevaluates the existence of a tumor. Many times this fact is neglected by both the pathologist and the performer of the biopsy. Considering that a needle prostatic biopsy may obtain fragments up to 20mm in length, the minimal accepted length would be fragments with 10mm. Its is very important that the performer of the biopsy be aware of the length of the fragments repeating immediately the biopsy from sites that the sample is insufficient. The pathologist must also be aware to this detail, informing the length of each of the fragments received for analysis, and commenting in the report whenever the sample is insufficient for an adequate estimation regarding existence of a neoplasia. This is critical when evaluating “insignificant” carcinoma according to the criteria proposed by Epstein in stage T1c (J Urol. 1998; 160:2407-11). When the tumor occupies more than 50% of the area of the fragment it is considered significant. Considering that it occupies 100% of the area of a fragment with less than 5mm length, obviously, this finding is not a criterion to exclude the tumor as “insignificant”.

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Prostate cancer involving the bladder neck: recurrence-free survival and implications for AJCC staging modifications

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Purpose: In the AJCC TNM staging system, bladder neck involvement by prostate cancer after radical retropubic prostatectomy is considered pT4 disease, suggesting a high risk for disease recurrence. However, recurrence risk with pathological invasion of the bladder neck (pT4) has not been definitely compared to recurrence risk of extraprostatic extension (pT3a) or seminal vesicle invasion (pT3b). Moreover, evidence to justify the higher (pT4) stage for bladder neck invasion in contemporary cancers is entirely lacking. We therefore compared recurrence risk in cases with bladder neck involvement to recurrence risk in cases with pT3a or pT3b disease.

Methods and Materials: The study cohort was composed of 1124 men with clinically localized prostate carcinoma treated with radical retropubic prostatectomy between 1994 and present. Prostate specific antigen (PSA)-recurrence was defined as 0.2ng/mL following surgery. Margins were evaluated for focal and extensive involvement. Bladder neck involvement, margin positivity, and all other pathology stage categories were assessed as covariates contributing to PSA-recurrence risk by Cox regression, and relative risk of these pT categories was tabulated.
Results: Bladder neck involvement was found in 61/1124 (5%) of cases; 46 and 15 of these had focal and extensive involvement of the bladder neck margin, respectively. Seminal vesicle invasion (pT3b) and extraprostatic extension (pT3a) were present in 76 (7%) and 278 (25%) cases, respectively. Cox regression analysis confirmed that pathology stage is a significant risk factor for PSA recurrence; however, the recurrence risk associated with bladder neck involvement (pT4) was less than that of seminal vesicle invasion (pT3b) and not substantially different from that of extraprostatic extension (pT3a).

Conclusions: The risk of recurrence conferred with bladder neck involvement (AJCC pT4) is not different that with extraprostatic extension (pT3a), or seminal vesicle invasion (pT3b). The AJCC staging system should be evidence-based; however, the current AJCC pathology staging system for bladder neck-involvement is contrary to available evidence; and reclassification of bladder neck involvement as part of the pT3 category, instead of pT4, should be considered.

Editorial Comment

Analyzing the category T of the TNM system of staging (proposed in 1997 or more recently in 2002), we almost overlook the fact that invasion of the bladder neck is considered stage pT4 and therefore, with worse prognosis than invasion of the seminal vesicle(s) (pT3b). This study arouses much interest when presented at the American Congress of Pathology this year in Chicago. A question raised refers to the representation of the bladder neck in the surgical specimen. According to the surgical technique used, including cases with total preservation, the bladder neck is variably represented in the specimen. All studies proposing changes in staging must be evaluated and confirmed by other authors. We had a great interest on this subject and compared recurrence and/or metastases following radical prostatectomy in patients with and without neoplasia in the bladder margin of the surgical specimen. The study was based in 141 patients with a follow-up ranging from 2 months to 62 months (median: 18 months). Recurrence was considered whenever the PSA level was ≥ 0.5ng/mL or 3 consecutive levels were increasing. The results showed no statistical difference related to recurrence comparing patients with (pT4) and without bladder neck involvement. On the other hand, the analysis of patients with seminal vesicle invasion (pT3b) showed a significantly higher recurrence of the disease.

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IMAGING

Extraprostatic spread of clinically localized prostate cancer: factors predictive of pT3 tumor and of positive endorectal MR imaging examination results

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Radiology 2002; 224:203-10

Purpose: To identify the factor(s) most predictive of pT3 tumor and those most predictive of a positive endorectal magnetic resonance (MR) imaging result in patients with clinically localized prostate cancer.
Materials and Methods: At multivariate analysis, five preoperative clinical parameters—prostate-specific antigen (PSA) level, digital rectal examination (DRE) result, Gleason score and number of involved sextants at transrectal US-guided biopsy, and endorectal MR imaging result—were used to predict pT3 tumor in 336 patients who underwent radical prostatectomy. On the basis of results of the first four examinations, multivariate analysis was performed also to determine predictors of a positive MR imaging study.

Results: Significant predictors of pT3 tumor were positive MR imaging result (P<2 x 10^{-8}), more than one sextant involved at biopsy (P<5 x 10^{-5}), and PSA level greater than 10 ng/mL (P<7 x 10^{-3}). Significant predictors of a positive MR imaging result were three or more sextants involved at biopsy (P<10^{-9}), positive DRE result (P<5 x 10^{-5}), and PSA level greater than 10 ng/mL (P<16 x 10^{-3}). In the subgroup of 175 patients who had at least three positive biopsy specimens, the sensitivity of MR imaging was 50% for detection of occult pT3 tumor and 69% for detection of extensive pT3 tumor. The overall specificity of MR imaging was 95%.

