

Sensitivity and Specificity of Ultrasonography in Predicting Etiology of Azoospermia

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OBJECTIVE	To determine the sensitivity and specificity of different ultrasound (US) modalities in predicting an obstructive vs a nonobstructive etiology of azoospermia.
MATERIALS AND METHODS	A total of 268 azoospermic men with available histopathologic slides were separated into obstructive (n = 104) and nonobstructive (n = 164) groups. Scrotal US studies, including color Doppler and transrectal US examinations, were performed in all patients and compared with the testicular biopsy results as the reference standard.
RESULTS	We found that a decreased testicular volume and intra- and extratesticular varicocele were the most common abnormalities detected using scrotal US in those with nonobstructive azoospermia. In contrast, epididymitis, spermatocele, and duct ectasia were the most common findings in those with obstructive azoospermia. The sensitivity and specificity of scrotal US in detecting nonobstructive azoospermia was 75% and 72%, respectively, and for detecting obstructive azoospermia was 29.8% and 87%, respectively. Prostatic midline cysts, ejaculatory duct calcification, dilated seminal vesicle, and/or vassal ampullae were the most common abnormalities detected using transrectal US for obstructive azoospermia. The sensitivity and specificity of transrectal US in detecting obstructive etiology was 45% and 83%, respectively, and for functional etiology was 39% and 88%, respectively.
CONCLUSION	Scrotal US was more sensitive in detecting functional azoospermia and more specific in detecting obstructive azoospermia. However, transrectal US was more sensitive in detecting obstructive azoospermia and more specific in detecting functional azoospermia. Both tests had greater specificity than sensitivity for obstructive azoospermia, indicating that US has the ability to exclude more than to diagnose cases of obstructive azoospermia. However, US is unlikely to completely replace testicular biopsy. UROLOGY 81: 967–971, 2013. © 2013 Elsevier Inc.

Infertility is defined as the inability of a sexually active couple to attain pregnancy after 1 year of unprotected sexual intercourse. In 40%-60% of cases of infertility, a contributing male factor is present.^{1,2} Azoospermia is defined as the absence of spermatozoa in the semen.³ Azoospermia is identified in semen analyses in 5%-10% of infertile men.⁴ This condition represents the final result of different testicular alterations, ranging from normal spermatogenesis with seminal tract obstruction or the absence of the vas deferens (obstructive azoospermia) to different abnormalities of the spermatogenic process, including hypospermatogenesis, maturation arrest, and a complete absence of germ cells, such as in

Sertoli cell-only syndrome (nonobstructive or functional azoospermia).^{5,6}

The distinction between obstructive and nonobstructive azoospermia is important because men with obstructive azoospermia might have cost-effective treatment options such as microsurgical reconstruction of the reproductive tract. However, for those with functional azoospermia, it might be reasonable to proceed directly to an advanced assisted reproductive technique such as intracytoplasmic sperm injection.⁷ Also, a real risk of failure to retrieve spermatozoa exists in men with nonobstructive azoospermia, and couples must be apprised of this risk before attempting assisted reproduction.⁸

For the definite diagnosis of obstruction, a testicular biopsy is required, with the finding of a good number of mature spermatid and spermatozoa in the seminiferous tubules.⁹ Because of the invasive nature of this procedure, the limited results of surgical treatment of obstructions of the seminal path, and alternative options such as assisted reproductive treatments, testicular biopsies are not routinely performed.¹⁰

Transrectal ultrasonography (TRUS) has conventionally been used as a first-line diagnostic modality to evaluate the prostate and document obstruction in the

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ejaculatory duct.^{11,12} Little has been published about the comparative sensitivity and specificity of ultrasonography (US) in detecting azoospermia vs the more definitive, but invasive, diagnostic testicular biopsy.¹³ Although scrotal color Doppler US is routinely performed to check for nonpalpable varicocele, it might also be helpful in distinguishing testicular failure from obstruction in patients with azoospermia, because it can directly demonstrate abnormalities in the proximal mediastinum testis, epididymis, and intrascrotal portion of the vas.¹⁴

The objective of the present study was to determine the sensitivity and specificity of scrotal US (including color Doppler US) and TRUS in the prediction of an obstructive or a nonobstructive etiology in infertile men with azoospermia compared with testicular biopsy as the reference standard.

