A PROSPECTIVE COMPARISON OF 3 DIAGNOSTIC METHODS TO EVALUATE EJACULATORY DUCT OBSTRUCTION

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ABSTRACT

Purpose: Various diagnostic tests are available to evaluate patients with ejaculatory duct obstruction (EDO). However, the most accurate diagnostic technique, defined as the one that best predicts a successful outcome after ejaculatory duct resection, is unclear. We prospectively performed transrectal ultrasound (TRUS) and 3 other tests in men with EDO and determined their relative value in this diagnosis.

Materials and Methods: Patients with suspected EDO on clinical evaluation that included TRUS proceeded to further intraoperative evaluation with duct chromotubation, seminal vesicle aspiration and seminal vesiculography. A comparative analysis of findings from each technique was performed and the success of subsequent transurethral resection procedures was assessed.

Results: All 25 patients had evidence of EDO on diagnostic TRUS, a finding that merited further evaluation with other modalities. However, TRUS findings correlated poorly with those of the other diagnostic tests. Obstruction on TRUS was confirmed in only 52%, 48% and 36% of vesiculography, seminal vesicle aspiration and duct chromotubation studies, respectively. A better correlation was observed between the dynamic tests of duct chromotubation and seminal vesiculography. Based on all diagnostic tests only 12 patients (48%) proceeded to duct resection, of whom 10 (83%) showed significant improvement in semen analysis parameters or clinical symptoms after the procedure.

Conclusions: A comparative analysis of 4 diagnostic techniques suggests that TRUS alone has poor specificity for EDO evaluation. Incorporating dynamic tests into the algorithm of EDO diagnosis may decrease unnecessary duct resection procedures and improve the success of the resection procedures that are indicated.

KEY WORDS: testis; ejaculatory ducts; spermatozoa; ultrasound, high-intensity focused, transrectal; infertility, male

Eiaculatory duct obstruction (EDO) is a cause of infertility in 1% to 5% of infertile men.¹ It is suspected in patients with normal, palpable vasa deferentia and semen analyses that reveal low ejaculate volumes combined with low or normal sperm concentration and low or absent motility.² Ejaculatory duct obstruction also presents as hemospermia and painful ejaculation. The causes of EDO are well described, including midline or eccentric cysts, duct calcification or stones and blockage due to post-infectious or postoperative scar tissue.¹ For affected patients transurethral resection of the obstructed ejaculatory ducts (TURED) durably improves semen quality and decreases urological symptoms.³ However, TURED is also associated with potential complications, including watery (urine) ejaculate, epididymitis and rarely urinary incontinence.⁴ Such risks emphasize the important role of careful diagnosis and patient selection in this condition.

The optimal method to evaluate ejaculatory duct obstruction is poorly defined. Transscrotal vasography is the most invasive technique used to diagnose EDO. Through antegrade or retrograde injection of contrast medium into the vas deferens or seminal vesicle (SV) vasography provides static anatomical and dynamic information about the reproductive tract. In the last decade transrectal ultrasonography (TRUS) has been widely used to evaluate EDO.^{5,6} Although it is less invasive than vasography, TRUS provides only anatomical

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information concerning the static dimensions and positions of reproductive tract organs. Indeed, the presence or absence of certain anatomical findings does not correlate well with true physical obstruction of the ejaculatory ducts.⁶ For example, TRUS accurately detects SV enlargement but not all patients with EDO have this finding. Also, not all patients with dilated SVs have EDO. Thus, although it is minimally invasive, TRUS may not be the best method to detect EDO.

SV sperm aspiration, and SV and ejaculatory duct chromotubation have also been used to diagnose EDO.⁷ The finding of sperm in aspirated SV fluid is suggestive of EDO and permits the differentiation of normal from obstructed ducts.⁸ Likewise urethral washout of colored reagents such as indigo carmine after TRUS guided antegrade injection of the SVs and ejaculatory ducts (chromotubation) may provide static and dynamic evidence of EDO.9 To our knowledge the relationship between and the value of these diagnostic techniques in EDO management is undefined. In this study we prospectively evaluated how TRUS findings compare with vasography, SV aspiration and chromotubation in a cohort of men with suspected EDO.

