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UROLOGICAL SURVEY

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ENDOUROLOGY AND LITHIASIS

Laparoscopic pyeloplasty for UPJ obstruction with crossing vessels: contrast-enhanced color Doppler findings and long-term outcome

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Urology, 59: 500-505, 2002

Objectives: To evaluate, in the present long-term follow-up study, contrast-enhanced color Doppler imaging (CDI) findings and the clinical outcome of patients with crossing vessels at the obstructed ureteropelvic junction (UPJ), who underwent laparoscopic pyeloplasty. In a previous study, contrast-enhanced CDI proved capable of detecting crossing vessels at the UPJ.

Methods: A total of 23 patients, who had undergone laparoscopic pyeloplasty and displacement of crossing vessels for UPJ obstruction at least 2 years before this study (mean 27 months), underwent contrast-enhanced CDI, intravenous urography, and renography. Contrast-enhanced CDI was performed using intravenously administered Levovist to assess the displacement of the vessels relative to the UPJ. All patients completed analog follow-up pain scales and quality-of-life assessment questionnaires.

Results: Contrast-enhanced CDI revealed a cranial displacement (mean 1.3 cm) of the crossing vessels from the UPJ in all 23 cases. Intravenous urography showed a decrease in the degree of hydronephrosis, with a success rate of 100% in low-grade and 86% in high-grade hydronephrosis. The split renal function improved from 39.7% to 48.1%. Analog pain scale measurements demonstrated a mean improvement in pain of 92% (range 73% to 100%) and a mean quality-of-life score of 94 (range 78 to 100).

Conclusions: Our series of patients with crossing vessels at the UPJ treated by laparoscopic pyeloplasty showed an excellent long-term successful outcome. Contrast-enhanced CDI allows for preoperative detection, as well as postoperative assessment, of the displacement of the crossing vessel. We recommend that the presence of a crossing vessel be routinely determined preoperatively, because it may influence the choice of treatment modality and thereby the clinical outcome.

Editorial Comment

This study demonstrated that preoperative evaluation for crossing vessels at UPJ and treatment of patients with such crossing vessels by laparoscopic pyeloplasty (Anderson-Hynes dismembered pyeloplasty, n = 4, or nondismembered Fenger-plasty, n = 19) resulted in up to a 100% success rate. The surgical technique was demonstrated previously and is quick and easy to perform (1). Also, the authors demonstrated that contrast-enhanced color Doppler imaging (CDI) allowed for preoperative detection, as well as postoperative assessment of the position and displacement of crossing vessels. Based on the high prevalence of crossing vessels in this study and a low rate of intrinsic stenosis, the authors strongly recommend the need for preoperative evaluation for the presence of a crossing vessel.

It is interesting to point out that anatomical studies demonstrated that in 65% of the cases there was a prominent artery, or vein, or both vessels in close relationship with the ventral surface of the UPJ, in normal kidneys (2). These vessels are not aberrant and do not cause UPJ obstruction.

Van Cangh et al. (3) obtained preoperative digital angiography in patients prior to endopyelotomy and found an associated vessel in 39% of patients with UPJ obstruction. These authors stated that the presence of an

anterior crossing vessel with either mild or severe hydronephrosis resulted in a success rate of only 50% and 39% respectively.

On the other hand, Gupta and Smith (4) stated that the current data suggest that the finding of crossing vessels preoperatively need not significantly influence the treatment rendered. Corroborating it, Nakada et al. (5) reported that helical computed tomography (CT) detected significant anterior or posterior crossing vessels in 38% of patients following successful endopyelotomy. In their opinion, the adverse influence of the crossing vessel is not sufficient to justify the added expense of preoperative angiography, spiral CT or endoluminal ultrasound. Also, documenting the presence of a crossing vessel is inadequate to confirm that the vessel is causing obstruction. None of the current UPJ imaging techniques can distinguish crossing arteries that are the direct cause of obstruction from those that are not. Therefore, in the absence of a prospective randomized trial comparing the results of open pyeloplasty and endopyelotomy, including the investigation of crossing vessels, it is controversial the importance of imaging these crossing vessels before surgery.

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Francisco J.B. Sampaio

Extracorporeal shockwave lithotripsy in patients treated with antithrombotic agents

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Objective: This study was performed in order to achieve safe SWL in patients using antithrombotic agents, trying to reduce to a minimum both the hemorrhage and the thromboembolic risks.

Patients and Methods: Between January 1996 and December 1999, 749 patients underwent electromagnetic SWL. Among them, 23 patients, 19 with renal and 4 with ureteral stones, were receiving antithrombotic drugs (aspirin, ticlopidine, dipyridamole). According to the cardiologist and hematologist, we divided these patients into two groups: group 1 had a low thromboembolic risk (previous myocardial infarction) and group 2 had a high thromboembolic risk (aortocoronary bypass, atrial fibrillation, cerebrovascular disease, peripheral occlusive arterial disease). Group 1: patients discontinued their antiplatelet therapy 8 days prior to SWL to permit a sufficient number of functioning platelets to remain. Group 2: patients suspended antiplatelet therapy, and unfractioned heparin 5000 IU tid (8 a.m., 4 p.m. and 12 p.m.) was administered for the 8 days prior to SWL. On the ninth day of withdrawal, SWL was performed in all the patients. Close follow-up was performed during the postoperative period (hemoglobin, hematocrit, kidney ultrasonography, plain abdominal film). The antithrombotic therapy was restored in all patients within 10 to 14 days of withdrawal.