Conclusion: Endorectal MR imaging seems to be indicated in carefully selected patients - specifically, those with 3 or more positive biopsy specimens, a palpable tumor, and/or a PSA level greater than 10 ng/mL.

Editorial Comment

There is still much controversies among urologists, whether endorectal MR imaging should or should not be used for staging prostate cancer. Although the number of urologists that use this method has been growing, this group is still a minority. The main reason for that is because they believe that MR imaging is not sensitive or specific enough to predict extraprostatic disease. There are several reasons to explain this situation: lack of consensus among radiologists regarding what are the specific signs of extraprostatic disease, the use of different equipments and different techniques thus resulting in distinct degree of accuracy, and MR imaging readers with no particular training and/or interest in uroradiology. All these factors are responsible for the significant differences in accuracy showed by several reports in the literature during the last decade.

The authors presented a rare prospective study where a multivariate analysis of 5 pre-operative clinical parameters (PSA, DRE, Gleason score, and number of positive sextants biopsies) was performed in a large series of 336 patients who underwent radical prostatectomy. The positive aspect of this study is that MRI was used in the best conditions in order to optimize its results and consequently obtain the maximum specificity possible. These conditions include: a)- experienced uroradiologists, b)- exclusion of indirect signs of extraprostatic extension and sole use of direct signs of capsular disruption or seminal vesicle invasion, c)- use of combination of endorectal coil and anterior surface coil, and d)- knowledge of all clinical information available before reading the MR imaging examination (DRE result, PSA level and sites of positive transrectal ultrasound biopsies). By using these criteria, the authors achieved a 95% specificity for MR imaging and as one should expect this high specificity was only accomplished at a cost of an undesirable relatively low sensitivity.

After the study performed by D’Amico et al. (1), showing the limitations of using the Partin’s probability plots and nomograms (2) the criteria for utilization of MR imaging for staging clinically localized prostate cancer has been changed. According the study by Partin et al, the risk of extraprostatic extension in these group of patients can be determined by the combination of DRE result, PSA level, and Gleason score. Results of the D’Amico study, demonstrated that in the group of patients with intermediate risk of pT3 tumor, as defined on the basis of a PSA level of 11-20ng/ml and Gleason score 5 -7, the addition of MRI increased the efficiency of extraprostatic tumor detection (overall accuracy 78-80%), relative to the elements indicated by Partin. Since the percentage of positive biopsy specimens(calculated on the number of sextants invaded by tumor), indirectly reflects tumor volume(3) and its propensity for extraprostatic extension, the authors applied this variable to patients with intermediate risk of extraprostatic disease pT3 tumors. Multivariate analysis results showed that the presence of at least 3 positive specimens was the most powerful predictor of a positive MR imaging result and also a useful tool to identify patients with a risk of extensive extraprostatic disease.
This manuscript confirmed previous studies by showing that endorectal MR imaging is a reliable method of predicting occult extraprostatic disease but, this method should not be used as a routine procedure in all patients with clinically localized prostate cancer. On contrary, it should be reserved for a selected group of patients.

References

Blunt renal trauma: minimally invasive management with microcatheter embolization - experience in nine patients
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Radiology 2002; 223:723-30

Purpose: To evaluate superselective embolization therapy for the management of arterial damage in patients with severe renal trauma.

Materials and Methods: Nine consecutive patients with renovascular injuries after blunt trauma underwent superselective embolization. Six patients had pseudoaneurysms or traumatic arteriovenous fistulas. Three patients had frank, uncontained extravasations (2 shattered kidneys, 1 complete pedicle avulsion) and were treated immediately after admission. Two patients were hemodynamically unstable. All patients underwent embolization with 3F coaxial microcatheters and polyvinyl alcohol particles (n=2) or 0.018-inch platinum microcoils (n=7). Procedural and medical success and complications (postembolization syndrome, abscess, permanent serum creatinine elevation, hypertension) were retrospectively assessed from the patients’ records. Mean clinical follow-up was 11.9 months (range, 1–50 months).

Results: In all cases, bleeding was effectively controlled with superselective embolization in a single session. There was no procedure-related loss of renal tissue in 8 cases; in 1 patient, a lower pole remnant of 20% of viable ipsilateral parenchyma was lost due to the procedure. In 1 patient, a coil migrated into a lumbar artery without causing clinical consequences. None of the patients developed abscess, hypertension, or procedure-related impairment of renal function.

Conclusion: Superselective embolization may be used for effective, minimally invasive control of active renovascular bleeding.
The choice of treatment (surgical or conservative) for major renal trauma still remains controversial, but in patients with hemodynamic stability, conservative treatment is increasingly accepted as the preferred approach to most renal injuries including grades III and IV. Recent studies have shown a higher nephrectomy rate in the case of primary surgical intervention compared to conservative management (1). Another important point to consider is that the conservative treatment is very well accepted because there is no increase of the immediate or long-term morbidity with this approach. When the patient present with injuries to the vascular pedicle, avulsion of the renal pelvis or life-threatening hemodynamic instability (Grade-V renal trauma), surgical treatment is usually indicated. Penetrating and iatrogenic renal vascular lesion (the latter usually due to percutaneous renal biopsy, percutaneous nephrolithotripsy or development of postoperative AV-fistula) has been treated by percutaneous superselective embolization with Gelfoam particles or micro-coils with prompt effect and minor adverse effect. The authors call the attention for the utility of this technique also for patients with noniatrogenic and blunt renal trauma, particularly in children. They concluded that superselective embolization should be considered a therapeutic option in patients with noniatrogenic and blunt renal trauma, in those institutions where well-trained interventional radiologist and technicians can be quickly available on a 24-hour basis.