MATERIALS AND METHODS

Patient diagnostic algorithm. Each of 25 subjects provided a urological history and underwent physical examination. EDO was suspected in patients with 1 or more of certain clinical symptoms, including hemospermia, painful ejaculation and/or infertility with characteristic seminal findings of low volume azoospermia or low volume asthenospermia (motility less than 30%) according to 1992 WHO guidelines. If ejaculatory duct obstruction were suspected, a diagnostic

TRUS was performed by a single investigator (KS). Table 1 lists TRUS findings considered abnormal and warranting further evaluation.

Patients with abnormal diagnostic TRUS were offered further diagnostic evaluation under general or spinal anesthesia. The figure shows the diagnostic algorithm. Each patient underwent repeat transrectal ultrasound, SV aspiration, seminal vesiculography and chromotubation of the ejaculatory ducts, followed by TURED if obstruction was diagnosed.

TRUS. Initial diagnostic TRUS was performed with the patient in the lateral decubitus position using a high resolution 7.5 MHz probe (Siemens, Issaquah, Washington). Using anesthesia TRUS was again performed in the transverse and longitudinal planes with the patient in the lithotomy position. Typically prostatic hypoechogenicity and size, SV width and ejaculatory duct diameter were assessed. Table 1 lists TRUS criteria considered suspicious for EDO.

TRUS-SV sperm aspiration. As proposed by Jarow,⁸ patients were asked to ejaculate within 24 hours of the scheduled examination under anesthesia to optimize differences in sperm aspiration findings between normal and obstructed patients. A simple bowel preparation was also prescribed that included a Fleet enema and 500 mg of ciprofloxacin (Bayer, West Haven, Connecticut) ingested within 8 hours of the procedure. Under TRUS guidance the SVs were accessed transrectally using a 17 cm 22 gauge spinal needle (Becton Dickinson, Franklin Lakes, New Jersey). Fluid was withdrawn for inspection under bright field microscopy at 400× magnification for the presence or absence of sperm. The finding of greater than 3 sperm per high power field was suggestive of obstruction.¹⁰

TRUS-seminal vesiculography. Immediately following SV sperm aspiration and scout plain x-ray of the kidneys, ureters and bladder each patient underwent seminal vesiculography through the pre-placed 30 cm spinal needle. Approximately 5 ml 50/50 volume per volume Hypaque (Amersham Health, Piscataway, New Jersey)-saline solution were injected in an antegrade direction into each SV. Prior to injection a small Foley catheter was placed transurethrally with 5 ml water in the balloon and light traction on the catheter to occlude the bladder neck. EDO was defined as the absence of contrast medium within the prostatic urethra after injection. This procedure was repeated on the contralateral side.

Chromotubation of the ejaculatory ducts. Following seminal vesiculography transrectal SV chromotubation was done. In this procedure, which was performed concurrent with cystoscopy, 5 ml indigo carmine or methylene blue diluted 1:5 with normal saline were injected in an antegrade direction into each SV. Under direct cystoscopic visualization of the verumontanum and ejaculatory duct orifices the absence of methylene blue emission from the duct was deemed suspicious for EDO. This procedure was repeated on the contralateral side.

If 1 or more of the described techniques suggested EDO, we proceeded with unilateral or bilateral TURED, as previously described.² A 50% increase in the total motile sperm count using the equation, volume \times concentration \times motile fraction, or the resolution of clinical symptoms defined improvement after TURED.



Diagnostic algorithm followed for all study patients with suspected EDO based on clinical history and TRUS findings. Decision to perform duct resection was based on findings of all tests.

RESULTS

Patient characteristics. A total of 25 consecutive patients suspected of having EDO based on history and initial TRUS findings were enrolled during 4 years. Mean patient age was 36 years (range 16 to 52). The presentation was infertility in 18 patients (72%), painful ejaculation in 2 (8%), hemospermia and azoospermia in 2 (8%), pain in 2 (8%) and hemospermia in 1 (4%).

