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ORIGINAL ARTICLE

Male Infertility

The performance of transrectal ultrasound in the diagnosis of seminal vesicle defects: a comparison with magnetic resonance imaging

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Obstructive azoospermia (OA) is one of the most common causes of male infertility. Transrectal ultrasound (TRUS) has been used to diagnose OA for many years. From 2009 to 2013, we evaluated a prospective cohort of 1249 patients with suspected OA using TRUS. It was found that dilation of the ejaculatory duct (ED) (29.9%, 374/1249) was the most common cause of OA, followed by seminal vesicle (SV) abnormalities (28.5%, 356/1249). A total of 237 patients were diagnosed with congenital defects (agenesis and/or hypoplasia) of the SV, constituting more than half of the cases of SV disease in OA (19.0%, 237/1249). In contrast to ED, congenital defects of the SV could not be corrected with surgical treatment. Therefore, it is meaningful to compare TRUS and magnetic resonance imaging (MRI) for accurate diagnosis of SV defects. Among our patients, 30 with agenesis or/and hypoplasia of the SV on TRUS were further evaluated using pelvic MRI within 2 years, with the objective of verifying the TRUS results. The concordance rate for diagnosing congenital defects of the SV was 73.3% (22/30). We concluded that TRUS is a reliable and convenient method for diagnosing agenesis or hypoplasia of the SV in OA patients with a high concordance with MRI while MRI is useful in patients with inconclusive TRUS findings.

INTRODUCTION

About 15% of couples are unable to conceive after 1 year of unprotected intercourse. It has been reported that 20% of infertility is male related, and 30%–40% is related to combined male-female factors.[1] The main cause of male infertility is low semen quality. Complete agenesis of sperm in the ejaculate is called azoospermia and is present in about 10%–15% of infertile men.[2] The etiology of azoospermia is extremely complex. Azoospermia is classified clinically as obstructive azoospermia (OA) and non-OA (NOA). Most OA patients have a normal testicular spermatogenesis. Microsurgical epididymal sperm aspiration or testicular sperm extraction combined with intracytoplasmic sperm injection can be performed for the treatment of this type of infertility.[3,4] In NOA, spermatogenesis is markedly diminished and there is little possibility of finding mature spermatozoon cells. The lack of mature sperm results in poor treatment outcomes. Exploring the causes of azoospermia and evaluating the status of testicular spermatogenic function can help identify the optimal treatment strategy for infertile couples.

Ultrasonography is widely used in the evaluation of male infertility.[5] Scrotal ultrasound (US) can be used to directly observe the testis, epididymis, spermatic vein and proximal vas deferens.[6] Using transrectal US (TRUS), it is possible to visualize the distal genital tract including the prostate, vas ampulla, seminal vesicles (SVs) and

ejaculatory ducts (EDs). TRUS has been identified as an important diagnostic tool in the evaluation of azoospermia, particularly when associated with low ejaculate volume.[7,8] TRUS is currently found to be more sensitive in detecting OA than scrotal US.[9] Magnetic resonance imaging (MRI) is characterized by high soft tissue contrast and multiplanar capability, and is superior to TRUS in evaluating the vas ampulla, SVs and EDs.[6] The use of MRI also provides more detailed visualization of the intra-abdominal segment of the vas deferens, which is important in the diagnosis of the congenital absence of the vas deferens.[10] Although MRI has many advantages, the high equipment and patient costs and the time delay before the results are available prevent it from being used as the initial evaluation method in male infertility.[6,11,12] Consequently, TRUS is more commonly used in the clinical diagnosis of OA because of its lower cost and ease of use. However, few studies have been carried out regarding the accuracy of TRUS in the diagnosis of OA.

The aim of the present study was to investigate the utility of TRUS in the diagnosis of OA. Our secondary aim was to assess the concordance of TRUS findings with those obtained using MRI in the detection of congenital defects of the SV in the subset of patients who underwent both imaging modalities. In addition, the reliability of TRUS in the evaluation of this disease was also assessed.