Results: Hematomas and thromboembolic events were not observed. At 3 months follow-up, 14 patients (61%) were stone free, 3 (14%) had lower 4 mm fragments and 6 (26%) had major residual fragments.

Conclusion: Our schedule for the suspension or substitution of antithrombotic therapy, although tested in a small number of patients, allowed us to perform SWL, without hemorrhagic or thromboembolic complications.

Editorial Comment

The most frequent side effect of SWL is hematuria. The treatment may cause microtrauma to the kidneys and urinary tract, with formation of intra or perirenal hematomas, as well as laceration of the transitional epithelium. In SWL of the kidneys, studies with computer tomography and magnetic resonance showed that the incidence of hematoma ranges between 20 and 25% (1). Patients with coagulation disorders or those with cardiovascular diseases under antithrombotic therapy have an increased risk of developing such complication. Therefore, it has been considered that congenital or acquired coagulation abnormalities represent a contraindication to the procedure.

In recent years, several works reported successful SWL in patients with coagulation disorders (2). In the present study, it is noteworthy that no peri or intrarenal hematoma was observed, although the post-treatment evaluation was performed only with ultrasound, that is less accurate than computer tomography. Furthermore, no patient presented hematuria for more than 2 days, and none had hemoglobin decrease larger than 1.5g.

This article, despite the small number of patients, demonstrates that, with adequate preparation (temporary suspension or partial decrease of antithrombotic medication) and careful application, SWL can be safely employed even in high-risk patients under antithrombotic therapy, without increase in hemorrhagic or thromboembolic complications.

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Artur Henrique Brito

UROLOGICAL ONCOLOGY

Variations in morbidity after radical prostatectomy

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Background: Recent studies of surgery for cancer have demonstrated variations in outcomes among hospitals and among surgeons. We sought to examine variations in morbidity after radical prostatectomy for prostate cancer.

Methods: We used the Surveillance, Epidemiology, and End Results-Medicare linked database to evaluate health-related outcomes after radical prostatectomy. The rates of postoperative complications, late urinary

complications (strictures or fistulas 31 to 365 days after the procedure), and long-term incontinence (more than 1 year after the procedure) were inferred from the Medicare claims records of 11,522 patients who underwent prostatectomy between 1992 and 1996. These rates were analyzed in relation to hospital volume and surgeon volume (the number of procedures performed at individual hospitals and by individual surgeons, respectively).

Results: Neither hospital volume nor surgeon volume was significantly associated with surgery-related death. Significant trends in the relation between volume and outcome were observed with respect to postoperative complications and late urinary complications. Postoperative morbidity was lower in very-high-volume hospitals than in low-volume hospitals (27 percent vs. 32 percent, $p = 0.03$) and was also lower when the prostatectomy was performed by very-high-volume surgeons than when it was performed by low-volume surgeons (26 percent vs. 32 percent, $p < 0.001$). The rates of late urinary complications followed a similar pattern. Results for long-term preservation of continence were less clear-cut. In a detailed analysis of the 159 surgeons who had a high or very high volume of procedures, wide surgeon-to-surgeon variations in these clinical outcomes were observed, and they were much greater than would be predicted on the basis of chance or observed variations in the case mix.

Conclusions: In men undergoing prostatectomy, the rates of postoperative and late urinary complications are significantly reduced if the procedure is performed in a high-volume hospital and by a surgeon who performs a high number of such procedures.

Editorial Comment

Surgeons with specific low-volume surgeries can perform some major surgical procedures, and these procedures can be performed at low or medium-volume hospitals with similar results that those obtained by expertise surgeons in very high-volume hospitals. However, this is not true for all major surgical procedures (1,2). Although peroperative mortality rate of radical prostatectomy is extremely low, late complications may be important, and consequently high morbidity rate may be found.

The authors suggested that patient morbidity after radical prostatectomy could be influenced by the surgeon’s experience and the medical and paramedical team’s experience enrolled on the surgical treatment of prostate cancer. However, this difference is widely ranged. The authors considered a very-high-volume surgeon and a low-volume surgeon those who had performed 33 to 121, and 1 to 10 radical prostatectomies in a 5-year period, respectively. Influence of surgeon’s experience is more important when overall postoperative complications is assessed, and they are significantly lower in the high-volume group. Interestingly, this is not the same with regard exclusively to the long-term continence rate.

Actually, most urologists are skilled to perform radical prostatectomy. However, they can keep in mind that to obtain good results depends not only of their self, since an adequate hospital environment (i.e., hospital structure and medical/paramedical team) is also essential.

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E. Alexsandro da Silva

PATHOLOGY

Stage pT1 conventional (clear cell) renal cell carcinoma: Pathological features associated with cancer specific survival

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Purpose: The features predictive of aggressive behavior in stage pT1 conventional (clear cell) renal cell carcinoma are not completely known. We evaluated pathological features in a large series of stage pT1 conventional renal cell carcinoma cases and examined the association of these features with cancer specific survival.