Reference

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Sonic hedgehog signaling from the urethral epithelium controls external genital development
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External genital development begins with formation of paired genital swellings, which develop into the genital tubercle. Proximodistal outgrowth and axial patterning of the genital tubercle are coordinated to give rise to the penis or clitoris. The genital tubercle consists of lateral plate mesoderm, surface ectoderm, and endodermal urethral epithelium derived from the urogenital sinus. We have investigated the molecular control of external genital development in the mouse embryo. Previous work has shown that the genital tubercle has polarizing activity, but the precise location of this activity within the tubercle is unknown. We reasoned that if the tubercle itself is patterned by a specialized signaling region, then polarizing activity may be restricted to a subset of cells. Transplantation of urethral epithelium, but not genital mesenchyme, to chick limbs results in mirror-image duplication of the digits. Moreover, when grafted to chick limbs, the urethral plate orchestrates morphogenetic movements normally associated with external genital development. Signaling activity is therefore restricted to urethral plate cells. Before and during normal genital tubercle outgrowth, urethral plate epithelium expresses Sonic hedgehog (Shh). In mice with a targeted deletion of Shh, external genitalia are absent.
Genital swellings are initiated, but outgrowth is not maintained. In the absence of Shh signaling, Fgf8, Bmp2, Bmp4, Fgf10, and Wnt5a are downregulated, and apoptosis is enhanced in the genitalia. These results identify the urethral epithelium as a signaling center of the genital tubercle, and demonstrate that Shh from the urethral epithelium is required for outgrowth, patterning, and cell survival in the developing external genitalia.

Editorial Comment

The literature concerning external genital development is controversial, owing largely to inconsistent descriptions of genital development. Development of penile urethra has been a particular area of controversy, with such fundamental issues as the embryonic origin of the distal urethral plate and morphogenesis of the tubular urethra remaining unclear. Despite external genital defects are among the most common congenital anomalies, the molecular mechanisms controlling early stages of external genitalia development is not well understood. Recent findings showed that the spongy urethra presents regional differences regarding to extracellular matrix molecules (1), and this could have a key role during urethral development because a normal interaction between epithelial and mesenchymal tissues in the tubercle is required for normal genital development.

The authors have provided the most accurate and comprehensive study of the embryology of the mouse external genitalia. The authors did not detect, at any stage studied, an ectodermal ingrowth from the apex of the mouse genital tubercle. This contrasts with previous reports that the distal urethra forms by apical ectodermal invagination.

However, the most impressing finding in the present paper is the superb description of the key role of Shh genes in the external genital development. Furthermore, these genes regulate the expression of several cytokines (i.e., FGF family). Another strong point in the present paper is the clear evidence showed by the authors that the urethral epithelium, but not genital mesenchyme, has polarizing activity. The authors’ results clearly identified the urethral epithelium as a signaling region in the genital tubercle, implicated Shh genes as the key urethral signal, and showed that Shh is essential for external development.

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HUMAN REPRODUCTION

Predictive value of testicular histology in secretory azoospermic subgroups and clinical outcome after microinjection of fresh and frozen-thawed sperm and spermatids

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Hum Reprod. 2002; 17:1800-10
Background: A retrospective study was carried out on 159 treatment cycles in 148 secretory azoospermic patients to determine whether histopathological secretory azoospermic subgroups were predictive for gamete retrieval, and to evaluate outcome of microinjection using fresh or frozen-thawed testicular sperm and spermatids.

Methods: Sperm and spermatids were recovered by open testicular biopsy and microinjected into oocytes. Fertilization and pregnancy rates were assessed.

Results: In hypoplasia, 97.7% of the 44 patients had late spermatids/sperm recovered. In maturation-arrest (MA; 47 patients), 31.9% had complete MA, and 68.1% incomplete MA due to a focus of early (36.2%) or late (31.9%) spermiogenesis. Gamete retrieval was achieved in 53.3, 41.2 and 93.3% of the cases respectively. In Sertoli cell-only syndrome (SCOS; 57 patients), 61.4% were complete SCOS, whereas incomplete SCOS cases showed one focus of MA (5.3%), or of early (29.8%) and late (3.5%) spermiogenesis. Only 29.8% of the patients had a successful gamete retrieval, 2.9% in complete and 77.3% in incomplete SCOS cases. In total, there were 87 ICSI, 39 elongated spermatid injection (ELSI) and 33 round spermatid injection (ROSI) treatment cycles, with mean values of fertilization rate of 71.4, 53.6 and 17%, and clinical pregnancy rates of 31.7, 26.3 and 0% respectively.

Conclusions: Histopathological subgroups were positively correlated with successful gamete retrieval. No major outcome differences were observed between testicular sperm and elongated spermatids, either fresh or frozen-thawed. However, injection of intact round-spermatids showed very low rates of fertilization and no pregnancies.

Editorial Comment

The chance of sperm retrieval is very different for men with obstructive and non-obstructive (secretory) azoospermia. Men with obstructive azoospermia have normal sperm production while those with non-obstructive azoospermia have testicular failure. However, direct evaluation of testis biopsy specimens demonstrates sperm in some men with non-obstructive azoospermia (NOA), which can be retrieved and used for intracytoplasmic sperm injection (ICSI). It means that NOA men may have marginal sperm production within the testis.

The present study shows that the findings of a diagnostic biopsy are helpful in evaluating the success of sperm retrieval. In addition, the chance of finding sperm is more likely if at least one area of spermatogenetic activity is identified, in spite of the testicular histology pattern. The authors also report their excellent results with ICSI using testicular fresh/frozen sperm, which is similar to fresh/frozen ejaculated sperm. Cryopreservation of testicular sperm is, therefore, an excellent option for NOA men, since these men have very limited sperm production, and repeated sperm extraction is not always successful.