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PATIENTS AND METHODS

Study population

We enrolled a prospective cohort of patients who were suspected of having OA in our center from May 2009 to May 2013. The criteria for OA were: (i) a chief complaint of infertility, with more than two semen analyses showing a low ejaculate volume (<2 ml), azoospermia and a low semen pH value (pH < 7); (ii) seminal plasma biochemistry testing that detected fructose and alpha-glucosidase levels of 0 or that were obviously lower than normal, and physical examination and scrotum US demonstrating a normal testis volume (US-derived volume of 15–23 ml);[13,14] (iii) testicular biopsy showing normal spermatogenesis; and (iv) testosterone (normal value: 3.5–9.8 ng ml^{-1}), follicle-stimulating hormone (FSH; normal value: 1.00–8.00 IU l^{-1}) and luteinizing hormone (normal value: 2.00–12.00 IU l^{-1}) levels in the normal range. Patients with testicular atrophy, cryptorchidism and other chronic organ diseases were excluded. This study was approved by the Institutional Review Board and all patients provided informed consent.

Transrectal ultrasound protocol

Transrectal ultrasound was performed using a 5.5–7.5 MHz, double plane probe (LOGIQ-400, Doppler Ultrasonic Diagnostic Apparatus, GE Company, Los Angeles, California, USA) in our department. Patients were instructed to abstain from sexual intercourse for 1 week before TRUS examination. They were placed in the left lateral decubitus position during the examination. The prostate was examined in the transverse and sagittal planes. Prostate volume was calculated, and the EDs identified. Normally, the ED was seldom observed using TRUS. However, when dilation occurred, the tubular structure could be seen.[15] When the measurement of the ED diameter was >1.6 mm, we defined it as a dilated ED.[16] SVs had a bow-tie appearance in transverse scans and an oval configuration.[17] SVs were observed in relation to their shape, echo intensity and anteroposterior/left-right diameters. Evaluation of the SVs was performed in the transverse and sagittal planes. The description of the echo texture and characteristics of the SV was consistent with previous studies.[18,19] SV hypoplasia was defined as the maximum width of <50% of normal, or <5 mm[8]. On the other hand, when the maximum width was >50% of normal, or >15 mm, we defined the SV as being dilated.[19,20] Mullerian cysts are funnel-shaped and usually located in the midline, between the posterior urethra and the verumontanum.[21]

Magnetic resonance imaging examination

Thirty patients diagnosed with agenesis or hypoplasia of the SV using TRUS imaging required MRI evaluation in <2 years of diagnosis. Patients were examined in the supine position. A standard six-channel, torso phased-array coil was used for imaging (3.0T, Siemens Magnetom TrioTim, Munich, Germany). The MRI protocols included T1-weighted (TR/TE600/21) axial images (slice thickness 3 mm; slice interval 0.4 mm) and fat-saturated T2-weighted (TR/TE 3500/95) images. Axial, coronal and sagittal images of the pelvis were obtained. Contrast-enhanced images (axial, coronal and sagittal) were acquired after intravenous bolus injection of paramagnetic gadolinium chelate (0.1 mmol of gadopentetate dimeglumine per kilogram body weight).

RESULTS

A total of 1249 male patients participated in the study. Patient age ranged from 26 to 47 years. All characteristics are listed in **Table 1**. Findings from TRUS imaging are detailed in **Table 2**. The most common findings in men with OA were dilation of the EDs (29.9%, 374/1249),

SV abnormalities (28.5%, 356/1249) and the presence of prostate midline cysts (22.3%, 279/1249). SV dilation and congenital defects were seen in 8.0% and 19.0% of the patients, respectively. A total of 56 patients had calcifications in the verumontanum or EDs. **Table 3** shows the findings in 30 patients with agenesis or hypoplasia of the SV on TRUS who underwent MRI. Five (numbers 7, 20, 21, 25 and 30) had unilateral congenital defects of the SV diagnosed using TRUS, but bilateral SV defects diagnosed using MRI. Three patients (numbers 13, 15 and 23) had seminal vesiculitis diagnosed using MRI, and SV agenesis and hypoplasia diagnosed using TRUS (**Figure 1**). The concordance rate for diagnosing congenital SV defects between these two methods was 73.3% (22/30).