Table 1 lists the frequency of findings detected on TRUS with ejaculatory duct dilatation the most common abnormality observed (18 of 25 cases). Of all patients 8 (32%) had 1 TRUS finding suggestive of obstruction, 9 (36%) had 2 abnormal findings, 5 (20%) had 3 findings suggestive of obstruction and 3 (12%) had 4 signs of obstruction.

Comparison of diagnostic techniques. All patients were deemed to have findings suggestive of EDO on initial TRUS. We compared the ability of adjunctive diagnostic techniques to confirm or refute the TRUS diagnosis. Tables 2 to 4 list patient findings and the results of diagnostic testing.

Initial TRUS findings poorly predicted the results of other diagnostic tests (table 2). Only 13 of the 25 patients (52%) were deemed to have obstruction on vesiculography, 12 (48%) had it on SV aspiration and 9 (36%) had it on chromotubation. Eight patients (32%) had no abnormal test other than TRUS. SV aspiration findings also correlated poorly with those of chromotubation and vesiculography. Notably obstruction based on chromotubation correlated well with ob-

TABLE 2. TRUS and other techniques for EDO

	No. TRUS (%)	No. SV Aspiration (%)	Chromotubation (%)	No. Vesiculography (%)
No. obstructed pts	25	12	9	13
SV aspiration:				
Obstruction	12(48)		6 (67)	8 (62)
No obstruction	13(52)		3 (33)	5(38)
Chromotubation:				
Obstruction	9 (36)	6 (50)		9 (69)
No obstruction	16 (64)	6 (50)		4(31)
Vesiculography:				
Obstruction	13 (52)	8 (67)	9 (100)	
No obstruction	12(48)	4(33)	0	

 TABLE 1. Type and frequency of TRUS findings in patients with suspected ejaculatory duct obstruction

Findings	No. Single Finding (%)	No. Multiple Findings (%)			
Ejaculatory ducts dilated greater than 2.3 mm	3 (12)	15 (60)			
Seminal vesicle enlarged greater than 1.5 cm	1 (4)	15 (60)			
Ejaculatory duct calcification/stones	1 (4)	7(28)			
Midline müllerian cysts	1 (4)	10 (40)			
Eccentric wolffian cysts	2 (8)	0			

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Pt No.	Vol (ml)	Density (million/ml)	% Motility	Total Motile Sperm Count (millions)
Preop:				
1	0.5	0	0	0
2	0.25	43	1	1.2
3	0.03	0	0	0
4	0.8	214	9	15.4
5	0.4	22	45	3.9
6	1.8	0.9	64	10.4
7	0.4	19	8	6.1
8	2.9	4	18	2.1
Postop:				
1	1.9	51	65	63
2	4	24.4	57	55.6
3	1.5	37	46	25.5
4*	1.9	183	3.5	12.2
5	2.3	21	40	19.3
6	4.1	27	44	48.7
7	6.3	62	18	70.3
8*	57	1	40	23

* No total motile sperm count improvement greater than 50%.

TABLE 4. Results of diagnostic tests

Pt No.	Aspiration	TRUS	Vesiculography	Chromotubation
1	Obstructed	Obstructed	Obstructed	Obstructed
2	Obstructed	Obstructed	Obstructed	Obstructed
3	Obstructed	Obstructed	Obstructed	Obstructed
4	Obstructed	Obstructed	Patent	Patent
5	Obstructed	Obstructed	Obstructed	Obstructed
6	Obstructed	Obstructed	Obstructed	Obstructed
7	Obstructed	Obstructed	Obstructed	Obstructed
8	Patent	Obstructed	Patent	Patent

struction on vesiculography (100%). When obstruction was suggested by vesiculography, it was confirmed equally but not consistently well with chromotubation (69%) and SV aspiration (62%).