In the last years, several points have become evident regarding spermatid injection. First, the technique of spermatid injection is very inefficient for producing normal fertilization. Second, the efficiency of embryonic implantation is extremely poor. Third, the nomenclature used by different investigators is highly variable; for one group spermatid is often what another call a testicular sperm. Four, it is widely believed that the identification of spermatids using standard optics or phase contrast microscopy is highly unreliable. Many investigators now believe that round spermatids, if present in a testis in the absence of spermatozoa, are usually undergoing apoptosis and are not capable of normal fertilization after injection into the oocyte. Therefore, microinjection of round spermatid should not be used, although further research is needed.

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Sperm aneuploidy rates in younger and older men
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_Hum Reprod_. 2002; 17:1826-32

Background: In order to assess the possible risk of chromosomal abnormalities in offspring from older fathers, we investigated the effects of age on the frequency of chromosomal aneuploidy rates of human sperm.

Methods and Results: Semen samples were collected from 15 men aged <30 years (24.8 +/- 2.4 years) and from eight men aged >60 years (65.3 +/- 3.9 years) from the general population. No significant differences in ejaculate volume, sperm concentration and sperm morphology were found, whereas sperm motility was significantly lower in older men (P=0.002). For the hormone values, only FSH was significantly elevated in the older men (P=0.004). Multicolor fluorescence in-situ hybridization was used to determine the aneuploidy frequencies of two autosomes (9 and 18); and of both sex chromosomes using directly labeled satellite DNA probes on decondensed sperm nuclei. A minimum of 8000 sperm per donor and >330 000 sperm in total were evaluated. The disomy rates per analyzed chromosomes were 0.1-2.3% in younger men and 0.1-1.8% in older men. The aneuploidy rate determined for both sex chromosomes and for the autosomes 9 and 18 were not significantly different between the age groups.

Conclusions: The results suggest that men of advanced age still wanting to become fathers do not have a significantly higher risk of procreating offspring with chromosomal abnormalities compared with younger men.

Editorial Comment

Numeric chromosomal anomalies (aneuploidy) result from nondisjunction during a meiotic division. It is well known that these anomalies increase with maternal age, which may be explained by oocyte aging. For example, the risk for Down syndrome for women in their 30s is 1/952, increasing to 1/378 at 35 years old, and 1/106 at their 40s (1). On the other hand, the association between paternal age and chromosomal abnormalities is not well established. Although others corroborate the findings of the present study, few chromosomes were analyzed, and very few patients were studied.

Not only aneuploidy may be sperm-derived but also structural anomalies and single gene defects (mutations). Contrary to the findings on paternal age and aneuploidy, a positive relationship exists between paternal age and the frequency of structural anomalies in sperm (2). However, there is no evidence that this age-related association leads to an increased frequency of offspring with structural anomalies.

Although the incidence of chromosomal disorders in children does not appear to exhibit an paternal age-related increase, there is no question of the association between single gene defects and advanced paternal age. Single gene defects are the result of errors in the DNA replication process. They can lead to an increase likelihood of autosomal dominant diseases, such as hemophilia A, Marfan syndrome, polycystic kidney disease, neurofibromatosis, achondroplasia, etc. It is estimated that the risk for a father over 40 years old to have a child with an autosomal dominant mutation equals the risk of Down syndrome for a child whose mother is 35-40 years old (3). Other anatomic birth defects, including ventricular and atrial septal defects, and situs inversus, may be also related to the increase in paternal age (4).

References
Urological Survey


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RECONSTRUCTIVE UROLOGY

Microsurgical replantation of sexual organs in three patients
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Scand J Urol Nephrol. 2002; 36:14-7

Objective: The present study deals with microsurgical replantation technique.
Material and Methods: The technique was applied in 3 patients whose sexual organs had been accidentally cut off.
Results: Necrosis of the sutured organs occurred in 2 cases. In 1 case, however, healing with proper miction and sexual function was achieved. Prolonged period (over 12h) from the accident to operation as well as the extensive injury of tissues with the vascular system crush were considered to be the main reason for failure.
Conclusions: Microsurgical reconstruction of penis and testes with the use of vessel grafts prolonged the hypoxia, which led to necrosis. Disturbances in vein blood outflow from the sutured organs contributed to this process as well. The third case resulted in success mostly due to quick intervention (5h from injury) as well as to proper microsurgical reconstruction of vessels, nerves, and urethra. In addition, suprapubic urine diversion was successfully applied and the urethra healed on the perforated catheter. Routine antibiotics as well as antithrombotic prophylactics were administered in all of the 3 cases.

Editorial Comment
The authors presented 3 cases of genital traumatic amputation (1 case of penis, scrotum and testis, and 2 cases of penile amputation). Only 1 case was successfully replanted. The authors concluded that quick intervention and proper storage of the amputated organs are of utmost importance for successful genital organs replantation. Since testes are more sensitive to anoxia and one gonad is sufficient for proper endocrine and reproductive function, the authors proposed to start the operation with one testis implantation followed by penis replantation, in cases of complete genitals amputation.

Penile amputation is an uncommon injury and 87% of the patients had psychiatric problems. Since 1970 in Thailand, there had been an epidemic of penile amputation as philandering punishment by humiliated wives. Dr. Kochakarn from Mahidol University, Bangkok, Thailand, reported recently an impressive personal series of 25 penile reimplantations (1,2). He reported that the amputated part can be maintained up to 16 hours or may be up to 24 hours at hypothermia. In short, his reimplantation technique is: urethral mucosa of both ends approximated by interrupted 6-0 chromic catgut and the adventitia and corpus spongiosum by 4-0 or 5-0
polyglycolic acid; under 8-16 X microscopic magnification, perform meticulous dissection to find the healthy dorsal arteries is vital for successful anastomosis by 11-0 monofilament nylon both dorsal arteries (1 mm in diameter) and dorsal vein (3 mm in diameter); perineurorhaphy of the dorsal nerve with 9-0 or 10-0 nylon suture; and finally, dartos fascia is approximated by interrupted 5-0 or 6-0 polyglycolic acid. A percutaneous suprapubic cystostomy catheter is inserted. The adequate cosmetic restoration of the penis is satisfying and erection returns in nearly all cases, making intercourse possible. Although the penile sensation showed some decreasing, the recovering is remarkable. The most common complication is skin loss.