Materials and Methods: Patients with solitary stage pT1 conventional renal cell carcinoma who underwent radical nephrectomy between 1970 and 1997 were eligible for study. For each of the 46 patients who died of renal cell carcinoma we selected a stratified random sample of at least 3 year matched controls who were still alive or dead of other causes. The study included 277 patients. We evaluated patient age at nephrectomy, sex, tumor size, Fuhrman grade, necrosis and sarcomatoid component. Univariate and multivariate Cox proportional hazards models were fit to assess the features associated with cancer specific survival.

Results: Multivariate modeling revealed that tumor size, Fuhrman grade and necrosis were jointly significantly associated with cancer specific survival. Of the 4.5, 5 and 6 cm. tumor size cutoffs examined on univariate analysis a cutoff of 5 cm. or greater was most predictive of cancer specific survival.

Conclusions: In stage pT1 conventional renal cell carcinoma Fuhrman grade, tumor necrosis and tumor size together were jointly significantly associated with cancer specific survival. Specifically of the tumor size cutoffs analyzed the 5-cm. cutoff was most predictive of cancer specific survival.

Editorial Comment

First comment refers to nomenclature. The term “conventional” has been proposed in substitution of the term “clear cell”. The reason for this is based on works of cytogenetics which show chromosomal alterations (deletion of chromosome 3p) shared by clear cell carcinomas and eosinophilic (granular) cell carcinomas. Therefore, in a pathology report the tumor is named conventional renal cell carcinoma. The pathologist may add to the report that the carcinoma shows only clear cells, eosinophilic (granular) cells or, more frequently, both cellular types. The most important comment refers to the tumor size cutoff for stage pT1. The proposed TNM staging system of 1997 drastically changed this cutoff. The tumor limit of 2.5 cm or less in greatest dimension for stage pT1 was increased to 7 cm or less in greatest dimension (an almost 3-fold increase). Cheville’s paper is the first one based on a large series to show that a cutoff of 7 cm prevents the detection of a group of patients with a worse cancer specific survival in stage pT1. The statistical analysis of this study showed that the 5-cm cutoff was most predictive of cancer specific survival.

Athanase Billis

IMAGING

Enhancement characteristics of papillary renal neoplasms revealed on triphasic helical CT of the kidneys

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Purpose: To determine whether renal tumor enhancement or heterogeneity on triphasic helical CT scans is predictive of the papillary cell subtype or nuclear grade of renal cell carcinoma.

Material and Methods: The CT scans of 90 consecutive patients with renal masses who had undergone triphasic renal helical CT before a complete or partial nephrectomy (12 with papillary renal cell carcinomas, 66 with nonpapillary renal cell carcinomas, and 12 with benign lesions), were reviewed. Three radiologists who were unaware of the patients' diagnoses retrospectively and independently measured the attenuation of each patient's tumor, abdominal aorta, and normal renal parenchyma on the scans obtained during all three phases. Ratios of tumor-to-aorta enhancement and tumor-to-normal renal parenchyma enhancement were calculated for both of the phases performed after contrast material had been administered. Tumor heterogeneity was calculated as the difference between the highest and lowest attenuation values divided by the value of the enhancement of the aorta. Values were correlated with cell type and nuclear grade found at surgical pathology.

Results: Low tumor-to-aorta enhancement and low tumor-to-normal renal parenchyma enhancement ratios on the vascular phase scans significantly correlated ($p < 0.001$) with papillary renal cell type carcinoma. Homogeneity and tumor-to-parenchyma enhancement ratios on the parenchymal phase scans also significantly correlated ($p < 0.001$) with papillary renal cell type carcinoma. Heterogeneity and tumor enhancement ratios did not correlate with the nuclear grade of the carcinoma.

Conclusion: Papillary renal cell carcinomas are typically hypovascular and homogeneous. A high tumor-to-parenchyma enhancement ratio (≥ 25%) essentially excludes the possibility of a tumor being papillary renal cell carcinoma. A low tumor-to-aorta enhancement ratio or tumor-to-normal renal parenchyma enhancement ratio is more likely to indicate papillary renal cell carcinoma.

Editorial Comment

Nowadays, nephron-sparing surgery is considered to be an effective and curative therapy for localized renal tumors. Patients that are at risk for damage the renal function due to systemic diseases are the classical indication for this surgical procedure, because it preserves nephrons and provides excellent survival rate. Although the performance of nephron-sparing surgery in patients with normal contralateral kidney is a controversial issue, current results have shown that it is safe, provides a low local recurrence rate (0%-3%) and a high free-cancer survival rate (90%-100%) (1,2). Thus, radiologists may provide to urologists the most common hypothesis of the pathological specimen, for example, angiomyolipoma, oncocytoma, RCC, etc. This radiological characterization of renal mass can be assessed by helical CT with 4 phases (one pre-contrast material injection, and three post-contrast: cortex-medulla enhancement; nephrography; and excretory).

The authors provided a review of the findings in the pre-operative helical CT of 90 consecutive patients with renal mass. A triphasic helical CT was performed in all patients because the excretory phase was excluded. The tumor-to-aorta enhancement ratio or tumor-to-normal renal parenchyma enhancement ratio were assessed for the pos-contrast phases. This study shown that the papillary RCC is typically hypovascularized and homogeneous. A high tumor-to-parenchyma enhancement ratio (≥25%) essentially excludes the possibility of a

tumor being papillary RCC. On the other hand, a low tumor-to-aorta enhancement ratio or tumor-to-normal renal parenchyma enhancement ratio is more likely to indicate papillary RCC. Thus, the authors recommend that when radiologists suspect of papillary RCC, urologists can be informed because this tumor is preferentially managed by nephron sparing surgery. Papillary RCC posses a better prognostic than other cell types of renal tumor, and it is related to bilateral and hereditary incidence.