TURED success and complications. Based simply on TRUS findings and clinical presentation all 25 patients would have proceeded to TURED. With the inclusion of other diagnostic techniques only 12 patients (48%) underwent TURED. Overall 10 of the 12 patients (83%) treated with TURED showed improvement postoperatively. Semen analyses were available before and after TURED in all 8 patients with infertility (table 3). In this cohort ejaculate volume normalized in all patients with low ejaculate volume preoperatively and 6 of the 8 (75%) showed improvement in semen quality. Mean ejaculate volume increased from 0.89 to 3.4 ml and the mean total number of ejaculated sperm improved from 3.5 million to 124 million. In 2 of the 12 patients TURED was performed for pain and they reported resolution of pain postoperatively. Two patients with hemospermia reported symptom resolution postoperatively. Two natural pregnancies were reported by patients after TURED. Each man had previously had infertility.

In men with infertility if the diagnostic findings of the dynamic test of chromotubation or vesiculography were considered individually in the decision to perform TURED, each predicted successful outcomes in all 8 successful TURED cases. TRUS alone would have predicted TURED success in 6 of 8 patients (75%) and SV aspiration alone would have predicted success in 7 of 8 (88%).

Four complications were noted in the 25 patients (16%), including 3 after TURED. Epididymitis following TURED resolved with antibiotic treatment. Two patients had limited hematuria requiring urological reevaluation and 1 who did not undergo TURED reported limited, low grade postoperative fever.

DISCUSSION

EDO is a complex and incompletely understood phenomenon. The reasons include not only the lack of a clear idea concerning the best way to make the diagnosis, but also the fact that the condition likely involves several different underlying pathological conditions. For example, our study in animal models led to the belief that some cases of ejaculatory duct obstruction may in fact represent a primary functional problem of the SVs and not involve physical obstruction of the ducts.¹¹ Such etiological complexity in this condition suggests that dynamic tests might add value to static tests and more accurately diagnose true EDO.

Of the modalities used to diagnose ejaculatory duct obstruction TRUS, magnetic resonance imaging¹² and SV aspiration¹³ are static tests that assess anatomical integrity. However, procedures such as vasography and SV chromotubation are considered dynamic in nature. Despite this wide variety of diagnostic techniques there have been no prospective comparative studies evaluating the sensitivity and specificity of these diagnostic tests in EDO. To our knowledge we report the first prospective comparative study of static and dynamic diagnostic tests for this urological condition.

Our data suggest that the use of TRUS as the only diagnostic modality leads to unnecessary and unsuccessful TURED procedures in cases clinically suspicious for EDO. Indeed, only 48% of the patients with positive TRUS findings eventually underwent TURED after further diagnostic testing. The addition of dynamic tests to the diagnostic algorithm for EDO showed that no physical obstruction exists in at least 50% of cases in which it is suggested by TRUS. This finding is in agreement with published clinical outcome data on patients who undergo TURED based on a TRUS diagnosis, of whom 30% to 35% show no improvement after surgery.¹⁴ In addition, by including dynamic tests in the decision to perform TURED improved outcomes were obtained in 83% of the cases, a value that compares favorably to that in previously published series. Lastly, if TURED were performed based simply on chromotubation or vesiculography findings, all successes and failures were accurately predicted. Briefly, these findings suggest an important role for dynamic diagnostic testing in patients with suspected EDO.

Despite the stated need for additional testing in EDO it is not clear from this study which test is the most appropriate to include. Evidence suggests that static tests (TRUS and SV aspiration) correlate poorly with dynamic tests (vesiculography and chromotubation) in EDO. Given this finding we observed that dynamic tests appeared to correlate better with SV aspiration than TRUS. In addition, the data suggest that dynamic tests correlate quite well with each other (vesiculography vs chromotubation). In men deemed to have obstruction on chromotubation all diagnoses were confirmed on vesiculography. Likewise, in men deemed to have obstruction on vesiculography the diagnosis was confirmed by chromotubation in 70%. Beyond this simple analysis it is difficult to ascertain the best dynamic test to include in the diagnostic algorithm of EDO.

The combination of findings that there is a poor correlation of static and dynamic tests and the fact that adding dynamic testing appears to improves outcomes after TURED suggests to us that functional EDO indeed exists clinically in men with EDO and it may require dynamic tests for an accurate diagnosis. Traditional static techniques to diagnose EDO appear unlikely to differentiate accurately between functional and physical obstruction.