MATERIAL AND METHODS

The present study was a prospective, cross-sectional study. It was conducted from March 2010 to May 2012 at our institutes. It included 268 azoospermic men (diagnosed after ≥ 2 semen analyses 1 month apart) who had undergone a previous diagnostic testicular biopsy with histopathologic slides available. Those patients having clinically evident small testes and those with clinically evident hypogonadism were excluded to avoid any bias during the US evaluation. The patients were divided into 2 groups according to the testicular histopathologic findings using modified Johnsen scoring⁹: a functional azoospermia group (n = 164) and an obstructive azoospermia group (n = 104). All patients included in the present study underwent complete history taking and general and genital examinations. Patients with clinically evident testicular atrophy or cryptorchidism were excluded. Those patients with retrograde ejaculation revealed by examination of postorgasmic urine were also excluded.

Scrotal US, including color Doppler US, was performed using a 7.5-MHz, high-resolution, linear array transducer (Sonoline Versa Plus, Seimens Medical System, Erlangen, Germany) with pulsed and color Doppler capabilities. The patient was placed first in the supine position. The scrotum was elevated with a towel draped over the thighs and the penis placed on the patient's abdomen and covered with a towel. Acoustic gel was used. The testes were examined using scrotal US for their size, volume, echogenicity, and perfusion. The testicular volumes were calculated using the US formula, length \times width \times height \times 0.71, and expressed in milliliters.¹⁵ The total testicular volume was calculated by summing the volumes of the 2 testes and was considered subnormal if < 20 mL.¹⁶ The presence of any paratesticular anechoic, tortuous tubular structures (ie, widened spermatic veins) was noted. Next, the patient was examined in the standing position. The color mode was used to evaluate the testicular veins. The veins were examined before, during, and after the Valsalva maneuver for their size and the occurrence of reflux. Spectral analysis was used to detect venous reflux and to determine its duration. Varicocele was diagnosed by US demonstration of ≥ 1 veins with a maximal diameter of > 3 mm and reflux > 1 second.¹⁷

TRUS was done using an AU5 ultrasound machine (Esaote Medical Systems, Genoa, Italy). A self-administered enema was routinely used before the examination. Patients were placed in the left lateral decubitus position. A digital rectal examination was performed for each patient to ensure the absence of rectal

abnormalities that could interfere with the scan. After adequate lubrication, the probe was gently inserted into the rectum up to the bladder. The seminal vesicles were examined for their size and echogenicity. The prostate was examined in the transverse and sagittal planes, searching for the ejaculatory ducts. Both vasa differentia were evaluated for their presence or absence, the echogenicity of their lumens, and their calibers.¹⁸

The local ethics committee at our institutes approved the present study, all patients provided written informed consent before enrollment in the study.

Statistical Analysis

The data was recoded and entered in the Excel 2007 software program, then cleaned, and transformed to the Statistical Package for Social Sciences software, version 16 (SPSS, Chicago, IL). Descriptive statistics are presented as frequencies and the mean \pm standard deviation. The chi-square test was used to compare the valid percentages of findings between groups. The data were considered significant when $P \leq .05$.

RESULTS

The study included 268 infertile male patients divided into 2 groups according to the testicular histopathology report: nonobstructive (group 1, n = 164) and obstructive (group 2, n = 104). Demographic data analysis revealed no significant difference between the 2 groups in the age distribution (mean 37.35 ± 7.19 years for group 1 and 36.51 ± 7.72 years for group 2; $P > .05$) or body mass index (mean 25.24 ± 2.56 kg/m² for group 1 and 26.67 ± 1.95 kg/m² for group 2; $P > .05$).

Scrotal US yielded significantly more common diagnoses suggesting a functional etiology in the functional azoospermia group, including a subnormal total testicular volume and intra- and extratesticular varicocele. In contrast, it yielded significantly greater findings suggesting obstructive etiology in the obstructive azoospermia group, including epididymitis, efferent duct ectasia, and spermatocele (Table 1).

TRUS yielded significantly more common diagnoses suggesting an obstructive etiology (with distal obstruction in the male genital duct) in the obstructive azoospermia group, including prostatitis, midline prostatic cysts, a dilated seminal vesicle and/or ampulla of vas, and ejaculatory duct calcification (Table 2).

The diagnostic power of scrotal Doppler and TRUS in detecting azoospermia vs testicular biopsy is presented in Table 3. Using scrotal Doppler US in the functional azoospermia group yielded positive data suggesting a functional etiology in 123 of the 164 patients, for a sensitivity of 75% and specificity of 72%. In the second group with obstructive azoospermia, we found scrotal US data in accordance with obstructive etiology in 31 of 104 patients, for a sensitivity of 29.8% and specificity of 87%. TRUS yielded positive data suggesting an obstructive etiology in 47 of 104 patients (45%) with obstructive etiology, for a sensitivity of 45% and specificity of 83% in obstructive azoospermia, while in functional azoospermia the sensitivity and specificity of TRUS were 39% and 88% respectively. Scrotal Doppler US was more sensitive in detecting

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