This paper presents some limitations, some of those discussed by the authors; a)- the enhancement rate of a renal mass depends on several points, but mainly of the quantity and the velocity of the administration of venous contrast, and therefore it can be different whether assessed with a 2mL/seg or 4mL/seg infusion rate; b)- the prevalence of this histological type of tumor was 14%, while the prevalence ranges from 5% to 15%. Negative and positive predictive values depend of the disease prevalence in the studied population; c)- the authors provided no comments on the value of the density of the papillary CCR in the pre contrast phase (hyperdenses solid mass represent frequently clear cell CCR, and moreover do not reference the chromophobic cell RCC that in our experience can be also homogenous and hypovascularized. Any way, this article is extremely important to call attention of the radiologist to provide, always possible, records that contains not only morphological findings, but histological hypothesis that surely will be useful in the choice of the best option for treatment.

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Adilson Prando

Directed biopsy during contrast-enhanced sonography of the prostate

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AJR, 178: 915-919, 2002

Purpose: To evaluate the value of directed biopsy for the detection of prostate cancer during contrast-enhanced endorectal sonography.

Materials and Methods: Forty patients were evaluated with harmonic gray-scale sonography. The evaluation was performed before administration of contrast agent, during continuous IV infusion of perflutren lipid microspheres, and again during bolus administration of the microspheres. Sextant biopsy sites were scored prospectively on a six-point scale for suggestion of malignancy at baseline during contrast infusion and after bolus administration. An additional directed core was obtained at 20 of the sextant biopsy sites based on contrast-enhanced imaging.

Results: Cancer was identified in 30 biopsy sites in 16 of the patients (40%). A suspicious site identified during contrast-enhanced transrectal sonography was 3.5 times more likely to have positive biopsy findings at than an adjacent site that was not suggestive of malignancy ($p < 0.025$). When a suspicious site was evaluated with an additional biopsy core, the site was five times more likely to have a biopsy with positive findings than a standard sextant site ($p < 0.01$). We found no difference in diagnostic accuracy between continuous infusion of contrast material and bolus administration.

Conclusion: Contrast-enhanced transrectal sonography improves the sonographic detection of malignant foci in the prostate. The performance of multiple biopsies of suspicious enhancing foci significantly improves the detection of cancer. There is no advantage to additional examination of the gland after bolus administration of contrast material.

Editorial Comment

The authors presented a study on 40 patients submitted to directed biopsy during transrectal sonography. A new echo-contrast (microbubbles lipidic suspension of perflutren) was used in addition to transrectal sonography software to obtain harmonic images. Theses images are produced by the emission in repetitive pulses (intervals of 0.2, 0.5, 1.0 and 2.0 seconds) after the intravenous infusion of the echo-contrast. When an abnormality was evidenced by the contrast, this one was target of an additional directed biopsy (1 or 2 cores). Identification of a suggest site has a positive predictive value of 3.5 time more likely to have positive biopsy findings at than an adjacent site that was not suggestive of malignancy ($p < 0.025$). Sextant biopsy of the prostate was performed when the sonography was normal. The positive rate of cancer was 40% (16/40 patients).

This article is important because address 2 points. Firstly, the value of the color Doppler during transrectal biopsy, which alone improves the cancer detection in 10-15% (1). Secondly, the improvement in the detection rate of prostate cancer using echo-contrast (2). Recently, we studied 50 consecutive patients who were evaluated using power-Doppler and echo-contrast, and we found positive biopsy in 43.5% (17% more than sextant biopsy). However, we used a different echo-contras (Levovist), which is constituted of microparticles of galactose in palmitic acid. It is important to note that, as in Brazil as in United States, sextant biopsy of the prostate is still the most common procedure performed for diagnosing cancer. Furthermore, as in 1997, only 20% of those perform sonography-guided biopsy (3).

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Adilson Prando

HUMAN REPRODUCTION

Serial ultrasonography, hormonal profile and antisperm antibody response after testicular sperm aspiration

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Hum Reprod, 16: 2632-2639, 2001

Background: In many fertility centres, intracytoplasmic sperm injection (ICSI) with epididymal or testicular spermatozoa is a routine treatment for men with azoospermia. In this prospective study, the physiological consequences after testicular sperm aspiration (TESA), using suction and a 19-gauge needle, were evaluated.

Methods and Results: Thirty-five consecutive men with azoospermia underwent TESA. Testicular ultrasonography with Doppler flow imaging was performed and testicular volumes were evaluated pre-operatively and 3 months after aspiration. If focal testicular lesions were found, further examinations were performed 6 and 9 months after TESA. Serum FSH, testosterone and antisperm antibodies (ASA) were analyzed. Focal testicular lesions were seen in four out of 61 testes (6.6%) at the 3-month investigation point. Three lesions were resolved after 6 months and all after 9 months. Testicular echogenicity remained unchanged in 50 cases (82%) 3 months after TESA. Four men (11.4%) reported severe subjective discomfort post-operatively, but only one had a medical consultation where an intratesticular haematoma was diagnosed. There were no significant changes in FSH and testosterone after surgery and testicular volumes were similar after 3 months. There were three borderline cases of ASA in serum, but none was classified as ASA-positive.