Table 1: Patient characteristics

Parameters	Values (mean±s.d.)
Age (year)	28±14
BMI	23.7±2.9
Testosterone (ng ml^{-1})	5.6±3.3
FSH (IU l^{-1})	4.3±3.8
LH (IU l^{-1})	3.6±2.3
Ejaculate volume (ml)	1.8±1.1
Semen pH	6.8±0.3
Fructose (μmol per sample)	8.1±5.3
Alpha-glucosidase (mU per sample)	12.9±6.8
Prostate volume (ml)	13.9±6.7
SV anteroposterior diameters (mm)	
Right	9.7±2.7
Left	10.3±3.4
SV longitudinal diameters (mm)	
Right	22.1±6.5
Left	23.4±5.9

SD: standard deviation; BMI: body mass index; FSH: follicle-stimulating hormone; LH: luteinizing hormone; SV: seminal vesicle

Table 2: The TRUS findings in male OA

TRUS findings	n
Dilation of ED	374
Prostate midline cyst	279
Müllerian cyst	59
Prostate cyst	34
ED cyst	186
Abnormalities of SV	356
Congenital defects	237
Bilateral hypoplasia of SV	67
Bilateral agenesis of SV	74
Unilateral hypoplasia, contralateral agenesis of SV	36
Unilateral absence, contralateral normal SV	33
Unilateral hypoplasia, contralateral normal SV	27
Dilation	100
Bilateral dilation of SV	54
Unilateral dilation of SV	46
SV cyst	19
Calcification	59
Calcification of verumontanum	32
ED calcification	27
Total number of pathological findings	1068
Total number of normal findings	282

ED: ejaculatory duct; TRUS: transrectal ultrasound; SV: seminal vesicle; OA: obstructive azoospermia. The total number of pathological findings was 1068. More than one abnormal characteristic per patient was found in 78 patients

Table 3: Comparison of TRUS and MRI

ID	Age	TRUS		MRI	
		Right	Left	Right	Left
1	26	Hypoplasia	Hypoplasia	Agenesis or hypoplasia	Agenesis or hypoplasia
2	22	Hypoplasia	Normal	Agenesis	Normal
3	27	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
4	32	Agenesis	Hypoplasia	Agenesis	Agenesis
5	33	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
6	28	Hypoplasia	Agenesis	Agenesis	Agenesis
7	23	Hypoplasia	Normal	Hypoplasia	Hypoplasia
8	24	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
9	36	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
10	27	Agenesis	Hypoplasia	Hypoplasia	Hypoplasia
11	27	Hypoplasia	Agenesis	Hypoplasia	Hypoplasia
12	27	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
13	26	Agenesis	Agenesis	Agenesis or hypoplasia	Seminal vesiculitis
14	21	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
15	24	Hypoplasia	Agenesis or hypoplasia	Hypoplasia	Seminal vesiculitis
16	30	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
17	33	Agenesis	Agenesis	Hypoplasia	Hypoplasia
18	40	Hypoplasia	Agenesis	Hypoplasia	Hypoplasia
19	26	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
20	22	Hypoplasia	Normal	Hypoplasia	Hypoplasia
21	26	Agenesis	Normal	Hypoplasia	Hypoplasia and seminal vesiculitis
22	28	Hypoplasia	Agenesis	Agenesis	Hypoplasia and seminal vesiculitis
23	27	Agenesis	Hypoplasia	Agenesis	Seminal vesiculitis
24	29	Hypoplasia	Hypoplasia or agenesis	Hypoplasia	Hypoplasia
25	32	Normal	Hypoplasia	Agenesis	Agenesis
26	26	Hypoplasia	Hypoplasia or agenesis	Hypoplasia	Hypoplasia
27	34	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
28	28	Hypoplasia	Hypoplasia	Hypoplasia	Hypoplasia
29	31	Agenesis	Hypoplasia	Agenesis	Agenesis
30	21	Normal	Agenesis	Agenesis	Agenesis

Case 7, 20, 21, 25 and 30 show conflicting findings on TRUS and MRI. Case 13, 15 and 23 show different findings associated with seminal vesiculitis. TRUS: transrectal ultrasound; MRI: magnetic resonance imaging