Study limitations exist. Because of the rarity of the diagnosis patient accrual is slow and prohibits a comprehensive analysis of success in hundreds of men. Also, the choice of positive TRUS findings as part of the inclusion criteria eliminates the study of individuals who may in fact have EDO but without TRUS evidence of the condition. If anything, capture of this cohort would likely further decrease the accuracy of TRUS for the diagnosis of EDO. Even when seminal vesiculography or chromotubation show a patent ejaculatory duct, patients with dilated SVs or ejaculatory ducts may have stasis of semen, which results in semen quality deterioration. The diagnostic studies evaluated cannot assess partial obstruction or atonic properties in the ductal system, which may cause seminal fluid stasis. Another limitation is that transscrotal vasography was not included among the diagnostic tests evaluated. In addition, outcomes in this study were driven by 2 large variables, that is not only diagnostic, but also the surgical technique of EDO treatment. Finally, another limitation might be that the study included several different clinical presentations of EDO. However, there is currently no evidence that infertility, hematuria or pain present as different underlying pathological conditions in this condition.

CONCLUSIONS

TRUS may not be the most accurate way to diagnose EDO because it may have poor specificity compared with other diagnostic methods. As additional dynamic diagnostic tests, it appears that chromotubation of the ejaculatory ducts and seminal vesiculography offer greater specificity than TRUS for diagnosing EDO. Incorporating functional tests in diagnosing EDO increases the effectiveness of TURED. In addition, these techniques can differentially localize sites of obstruction to determine better individuals who might respond to TURED treatment.

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EDITORIAL COMMENTS

The authors expand our knowledge base in a poorly understood area of andrology. The 25 men in this prospective study of EDO had a variety of presenting complaints, ie hemospermia infertility and painful ejaculation, signifying the heterogeneity of this condition. Since the majority of these men had spermatozoa in their preoperative ejaculates, it does not indicate complete but a variation of partial EDO.

What is clear from this communication is that, as a screening tool, TRUS has low specificity (less than 50%) and additional dynamic tests are needed before considering TURED.^{1,2} As a corollary, 10 of 12 TURED were successful but there were still 4 minor complications (less than 30%).

Percutaneous vasography is no more invasive than transrectal SV and unfortunately it was not included in this study. Percutaneous vasography can use a combination of diluted hypaque and methylene blue for x-ray or direct cystoscopic viewing at TURED. In addition, if semen is not encountered at percutaneous entry into the vas deferens, secondary proximal (epididymal) obstruction must be considered in cases of obstructive azoospermia.

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EDO is an extremely rare but clinically important cause of male infertility, accounting for less than 1% of patients seen. The management of complete EDO is simplified since the results of diagnostic tests are unequivocal and patients are sterile in the absence of treatment. Patients with complete EDO have azoospermia, low ejaculate volume (with acidic pH), active spermatogenesis, sperm present in the ductal system proximal to the obstruction and complete obstruction on vasography. In contrast, patients with partial EDO have variable clinical findings and may be fertile without treatment, and there is no established method for diagnosis. In the absence of an agreed upon gold standard for diagnosis the outcome of therapy was appropriately used by the authors as the best determinant of whether a patient actually had obstruction. However, a flaw of this method of analysis is that a poor outcome may be reflective of a failure of treatment rather than a failure of diagnosis. Moreover, although it is understandable, the authors did not treat all patients entered into this study, hence prohibits full evaluation of these tests. The authors found that contrast medium and colored dye studies were the most accurate of the studies assessed and they had comparable results. It is not surprising that these tests had similar results since they are anatomical studies analogous to vasography. However, it is surprising to me that either of these tests was positive in oligospermic cases with partial obstruction since dye and contrast molecules are significantly smaller than sperm. In fact, the reason that partial obstruction is so difficult to diagnose is that vasography cannot distinguish between partial obstruction and the normal condition. The dye and contrast tests used in this study are not dynamic tests, as suggested by the authors. A true dynamic pressure flow study analogous to the Whitaker test has not yet been developed for the ejaculatory ducts. At this point I still consider partial EDO to be an investigational diagnosis and I caution against the over diagnosis and treatment of this controversial clinical entity.