Conclusions: The puncture method of testicular sperm aspiration seems to be a safe method for sperm retrieval, with minimal physiological consequences.

Editorial Comment

Percutaneous testicular sperm aspiration (TESA) has been used by many groups to obtain spermatozoa for assisted reproduction (intracytoplasmic sperm injection) in men with azoospermia. Some are against this method, preferring to perform an open biopsy (TESE), maintaining that TESA, as a “blind” procedure, can damage intratesticular vasculature, and may cause acute (hematoma) and/or chronic (spermatogenesis impairment) complications.

In this prospective study, the authors have observed only one case of intratesticular hematoma among 61 aspirations performed, and have not observed short and medium term alterations in the hormone profile, antisperm antibodies, testicular volume and echogenicity of the testicular parenchyma. From the individuals with nonobstructive azoospermia, TESA was successful to obtain spermatozoa in 36% (9/25) of them. In a group of non-selected azoospermic men, the recovery rate obtained in the present study was similar to the one obtained with open biopsy.

As TESA is a minimally invasive procedure, practically free of complications, and which allows ready return to daily activities, this has been considered the first option to obtain testicular spermatozoa for a growing number of authors. However, the results of the present study allows us to speculate that if the process needs to be repeated, it is wise to await a 6 month interval, once during this period focal intratesticular lesions are observed.

Sandro C. Esteves

Long-term outcomes of elective human sperm cryostorage

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Hum Reprod, 16: 2621-2627, 2001

Background: Sperm cryopreservation allows men with threatened fertility to preserve their progenitive potential, but there is little data on long-term outcomes of elective sperm cryostorage programs.

Methods and Results: Over 22 years, 930 men sought semen cryostorage in a single academic hospital, of which 833 (90%) had spermatozoa cryostored. Among 692 (74%) men surviving their illness, sperm samples were discarded for 193 (21% of all applicants, 28% of survivors) and cryostored spermatozoa were used for 64

men (7% of all applicants, 9% of survivors) in 85 treatment cycles commencing at a median of 36 months post-storage (range 12–180 months) with nearly 90% of usage started within 10 years of storage and none after 15 years. Pregnancy was most efficiently produced by intracytoplasmic sperm injection (median three cycles) compared with conventional IVF (median eight cycles) or artificial insemination (median more than six cycles; $p < 0.05$). A total of 141 (15%) of men had died and of these, 120 (85% of those dying) had their spermatozoa discarded; requests to prolong cryostorage were received from relatives of 21 men (2% of all applicants, 15% of deceased) of which three cases had spermatozoa transferred for use with no pregnancies reported. Sperm concentration was lower for all cryostorage groups compared with healthy sperm donor controls ($p < 0.05$). Following orchidectomy, men with testicular cancer had sperm density approximately half that of all other groups of men seeking cryostorage ($p < 0.05$), the lowering attributable to removal of one testis rather than in defects in spermatogenesis.

Conclusion: Elective sperm cryopreservation is an effective, if sparsely used, form of fertility insurance for men whose fertility is threatened by medical treatment and is an essential part of any comprehensive cancer care program.

Editorial Comment

Infertility is expected in most cancer patients submitted to chemotherapy and/or radiotherapy. Even though they may recover their fertility after treatment, approximately 50-95% of them will remain irreversibly infertile and many with azoospermia. In the past, due to the limitations of assisted reproduction techniques, it was uncommon to offer cryopreservation to men with low pre-treatment semen quality, which is indeed very frequent, mainly in men with testicular cancer and Hodgkin's disease. Today, with the advent of intracytoplasmic sperm injection (ICSI), low sperm quality does not limit pregnancy chances. Therefore, the best pregnancy results with ICSI are expected in this study (pregnancy rate: ICSI = 42.8%, average of 3 attempts; IVF = 21.4%, average of 6 attempts; artificial insemination = 31.4%, average of 8 attempts).

Interesting aspects of this study are also the casuistic and the long follow-up, which allow the evaluation of the natural fate of the cryopreserved semen. More than 90% of the individuals had cancer, of which 74% are still alive 22 years later, which reflects the survival improvement with the modern oncologic treatments. Less than one third of the individuals who survived discarded the semen during this period, which reinforces the importance of this form of fertility preservation. From these men, 59% did it because they had recovered their fertility. The use of cryostored spermatozoa was high (9%) when compared to other studies (mean of 3%).

Although less than 10% of the individuals used the cryopreserved semen, the costs of cryopreservation and storage are insignificant when compared to the costs with the treatment, which motivated the cryopreservation. As it is practically impossible to determine which men will recover their fertility after treatment, cryopreservation must be offered as means to preserve future fertility. What is observed in the data presented, and in many other studies, is that the practice of elective semen cryopreservation is still little divulged, in view of the high number of new cases of cancer affecting men in reproductive age. Therefore, as emphasized by the authors in the discussion, it is important to run informative campaigns with all physicians.