DISCUSSION

The development of assisted reproductive techniques has changed the management of infertile couples, allowing more couples to be treated. Treatment of male infertility has resulted in a >50% birth rate.[21] Impaired sperm production and function are the main reasons for male infertility. Impaired sperm production can occur because of problems at the pretesticular, posttesticular or testicular level. Pretesticular level disorders include hypogonadotropic hypogonadism, coital disorders and ejaculatory disorders. Primary testicular dysfunction constitutes about 75% of all male infertility. Cryptorchidism, orchitis, testis trauma, medications and genetic disorders are common etiological factors.[22] Varicoceles are considered a phenomenon associated with male infertility because of their effect on spermatogenesis.[23] Posttesticular etiological factors include obstructive lesions of the seminal tract, infections, inflammatory diseases of the accessory glands and autoimmune infertility.[22]

Patients were observed in the current study from 2009 according to the WHO 1999 criteria. To further distinguish between obstructive and
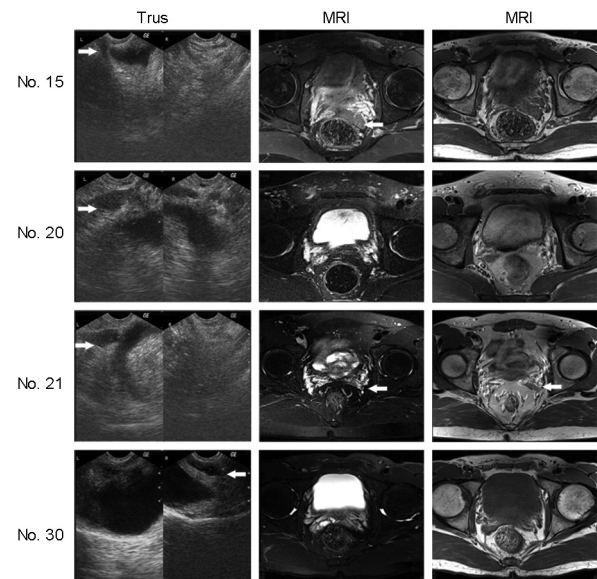
Figure 1: Patient number 15 – Transrectal ultrasound (TRUS) image showing left seminal vesicle (SV) agenesis or hypoplasia (arrow). The magnetic resonance imaging (MRI) was compatible with seminal vesiculitis (arrow). Patients 20 and 30 – The SVs appeared unilaterally normal on TRUS images (arrow), while MRI demonstrated agenesis or hypoplasia (arrow) on the same side. Patient 21 – A normal left SV can be seen on TRUS image (arrow), while the MRI was interpreted as hypoplasia of the SV and seminal vesiculitis.

nonobstructive causes of azoospermia, patients with normal testicular size and normal serum FSH level were required for testis biopsy; this strategy is also consistent with the American Urological Association male infertility guidelines.[24] We found the most common radiologic finding in OA to be dilation of the ED. Distal obstruction, congenital malformations or pressure originating from local inflammation can lead to dilation.[16] We found that the dilation of the ED also occasionally consisted of dilation of SVs (unilateral or bilateral). Cysts of the Müllerian duct or ED might also contribute to the dilation of the ED.

The SVs are a pair of accessory glands that are critical to normal male reproductive function. SV secretions are necessary for semen coagulation, the promotion of sperm motility, increases in the stability of sperm chromatin, and the suppression of immune activity in the female reproductive tract. Hypofunctioning SVs might be an important factor in male infertility.[25] Recently, Lotti *et al*.[17] reported that the SV ejection fraction (SVEF) could be used to assess SV emptying. In the present study, a series of SV parameters were studied in detail with the aim of evaluating the volume and emptying characteristics of the SV. As a new parameter, SVEF has been identified for assessing SV emptying. A cut-off value of 21.6% for the reduction in the SVEF was confirmed to correlate with prostate-vesicular and epididymal US abnormalities. In fact, to date, few studies have focused on the SV volume. According to the study of Lotti *et al*.[17] SV volume and SVEF, instead of the traditionally used anterior and posterior diameters, seem to be more useful in assessing SV emptying and should be advocated. More interestingly, this parameter might change in infertile patients with type 2 diabetes mellitus, which indicates further investigation of SV US features in diabetes mellitus will be necessary for future studies.[26] We analyzed the TRUS results from 1249 patients and found abnormal SVs (28.5%, 356/1249) to be the second most common US finding. Androgen is necessary for the growth of the SV. Increasing endogenous