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TRUS is often used to evaluate for EDO. I have noted, in fact, that TRUS is routinely used by some urologists on all of their patients with infertility, making it as integral to their evaluation as a history, physical examination, and 2 semen analyses. It is not unreasonable given literature that describes EDO as a common cause of infertility, urologist skill with a resectoscope, and dramatic results that have been reported for some patients. However, the enthusiasm for diagnosing EDO has been tempered by the lack of reliable TRUS criteria to make the diagnosis. In this study the authors tried to clarify how we diagnose EDO. They compared TRUS with SV aspiration (greater than 3 sperm per high power field suggests obstruction when the patient ejaculated less than 24 hours before examination) and 2 dynamic tests, namely seminal vesiculography and chromo-tubation of the ejaculatory ducts (injecting dye in the SVs and cystoscopically looking for efflux at the verumontanum). They found that TRUS is a poor method for diagnosing EDO and the addition of dynamic tests may help in the diagnosis.

There are some flaws to the study. Abnormal TRUS is part of the inclusion criteria and the authors admit that some patients may have EDO in the presence of normal ultrasound. It is also not clear how the authors selected 12 of 25 patients studied for TURED since 17 had some abnormal test besides TRUS, and yet only 12 of the 17 underwent treatment. I am also not sure why patient 8 with normal ejaculatory volume, and all 3 comparison tests showing him to have no unobstruction underwent TURED (tables 3 and 4). He seems unobstructed and is listed as having no improvement in his total motile sperm count, and yet the total motile sperm count increased 10-fold. Obviously, the selection of infertile patients for the evaluation and treatment of EDO still involves a sixth sense.

The bottom line is that EDO is likely not common. I would love to say that it is rare but since we have no gold standard to diagnose it, I cannot. We need to understand EDO and partial EDO better, and we need a better test to diagnose it. Until then I think that we should all approach EDO with some trepidation. It is 1 thing when someone has a low volume ejaculate, azoospermia and a large midline müllerian duct cyst on TRUS that is begging to be resected. If it does not work, you lose nothing, unless there is a complication in a healthy young male, of course. However, too often we are resecting someone who may or may not have EDO, and who has a low sperm concentration or sperm motility. You may convert these cases to azoospermia. I recommend in this era of escalating health care costs that we should be more selective when doing TRUS. I also recommend, in this era of litigation that we cautiously limit TURED to those with signs and symptoms of EDO in the presence of azoospermia, or total motile sperm counts too low to have much of a chance of pregnancy doing intrauterine insemination. If repeat cycles of intrauterine insemination have failed, ie TURED is a last resort before proceeding to in vitro fertilization and intracytoplasmic sperm injection. I look forward to the day when we can be less cautious, when we have a gold standard to make an accurate diagnosis. These authors have helped us toward that goal.

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REPLY BY AUTHORS

Our study is clearly not perfect but we believe that it is an important "first punch" effort to prospectively tackle the problem of how to make the difficult diagnosis of ejaculatory duct obstruction. What has become apparent from our report and the discussion it has generated is that 1) the actual prevalence of ejaculatory duct obstruction among healthy and infertile men is not clearly defined, 2) diagnostic TRUS suggests that more men have EDO than might really be the case, 3) adding a more "dynamic" diagnostic assessment of the ductal system (and we can argue what this might be) should improve our ability to diagnose and treat this condition accurately and 4) dynamic testing should also help us solve the problem of whether the "unicorn" cases of partial ejaculatory duct obstruction are real or mythical entities. Although not discussed in this article, our study revealed that partial obstruction due to unilateral duct blockage is a verifiable and treatable condition.

Thus, a framework has been built for us to advance our current understanding of this condition. If this small effort leads others to ponder and investigate this issue in a similarly rigorous way, then one cherished goal of publishing our results will have been accomplished.