Sandro C. Esteves

PEDIATRIC UROLOGY

Heredity of hypospadias and the significance of low birth weight

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J Urol, 167: 1423-1427, 2002

Purpose: We analyzed a large group of patients with hypospadias regarding familial aggregation, phenotype, twin rate and ethnic origin and assessed the correlation of low birth weight with hypospadias.

Material and Methods: We mailed questionnaires to 2503 boys operated for hypospadias in Sweden asking for additional cases of hypospadias in the family, the number of brothers in the nuclear family, and birth weight of the boys with hypospadias and their brothers.

Results: Of the boys 7% reported 1 or more additional family members with hypospadias. The birth weight of the boys with hypospadias was significantly lower ($p = 5x10^{-13}$) than the birth weight of their unaffected brothers. Phenotyping of 676 individuals revealed glandular hypospadias in 53%, penile forms in 39%, penoescrotal or perineal variants in 6%, cleaved prepuce as the only manifestation in 2%. There were 50% more twins than expected compared to the general population and established zygosity in 83% (67% monozygotic, 33% dizygotic). Non-Swedish ethnicity was noted in 22% of the subjects, a third of who were from Middle Eastern Countries.

Conclusions: We present data on heredity, birth weight, phenotype and ethnic origin in a large group of patients with hypospadias. The finding of additional members with hypospadias in 7% of the families supports the concept that genetic factors are involved in pathogenesis. The strong association with low birth weight may be explained by genetic and environmental factors.

Editorial Comment

The authors presented a detailed retrospective study on incidence rate of hypospadias, and evaluated heredity, phenotype, twin incidence, and the correlation between low birth weight with hypospadias in more than 2,500 patients with hypospadias, who were born in Sweden.

The major issue in the article is the relation of hypospadias and low birth weight. Masculinization of the male external genitalia begins in the 8th gestational week, and depends of the synthesis and circulating testosterone. Currently theory correlates fetal weight with higher incidence rate of hypospadias, and is based on placental insufficiency, which decreases the secretion of chorionic gonadotrophin (release hormone of androgen), and as a result influences the urethral plate opening and therefore hypospadias. This theory can be also applied to the incidence of chryptorchidism in low birth weight. Previous authors demonstrated that as higher the fetal weight, higher the number of descended testis in humans (1,2). Retrospective studies, as the present article, are essential to determine the influence of low birth weight in chryptorchidism.

The large number of patients that were retrospectively analyzed can be highlighted, confirming the importance of an organized database, which is fundamental to perform clinical studies.

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Luciano Alves Favorito

Adult testicular torsion

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J Urol, 167: 2109-2110, 2002

Purpose: Testicular torsion in adulthood is thought to be relatively unusual. We compared a series of men 21 years old or older with testicular torsion with a concurrent series of younger patients with torsion.

Material and Methods: We reviewed the medical records of patients admitted with testicular torsion in a 9-year period to hospitals affiliated with our institution. Data included patient demographics, history, physical findings, radiographic results if any, operative findings and outcome (testicular salvage versus loss).

Results: The charts of 48 patients were evaluated. Excluded from study was a neonate with torsion and 3 males who underwent delayed surgery for presumed missed torsion. Of the remaining 44 patients we compared 17 who were 21 years old or older (range 21 to 34) with 27 younger than 21 (range 8 to 20). The salvage rate differed in the 2 age groups with 70.3% of testes salvaged in the younger group versus only 41% in the older group. A factor affecting salvage in each group was time to presentation. In the older age group patients in whom the testis was lost had a significantly higher mean delay in presentation than those in whom it was salvaged (102 versus 11 hours). A similar pattern was noted in the younger group with a mean time to presentation of 108 and 6.5 hours in those with testicular loss and salvage, respectively. Mean time between presentation and operation was 7.1 hours in the older and 4.8 in the younger group, which was not statistically different. A significant difference was noted in the degree of spermatic cord twisting. The cord was twisted a mean of 585 degrees in the adults versus 431 in the younger group.

Conclusions: Testicular torsion in adults was more common in our series, than expected. Salvage of the affected testis was better in younger patients, presumably due to less twisting of the cord.

Editorial Comment

The authors reviewed their experience on testicular torsion affecting children and adults. This article is interesting and has merit, and gives more evidence to the fact that testicular torsion is not exclusively a children condition. The authors evaluated important aspects, as time to presentation and the degree of spermatic cord twisting. However, epidydimal and tunica vaginalis anatomy were not recorded to provide a comparison between groups.

Etiology of spontaneous testicular torsion is based on anatomical changes. Epidydimal and tunica vaginalis anatomy can be abnormal and promote torsion (1). The testis is commonly attached in the tunica vaginalis. If one of those structures were abnormally attached, testis would present an excessive mobility. There are 2 kinds of torsion regarding to tunica vaginalis anatomy: intravaginal and extravaginal torsion. These aspects were not discussed in the article. A third kind of testicular torsion occurs in the mesorchyum, which is the region between the testis and epidydimis. When epidydimal disjunction is present, the mesorchyum is large and therefore favoring testicular torsion. This is a very frequent alteration in patients with cryptorchidism (2-3).

We evaluated 16 cases of spontaneous testicular torsion. Patients' age ranged from 13 to 27 years old (mean age 15.6), and we found that the tunica vaginalis was normal in only one case (3.1%). Extravaginal torsion occurred in 2 cases (6.2%), large mesorchyum was present in 3 cases (9.3%), and intravaginal torsion occurred in 26 cases (81.25%). These results provide evidence that anatomical anomalies of paratesticular structures play important role in the pathogenesis of testicle torsion.