References

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Vaginal reconstruction for ambiguous genitalia and congenital absence of the vagina: a 27-year experience
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Background/Purpose: Gender assignment to a neonate with ambiguous genitalia is crucial. Patients with an absent vagina require the construction of an artificial vagina. In an effort to improve care, the authors have categorized their experience with this group of children.
Methods: Since 1974, we cared for 114 patients with anomalies of the genitalia. There were 53 genotypic girls with congenital adrenal hyperplasia (CAH), 16 genotypic boys with testicular feminization syndrome (TFS), 13 with mixed gonadal dysgenesis (MGD), 9 with Mayer-Rokitansky syndrome, and 4 true hermaphrodites. The remaining 19 had other genital abnormalities.
Results: After 1980, patients with CAH underwent clitoral recession and vaginoplasty. All patients with TFS were raised as girls and underwent orchidectomy. Eleven of the MGD patients were given a female sex assignment and underwent gonadectomy. Twenty-eight patients underwent intestinal vaginoplasty including 8 of the TFS patients, 9 with Mayer-Rokitansky syndrome, 8 patients with cloacal anomalies, 2 patients for rhabdomyosarcoma, and 1 of the MGD patients.
Conclusions: 1) This review emphasizes the range of diagnoses the surgeon must be prepared to address in patients with ambiguous genitalia. 2) Colovaginoplasty is an excellent procedure for replacement of a completely absent vagina. 3) Continued evaluation of this group will delineate appropriate timing and choice of procedure.

Editorial Comment
A correct diagnosis and gender assignment is imperative to be performed in those patients suffering from ambiguous genitalia. Gender assignment is based on the possibility to reconstruct a normal individual
with normal sexual function. There are several developmental anomalies on which vaginoplasty is needed, and numerous techniques to perform it are described. However, no one surgical procedure can be applied to reconstruct all cases of ambiguous genitalia. The wide anatomical variability imposes an individualized approach in these patients.

The authors showed an expressive series of patients suffering of ambiguous genitalia. They have performed several procedures to correct several developmental anomalies, which have developed with ambiguous genitalia. While most patients with a diagnosis of congenital adrenal hyperplasia and clitoral hypertrophy underwent a clitoral resection and vaginoplasty before the age of 6 months, patients with testicular feminization syndrome underwent reconstruction much later, 60% after the age of 15. It is a key point to perform the surgical procedure in the appropriate moment and thus, avoiding undesirable psychological effects caused by ambiguous genitalia. Furthermore, the printing issue has an important role in the gender reassignment, no matter whether genotype is male or female.

The authors’ results of long-term vaginoplasty with colon are very interesting. Eighteen of 26 women are sexually active and have none complications and none of their patients have experienced excessive mucus production from the neovagina.

Perhaps, the most important message from this article is that the surgeon needs to be aware of the great variety of diagnoses and surgical options to correct ambiguous genitalia.

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Multi-institutional experience with buccal mucosa onlay urethroplasty for bulbar urethral reconstruction
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Purpose: Buccal mucosa has been advocated as an ideal graft material for urethral reconstruction. We report our multicenter experience with buccal mucosa ventral onlay urethroplasty for complex bulbar urethral reconstruction in adults.

Materials and Methods: A retrospective analysis of patients who had undergone buccal onlay urethroplasty at 4 military medical treatment facilities participating in the Uniformed Services Urology Research Group was performed. The database generated included demographic data, genitourinary history, preoperative symptoms (American Urological Association symptom score), preoperative urinary flow rate, stricture length and operative statistics. Postoperative followup data included symptom score, flow rate, retrograde urethrogram results, and complications.

Results: A total of 53 patients (average age 32 years, range 17 to 64) underwent buccal mucosa graft urethroplasty between January, 1996 and March, 1998 for refractory strictures. Sixteen patients had undergone an average of 2.2 prior endoscopic procedures (range 1 to 7). Average stricture length was 3.6 plus or minus
standard deviation 1.8 cm. (range 2 to 7.5) as measured on preoperative retrograde urethrogram. Followup averaged 25 months (range 11 to 40 months). Average symptom scores decreased from 21.2 (range 14 to 33) preoperatively to 5.4 (range 3 to 8) postoperatively (p<0.001). Average peak urinary flow rates increased from 7.9 preoperatively to 30.1 ml. per second postoperatively (p<0.001). Postoperative retrograde urethograms were available for 34 patients and were normal in 24. The overall complication rate was 5.4%. Three patients required endoscopic incisions. One patient has a recurrent narrowing and treatment is considered a failure. There were 4 sacculations (7.5%) and 6 narrowings, 3 of which required further treatment. Of the patients 50 required no additional procedures (94.3%).

Conclusions: Buccal mucosa grafts used as a ventral onlay for bulbar urethral reconstruction yield reproducibly excellent results with minimal morbidity and low complication rates. Longer followup will be required to confirm the durability of our results.