testosterone production can increase SV secretory activity.[27] Rat castration is associated with a decrease in SV blood flow and density of the capillary vessels.[28,29] Congenital SV agenesis or hypoplasia is associated with mutations in the *CFTR* gene. Mice with a homozygous or heterozygous deletion of the *ARID4A* gene have SV agenesis.[30] This finding has not yet been observed in humans. Many patients with congenital agenesis of the SV have normal spermatogenic function. Microsurgical epididymal sperm aspiration and testicular sperm extraction combined with intracytoplasmic sperm injection have been used to treat these patients.[31]

Evaluation of male infertility includes a full medical history, physical examination, and hormone and semen analysis. Scrotal ultrasonography, TRUS, MRI, vasography and seminal vesiculography have been used in adjunct imaging studies. Each method has its own advantages and indications. MRI effectively visualizes the anatomy of the prostate, SVs and vas deferens;[6,32] it also facilitates an objective examination and is reliable in the diagnosis of SV abnormalities. 1H magnetic resonance spectroscopy has been reported as a noninvasive method for identifying and localizing spermatogenesis in testes with NOA.[33] However, MRI is expensive and inconvenient, and is not routinely used in the initial evaluation. The use of TRUS for posttesticular diagnosis in patients with infertility is well established.[6] TRUS is especially recommended in patients with low seminal volume and those suspected of having SV obstruction.[9,20,31]

There have been few reports regarding the accuracy of TRUS in the evaluation of congenital defects of the SVs. The treatments for SV agenesis and hypoplasia are almost identical, and unfortunately this disease cannot be corrected by surgical treatment. For this reason, we combined SV agenesis and hypoplasia as congenital SV defects. Radiologic interpretation of each study was blinded to the results of the other study. We found that most diagnoses were identical (22/30). Three cases were indicated to have a normal SV on one side of the body and defects on the other side using TRUS, but were verified as having SV defects on both sides using MRI; it was shown that the apparently normal SVs on TRUS were proved to be a lump of vessels at the anatomical site of the SV. The low resolution of gray-scale sonography in distinguishing blood vessels may explain this difference. Color Doppler US might improve the sensitivity and specificity of male infertility evaluations. MRI also easily identifies seminal vesiculitis and associated hemorrhage that are missed using TRUS.[34,35] This could explain the diagnosis of seminal vesiculitis in three patients using MRI, but not TRUS. Certainly, according to the recent study of Lotti *et al*.[17] traditional definitions such as SV dilation and hypoplasia, imaged using either US or MRI, were not as effective as the SVEF in evaluating SV emptying. More studies involving this new parameter in comparisons between TRUS and MRI in OA will be required in the future.

Some limitations need to be considered regarding our study. First, since this work began in May 2009, we did not update the criteria for low ejaculate volume (<1.5 ml), which was subsequently recommended by WHO in 2010. Second, as the abnormal karyotype or Y chromosome microdeletion are most likely to appear in NOA and severe oligospermia,[36] we did not include an analysis of these genomic abnormalities in the current study.

Taken together in our study, we found that SV agenesis and hypoplasia were important causes of OA. TRUS was found to be a reliable, convenient and economic modality for the diagnosis of agenesis or hypoplasia of the SV. MRI might only be required for patients where the TRUS findings were not conclusive. More investigations need to be carried out in the future.

AUTHOR CONTRIBUTIONS

XC participated in data collection, carried out data evaluation and drafted the manuscript. HW was involved in raw data collection. RPW, HL, XPM, CQM and HZZ helped with the TRUS and MRI analysis. SPQ participated in study coordination. DHW conceived of the study, participated in its design and coordination, and helped to draft the manuscript. All authors have read and approved the final version of the manuscript.

COMPETING INTERESTS

All authors declare no competing interests.

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