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RECONSTRUCTIVE UROLOGY

Continent catheterizable conduits: which stoma, which conduit and which reservoir?

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BJU, Int 89: 86-89, 2002

Objective: To assess the outcome of the various methods used in creating continent catheterizable conduits.

Patients and Methods: The case notes were reviewed from 89 patients who underwent the formation of 112 continent catheterizable conduits.

Results: Sixty-five conduits were Mitrofanoff and 47 were antegrade colonic enema (ACE); 21 patients had both. At a mean follow-up of 34 months, 95 (85%) conduits were still in use. There was no difference in complications between the Mitrofanoff and ACE conduits; 109 (97%) conduits were continent and stomal stenosis occurred 35 (31%). There was no significant difference relating to the conduit used, the reservoir, the stoma type or the stoma site. Only 39% of patients required no revisional surgery.

Conclusion: Although urinary and fecal continence can be achieved in most patients there is a high burden of complications and revisional surgery. All patients should be counseled accordingly.

Editorial Comment

The use of Mitrofanoff principle and Malone's surgery (antegrade colonic enema - ACE) improve the quality of life for patients who suffer from urinary and fecal incontinence. Some modifications of the original techniques were described, including two Brazilian contributions (1,2). However, the appendix remains the safest material to perform a catheterizable conduct (3).

The authors presented their great experience, mainly on the surgical treatment of neurogenic fecal incontinence (ACE). These procedures present high complications rate, and frequently surgical revision is needed. In the present series, only 39% of patients did not need surgical revision. It is important to be noted that there was not difference with regard to conduct stenosis when the stoma was placed in the umbilicus or in the abdominal wall, as well when the conduct was implanted in the original or bowel augmented bladder. Dissatisfaction with the washout regime and difficulty for catheterizing are important factors to promote refusing to use the conduit. The authors showed a low rate of dissatisfaction (15%) enough to no more use the conduit, after a mean follow-up of 34 months.

A high quality information can be addressed to patients and their parents before these surgical procedures be performed. This is a key point to obtain success. This is especially important with regard to the ACE, in which dissatisfaction is the main cause for abandoning the conduct catheterization.

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E. Alexsandro da Silva

Kidney transplantation in children weighing less than 15 Kg: Donor selection and technical considerations

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Transplantation, 73: 409-416, 2002

Objectives: The aim of the study was to analyze patient and donor data influencing outcome in children that weighed less than 15 Kg.

Methods: Sixty-eight kidneys were transplanted in sixty-four children that weighed less than 15 Kg. In forty-four cases, kidneys came from cadaveric donors and in twenty-four cases, from living-related donors. Grafts were placed transperitoneally via midline incision (n = 16) or extra-peritoneally in the iliac fossa (n = 52). Vascular anastomoses were routinely performed in the aorta and vena cava even when the extra peritoneal approach was used.

Results: Vascular thrombosis was observed in two (3%), urinary leaks in five (7%) and stenosis in four (6%) patients. In six children, whose grafts came from adult donors and were placed in their iliac fossa, wound closure needed to be performed using an absorbable mesh to prevent organ compression. Normal graft function occurred immediately in sixty cases (88%). Immediate graft function was significant more frequent among patients who received kidneys from living-related donors (100%) than from cadaveric donors (82%). The 1-, 5- and 10-year patient survival rate was 93%, 91% and 91% respectively. The 1-, 5- and 10-year graft survival rate was 92%, 85% and 85% respectively. There was no significant difference in patient and graft survival when organs from living-related and cadaveric donors were compared. Within the cadaveric group, graft survival was improved using kidneys from donors older than twelve years compared to younger donors.

Conclusion: Despite size discrepancy between recipients and grafts, kidney transplant is feasible in children that weigh less than 15 Kg by using an improved surgical technique even when adult organs are placed in the iliac fossa.

Editorial Comment

Kidney transplantation is considered the preferable treatment option in pediatric patients with end-stage renal insufficiency. Small children, nevertheless, represent a challenging patient group because of discrepancy size between recipients and donor organs. When kidneys from adult donors are transplanted to small children, most centers prefer the transperitoneal approach (1). The authors present in this paper a modified technique to allow placement of renal transplants extraperitoneally in the iliac fossa even in very small children.

There are many advantages to using extra peritoneal access without an increase in surgical complications or technical difficulty. Absent gastrointestinal complications, an easier way to perform percutaneous biopsy, treatment of any surgical complication with no need for repeated laparotomy and the possibility of using the peritoneal cavity when dialysis is needed postoperatively are attractive justifications for extra peritoneal access (2).

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Ioannis Antonopoulus

INVESTIGATIVE UROLOGY

Spermatogenesis, fertility and sexual behavior in a hypospadiac mouse model

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Purpose: Administering of flutamide to pregnant mice causes hypospadias in male offspring. We investigated spermatogenesis, fertility and sexual behavior in this hypospadiac mouse model.

Materials and Methods: Male offspring exposed to flutamide during the embryonic period were divided into hypospadiac group 1 and normal external genitalia group 2. Control group 3 consisted of male offspring not exposed to flutamide. We analyzed the spermatogenesis, epididymides sperm motility, in vitro fertilization rate and sexual behavior of each mouse.