Editorial Comment

In this multi-institutional study the results of 53 patients who underwent buccal mucosa craft urethroplasty in complicated stricture disease were studied. The minimum follow-up in these patients was close to 1 year. The results were respectable. Eleven percent of the patients had some form of recurrent stricture, but only half of them (6%) needed further treatment leading to a success rate of 94%. The fact that there were several surgeons and centers involved, that the means success rate is probably not due to the unpublished expertise of a single surgeon but rather due to other factors common to all centers involved, such as ventral onlay of the buccal mucosa, meticulous harvesting and preparation, careful suturing technique and maybe even the short hospital stay of the patients. The excellent results of this study confirm the biological properties of the oral cavity epithelium as a viable option for urethral reconstruction which will be with us at least in the near future.

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Critical evaluation of the problem of chronic urinary retention after orthotopic bladder substitution in women
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Purpose: We studied the possible causes of chronic retention after radical cystectomy and orthotopic bladder substitution in women.

Materials and Methods: Between January 1995 and January 2001, 136 women with a mean age plus or minus standard deviation of 52 ± 8 years underwent standard radical cystectomy and orthotopic substitution for organ confined bladder cancer. Videourodynamics, pelvic floor electromyography, pelvic floor magnetic resonance imaging and pan-endoscopy were done. In the last 37 cases some technical modifications were adopted to circumvent the development of chronic urinary retention.
Results: One woman died postoperatively of massive pulmonary embolism. Of the 100 patients evaluable at a mean followup of 36 months 95 were continent in the daytime, 86 were continent at night, 2 were completely incontinent and 16 were in chronic retention. Videourodynamic showed that retention was mechanical in nature due to the pouch falling back in the wide pelvic cavity, resulting in acute angulation of the posterior pouch-urethral junction. In addition, herniation of the pouch wall through the prolapsed vaginal stump was observed in most cases. Pelvic floor electromyography demonstrated complete pelvic floor silence during voiding. No abnormality of the pelvic floor or rhabdosphincter was noted on magnetic resonance imaging. Videourodynamics showed that retention was mechanical in nature due to the pouch falling back in the wide pelvic cavity, resulting in acute angulation of the posterior pouch-urethral junction. In addition, herniation of the pouch wall through the prolapsed vaginal stump was observed in most cases. Pelvic floor electromyography demonstrated complete pelvic floor silence during voiding.

Editorial Comment

Orthotopic bladder substitution in women is now an accepted form of urinary diversion in many centers worldwide. Favorable results in several hundred women published in the recent literature give evidence not only of the feasibility but also of oncological safety and good functional outcome of urethra-sparing cystectomy with subsequent anastomosis of a low pressure intestinal reservoir.

One of the few drawbacks of orthotopic neobladders in women -contrary to initial speculations -is not an increased rate of urinary incontinence but urinary retention. The authors which have a large experience with this type of surgery tried to find an answer to this problem by altering their surgical technique over the years. They evaluated one hundred patients with a mean follow up of 36 months. 95% were continent in the daytime, 86% were continent at night and 16% had chronic retention. They changed their technique by trying to improve positioning and suspension of the neobladder. This was achieved by anchoring the vaginal stump with the help of the preserved round ligaments, cushioning of the neobladder floor with a pedicled flap, bringing down the remnant peritoneum over the anterior rectal wall to the vaginal stump, and suspending the pouch near its dome to the back of the rectus muscle. Thus the incidence of chronic retention decreased from 18.7% (14 of 75 cases) before to 8% (2 of 25) after modifications. Furthermore, after vaginal wall descent was mechanically corrected by a pressary there was significant improvement in evacuation.

Conclusions: Strong evidence was provided that chronic urinary retention after orthotopic substitution is due to anatomical rather than to functional or neurogenic reasons. Modifications to increase back support of the pouch with ventral suspension near its dome and support the vaginal stump are recommended to avoid this complication.

Editorial Comment

Orthotopic bladder substitution in women is now an accepted form of urinary diversion in many centers worldwide. Favorable results in several hundred women published in the recent literature give evidence not only of the feasibility but also of oncological safety and good functional outcome of urethra-sparing cystectomy with subsequent anastomosis of a low pressure intestinal reservoir.

One of the few drawbacks of orthotopic neobladders in women -contrary to initial speculations -is not an increased rate of urinary incontinence but urinary retention. The authors which have a large experience with this type of surgery tried to find an answer to this problem by altering their surgical technique over the years. They evaluated one hundred patients with a mean follow up of 36 months. 95% were continent in the daytime, 86% were continent at night and 16% had chronic retention. They changed their technique by trying to improve positioning and suspension of the neobladder. This was achieved by anchoring the vaginal stump with the help of the preserved round ligaments, cushioning of the neobladder floor with a pedicled flap, bringing down the remnant peritoneum over the anterior rectal wall to the vaginal stump, and suspending the pouch near its dome to the back of the rectus muscle. Thus the incidence of chronic retention decreased from 18.7% to 8% in their last 25 cases.

This is truly an improvement and the modifications specified in the paper should be taken up by all surgeons. However, an 8% retention rate is still higher than in most series for male patients therefore it does not exclude functional and neurological reasons. It is difficult to believe that the angulation between the remnant urethra and the intestinal pouch should be the only reason. As outlined in the previous literature (which is well quoted in this paper) 3 major factors may be responsible for the higher incidence of urinary tension in females: 1) an undefined level of urethral dissection in females (due to the absence of the prostate), 2) partial autonomic denervation of the urethral smooth musculature, which plays a larger role in women due to its presence almost in the entire length of the urethra, and 3) mechanical obstruction of the neobladder outlet which includes mucosal intestinal folds, an acute urethro-intestinal angle and hypermobility of the urethra.
This paper shows valuable modifications in the technique of orthotopic bladder substitution in women, but it does not completely solve the problem by just trying to see only mechanical reasons for it.