Results: There were no significant differences in the weight of the testes or mean seminiferous tubular diameter in the groups. The number of apoptotic germ cells per unit area was not significantly different in the 3 groups. In groups 1 to 3 there were no significant differences in the mean epididymides sperm motility rate plus or minus standard deviation (62.6% ± 10.0%, 57.2% ± 7.0% and 67.0 ± 7.6%) or in the in vitro fertilization rate (52%, 48% and 48%, respectively). However, there were significant differences in groups 1 to 3 in mean mounting frequency (0.29 ± 4.0 and 12.4 ± 4.5 times per hour) and mean intromission frequency (0.24 ± 3.5 and 3.8 ± 1.5 times per hour, respectively). Females coupled with group 1 or 2 male mice did not achieve pregnancy.

Conclusions: These results suggest that spermatogenesis, sperm motility and fertilization in vitro were unaffected in hypospadiac mice but sexual motivation and arousal were deficient.

Editorial Comment

The etiology of hypospadias is not completely understood. However, androgen insensitive, deficiency of 5-α-reductase, and chromosomal anomalies may be the most important causes.

The authors assessed spermatogenesis, sperm motility, fertility and the sexual behavior of flutamide-induced hypospadiac mouse. This experimental model is far adequate, since that it is well established in the

literature that the administration of antiandrogens in the pregnant mice can cause hypospadias. The parameters evaluated were assessed by sophisticated techniques, for example, in vitro fertilization and embryo transfer. Among all parameters evaluated, only sexual behavior was abnormal. Hypospadiac animals presented no interest in female mice, and mice that presented normal genitalia, but were submitted to intra-uterus exposure to flutamide, presented abnormally high frequency of mounting and intromission. Thus, based on these results, studies to evaluate the sexual differentiation in brain areas related to sexual behavior can be very interesting. Moreover, sexual behavior seems to be an educated behavior, and it can be better successively. Thus, the evaluation of sexual behavior for several times in the same animal becomes also important.

Although all male offspring, in which intra-uterus flutamide was administered, presented internal urogenital changes, only 50% showed morphological alterations of the urethra conspicuous enough to characterize it as hypospadias. This states this experimental model as limited and specific, because flutamide acts only in a determined moment in the cascade of molecular events that occur in the urogenital embryogenesis. Albeit this experimental model does not represent an exact reflex of what occur in humans, mainly with regard to etiology, it is an interesting model to evaluate clinical problems of hypospadias (i.e., fertility and sexual behavior).

Cristiane Ramos

Vascular endothelial growth factor and signaling in the prostate: more than angiogenesis

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In cloning tyrosine kinase genes in dog prostate cells, a fragment of the vascular endothelial growth factor (VEGF) receptor 1 or Flt-1 was sequenced. To test for a functional protein, Flt-1 antibodies were used to probe immunoprecipitated tyrosine phosphorylated proteins. Western blotting revealed a major 170–180 kDa band and a few bands below 116 kDa in dog prostate and human prostatic carcinoma PC-3 cells, with higher levels in PC-3. Similar results were obtained with human placental membranes used as a source of Flt-1. That the major Flt-1 tyrosine phosphorylated protein was likely VEGF-R1 and part of VEGF signaling pathways was shown by enhanced level of only this protein when PC-3 cells were exposed to VEGF. Accordingly specific cell surface receptor complexes, displaced by VEGF but not EGF and compatible with Flt-1 in size, were revealed by chemical cross-linking after ^{125}I-VEGF binding. Similarly to the prostatic neuroproduct, gastrin-releasing peptide/bombesin, VEGF directly triggered the tyrosine phosphorylation of focal adhesion kinase and stimulated PC-3 cell motility. The titration of prostate tissue sections with VEGF-A antibodies revealed a confined staining in chromogranin A and/or serotonin positive neuroendocrine (NE) cells, including in primary tumors and lymph node metastases. Given that NE differentiation is associated with advanced disease, that NE cells are a significant source of VEGF in prostatic tumors, and that VEGF directly act on prostate cancer cells in vitro, VEGF-A may be more than angiogenic in prostate cancer and hence favor progression by affecting tumor cells.

Editorial Comment

Recently, angiogenesis has been recognized as an important factor in tumor growth and metastasis. Increased vascular density has been shown to correlate with poor prognosis in a variety of human cancers, including prostate cancer (1). Several angiogenic factors have been identified in prostate cancer, and this has opened new perspectives in therapeutic research. Since diverse cytokines and growth factors from other families affect endothelial cell functions and that anti-angiogenic factors and their signaling receptors were recently identified, the network of new blood vessels feeding tumors reflects the overall action of pro- and anti-angiogenic factors on receptors and signaling partners, which ultimately affects progression.

The authors reported on a functional fragment of the vascular endothelial growth factor receptor 1 (VEGF-R1 or Flt-1) activated by VEGF-A in human prostate cancer cells that express specific receptors on their surface. VEGF-A also triggered signaling through focal adhesion kinase (Fak) and activated prostate cancer cell motility. This is very important because was the first time that researchers have demonstrated the direct effects of VEGF on human prostate cancer cells. Thus, in additional to angiogenesis, VEGF may favor progression by acting on prostate cancer cells.

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