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FEMALE UROLOGY

Early results of pubovaginal sling lysis by midline sling incision  
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Urology. 2002; 59: 47-51

Objectives. To describe a simplified technique and results of pubovaginal sling lysis by incision of the sling in the midline by way of a transvaginal approach.

Methods. We reviewed the charts of 19 women who underwent pubovaginal sling lysis for obstruction. Patients presenting with retention, incomplete emptying or storage, or voiding symptoms suggesting obstruction after pubovaginal sling placement were evaluated with videourodynamic studies and cystourethroscopy. The diagnosis of obstruction was made on the basis of a combination of clinical, urodynamic, and endoscopic findings. All patients underwent a midline incision of the sling by way of a transvaginal approach without formal urethropexy.

Results. The mean patient age was 57 years. Fifteen women (79%) had an autologous rectus fascial sling, 3 (16%) an allographic fascia lata sling, and 1 (5%) a polypropylene sling. Twelve women (63%) presented with urinary retention and required catheterization to empty. The other 7 women presented with obstructive and/or irritative symptoms without the need to catheterize. The mean time to sling lysis was 10.6 months from the initial surgery. The mean follow-up was 12 months (range 1 to 55). Overall, sling lysis was successful in 84% of the women. Stress incontinence recurred in 17%. No significant perioperative complications occurred.

Conclusions. Pubovaginal sling lysis without formal urethropexy appears to be a safe and effective method of relieving obstruction. The success and recurrent stress incontinence rates are comparable to those with formal urethropexy.

Editorial Comment

The success of urethropexy, be it formal release of adhesions with placement of an interposition flap or simple sling incision, is judged by the resolution of the symptoms attributed to the iatrogenic obstruction with the continuation or achievement of urinary continence. The importance of this paper is in that it illuminates the possibility of addressing iatrogenic outlet obstruction in minimally invasive fashion with a potentially diminished period of convalescence.

Most surgeons have traditionally initially opted for vaginal approaches to urethropexy reserving retropubic urethropexy for nonfavorable vaginal anatomy and presumed marked retropubic scarring (1).
method mirrors other approaches of transvaginal urethrolysis with the usual focus on identification of an obstructing suture or sling with division of same (2-5). This approach does not depend on access to the retropubic space for reduction of retropubic fibrosis and scarification and thus optimizes the potential for postoperative urinary continence (2,6). Indeed, the postoperative urinary continence rates from simple sling incision (83%) mirror those rates found with other reported urethrolysis series (1-6).

Another noteworthy point of this report is the length of time between the placement of the obstructing suburethral sling and the time of simple sling incision (mean=10.6 months). Intuitive reasoning would have wagered that by 3 months, fibrosis would be set and a suburethral sling incision would not have yielded the rate of success that was achieved (84%). Perhaps, this paper will allow one to have a deeper appreciation of the subtle difference between the fibrosis of support and that of obstruction (7,8).

In addition, another value of consideration of this approach is that it does not require the surgeon to contemplate a synchronous resuspension procedure. This differs from a previous report that noted the placement of an interposition graft at the time of sling release (9).

In summary, this operative approach is very appealing because simple things are easy to do and complex things are not. Though in the past some have argued that to all difficult problems there is a simple solution which usually does not work, this report will embolden all of us to simply incise the sling if we feel it is obstructive and not worry if it greater than one or two months postoperatively.

References
Early hospital discharge for intravesical ureteroneocystostomy
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J Urol. 2002; 167:2556-9

Purpose: Inpatient stays of 3 to 5 days are common in the surgical management of vesicoureteral reflux and often include the use of bladder catheters, ureteral stents and perivesical drains. We reviewed our recent experience, in which patients undergoing routine ureteroneocystostomy were often discharged home on postoperative day 1 to determine the safety and efficacy of our management.

Materials and Methods: Between July 1998 and March 2001 patients who underwent intravesical ureteroneocystostomy at 2 major tertiary care institutions were identified. Patients who also underwent simultaneous additional operative procedures, bilateral ureteral duplication or ureteral tapering were excluded from study. Data recorded included patient demographics, the procedure, operative and postoperative pain, nausea and bladder spasm management, hospital stay, post-hospital discharge problems and operative success.

Results: Of the 113 patients with complete data available for analysis 101 received ketorolac postoperatively, including 75 females and 26 males with a mean age of 5.01 years (range 6 weeks to 16 years). There were 67 bilateral and 34 unilateral reimplantations. No ureteral stents or perivesical drains were placed. A perioperative urethral Foley catheter was removed on postoperative day 1 in all except 3 cases. Caudal analgesia with 0.25% bupivacaine before or after the operation was given in 91% of cases as a single injection. Epidural catheters were not used. In the ketorolac group average hospitalization was 29.5 hours (range 14 to 72). Of the 101 patients 58% were discharged home within 24 hours (average 21.3) and a further 11% were discharged home within 36 hours (average 27.4). All except 4 patients (4%) were discharged home within 48 hours of surgery. In the 12 patients who did not receive ketorolac average hospital stay was 43.8 hours (p<0.001). Gender did not affect the duration of hospitalization. Patients younger than 1 or older than 5 years old had a longer hospital stay than children between 1 and 5 years old (average 32.8 versus 25.5 hours). All patients received anticholinergics. The 9 complications (8%) involved urinary tract infection in 3 cases, and persistent nausea and vomiting, medication reaction and reoperation for clot evacuation in 1 each. Postoperatively 3 patients had persistent refluxing ureters.

Conclusions: Routine surgical repair of vesicoureteral reflux can be successful with early bladder catheter removal and without stents or drains, necessitating only overnight hospitalization in the majority of patients. Ketorolac can be given safely in children with minimal risk and when combined with caudal analgesia it facilitates early discharge home.

Editorial Comment
We are witnessing an explosion of new inventions in the medical field, that include new surgical techniques, new pharmaceuticals in addition to many other advances. These improvements in technology should result not only in better patient outcomes, but in reduced patient and family morbidity as well. Nonetheless, often there are precious little data documenting the efficacy of these advances. This is particularly concerning when the advances may also jeopardize the health of the patients.

The field of Pediatric Urology has been a leader in reducing patient morbidity. Many procedures are already performed as an outpatient, e.g. hypospadias repair, and orchiopexy. In contrast, ureteroneocystostomy is most often performed via a transvesical approach, resulting in a longer hospitalization and recovery period. The main factors that limit early recovery and discharge from hospital are the presence of a Foley catheter and/
or a perivesical drain, bladder spasms and pain. This article reports a shortened hospital stay (over 95% of patients were discharged in 48 hours) after ureteroneocystostomy, utilizing newer pain management techniques. In addition, there were few re-admissions to the hospital and no more than standard complications.

There are several weaknesses of the study. Although it is intuitive that better pain management is beneficial, the authors present little objective data on the success of their pain management (i.e. there were no pain scales used). Furthermore, patients were not randomized to one protocol vs. another. Hence any cause-effect relationship between early discharge and the pain management is not clear. The cause might just as well have been better surgical techniques, improved postoperative nursing or more successful education and discharge planning (or all of the above). Furthermore, although early discharge may be cost-effective and safe, there are no data presented on patient satisfaction. Were patients/families happy with their care or did they feel rushed out of the hospital with significant negative consequences for the family left to deal with the patient at home? (1) Nonetheless, the authors’ experience is similar to others, indicating that early discharge truly is feasible and safe after ureteroneocystostomy. Further studies of the outcome of the use of newer technologies should be encouraged.

Reference

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Increased urinary nitrite excretion in primary enuresis: effects of indomethacin treatment on urinary and serum osmolality and electrolytes, urinary volumes and nitrite excretion
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Objectives: To assess urinary nitrite excretion, a stable end product of nitric oxide (NO), in patients with enuresis and in normal controls, and to evaluate the effects of indomethacin (a potent prostaglandin synthesis inhibitor) on urinary nitrite excretion, other urinary variables and bladder capacity.

Patients and Methods: The study comprised 10 patients with primary enuresis and 10 normal comparable controls (age range 6-14 years). Nitrite was assayed in “spot” morning urine samples in both the enuretics and normal controls. Enuretics were then given 50mg indomethacin suppositories each night; urine volume, urinary osmolality and electrolytes, serum osmolality and electrolytes and urinary nitrite were assayed before indomethacin treatment and after 15 days of treatment.

Results: The mean (sd) urinary nitrite excretion was 24.4 (19.6) micromol/L in normal children and 275.9 (111.2) micromol/L in enuretics (p<0.05). With indomethacin, the urinary nitrite concentration was significantly decreased to 141 (45.1) micromol/L (p<0.05) and associated with a significant reduction in bed-wetting episodes and voiding frequency. The functional bladder capacity was <70% of the predicted value for age in 6 of the patients; they had significant improvements on indomethacin, to values similar to those in
patients with a nearly normal functional bladder capacity. Indomethacin decreased the 24-h urinary volume by 41%, the night volume by 40%, clearance of free water by 46% and increased the day:night urinary volume ratio by 55%. The absolute amounts of urinary calcium, magnesium, phosphorus, urea, creatinine, and glucose were lower on indomethacin, although not statistically significantly so. Indomethacin decreased the 24-h urinary and “spot” morning osmolality and osmotic clearance. There were no significant changes in serum osmolality and electrolyte concentrations. Indomethacin also decreased the absolute amount of urinary sodium, chloride and potassium, fractional sodium and potassium excretion, and filtered sodium. Creatinine clearance was decreased by 20% (p>0.05) and normal 24-h urinary protein was significantly lower, by 47%, after indomethacin treatment (p<0.05).

Conclusion: Urinary nitrite excretion increased significantly in patients with primary nocturnal enuresis; indomethacin markedly reduced bed-wetting episodes and decreased the frequency of voiding in enuretics with small or normal functional bladder capacity, which was associated with a significant decrease in urinary nitrite excretion. Indomethacin reduced bed-wetting by decreasing the urine volume, clearance of free water and urinary electrolytes, and through possible effects on bladder and urethral contraction, by inhibiting NO and prostaglandin synthesis. NO and prostaglandins might be important in the pathogenesis of primary enuresis.

Editorial Comment
Primary enuresis is a common problem of childhood and adolescence with a relatively benign character. However, the psychosocial consequences of the disease are often detrimental. Although many etiologic factors have been implicated as causes of primary enuresis, the exact cause remains obscure in most instances. The most common belief is that the disease has a multifactorial origin, including central nervous system, kidney and bladder, as well as psychosocial and behavioral components.

This article is significant from 2 standpoints: First, it reviews the literature in detail; kidney and bladder function of the enuretic child are emphasized. Secondly, the authors propose a new concept for the etiology of primary enuresis. The effects of nitric oxide (NO) in the urogenital system have been studied extensively during the last decade, but new effects are being uncovered regularly. From this point of view, the idea of investigating the role of the NO system in enuresis is novel. It is well accepted that there are significant interactions between NO and prostaglandins and similarly, between prostaglandins and anti-diuretic hormone (ADH), but there have been no comprehensive studies of their role in enuresis.

A weakness of this study is that too many parameters were checked, considering the number of patients (only 10 patients in each of the 2 groups). This limits the generalization of the results, but nonetheless the suggestion that the NO system may be involved in enuresis is worth pursuing further.

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