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Multiple needle-pass percutaneous testicular sperm aspiration as first-line treatment in azoospermic men

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SUMMARY

Percutaneous testicular sperm aspiration (TESA) has been known for decades as a simple, minimally invasive approach to sperm retrieval in azoospermic men. Because of lower reported sperm retrieval rates (SRR) when compared with microdissection testicular sperm extraction (mTESE), many centers now use mTESE as the first choice for retrieving spermatozoa in nonobstructive azoospermia (NOA). Objectives of this study were to evaluate the outcome and safety of TESA and mTESE in the treatment of azoospermia and to investigate the usefulness of a prognostic TESA to individualize protocols for couples and limit the use of invasive testicular procedures. IRB approval was obtained to retrospectively evaluate 208 patients undergoing multiple needle-pass TESA between 1999 and 2014. Prognostic TESA was performed on 125 men with NOA and 82 with obstructive azoospermia (OA). Nine NOA men and 31 OA men with previously demonstrated spermatozoa had a subsequent therapeutic TESA while nine NOA men with a failed TESA proceeded to mTESE. Main outcome measures were complication rates and SRR. SRR of the prognostic TESA was 30% (38/125) for NOA men and 100% (82/82) for OA men. Eight/nine NOA men and 31/31 OA men had spermatozoa found for intracytoplasmic sperm injection in a subsequent therapeutic TESA. In nine NOA men in whom a TESA produced no spermatozoa, only one had spermatozoa found with mTESE. Overall complication rates of TESA and mTESE were 3% (7/267) and 21% (3/14), respectively. TESA provides reasonable SRR and is a safe procedure. Successful prognostic TESA indicates future success with therapeutic TESA. Men with a failed TESA have a limited chance of sperm retrieval using mTESE. Approaching azoospermic men with an initial prognostic TESA followed by either therapeutic TESA and/or mTESE is an efficient algorithm in the management of azoospermia and limits the use of more invasive procedures.

INTRODUCTION

Azoospermia is defined as the absence of spermatozoa in the ejaculate verified in at least two samples, including assessment of the centrifuged pellet (WHO 5th edition). The condition is observed in 1% of the general population and affects 10–15% of infertile men (Willott, 1982; Jarow *et al.*, 1989; Gudeloglu & Parekattil, 2013). Azoospermia is divided into obstructive azoospermia (OA) and nonobstructive azoospermia (NOA), of which the latter constitutes 60% (Willott, 1982; Jarow *et al.*, 1989; Gudeloglu & Parekattil, 2013).

In OA one can attempt reconstructive surgery of the efferent ducts to allow spermatozoa to reach the ejaculate (Wosnitzer & Goldstein, 2014). In non-reconstructible cases it is relatively simple to obtain spermatozoa from the testis or epididymis and the outcomes of the available surgical methods seem to be similar (Wald *et al.*, 2007). This is not the case in NOA where sperm production is either absent or markedly reduced. In NOA patients the focus has been on percutaneous testicular sperm aspiration (TESA), conventional open testicular sperm extraction (cTESE), and microdissection testicular sperm extraction (mTESE). However, no consensus on a sperm retrieval protocol for these men has been reached.

TESA is a minimally invasive option in which a biopsy needle is used to aspirate testicular tissue, usually under local anesthesia in a clinic setting. Meanwhile, cTESE is a more invasive open procedure, with the risk of complications in the form of testicular vessel damage (Schlegel, 2009). The more complex mTESE is also an open procedure but the risk of complications is reduced as less tissue is removed (Amer *et al.*, 2000; Okada *et al.*, 2002; Ramasamy *et al.*, 2005). Overall sperm retrieval rates (SRR) for TESA, cTESE, and mTESE are usually reported around 25%, 49%, and 52%, respectively, but significant variations exist (Donoso

et al., 2007; Dabaja & Schlegel, 2013; Deruyver *et al.*, 2014). These variations become apparent in studies comparing TESA and cTESE where SRR ranges from 11 to 60% in TESA and 43–72% in cTESE (Friedler *et al.*, 1997; Ezeh *et al.*, 1998; Rosenlund *et al.*, 1998; Khadra *et al.*, 2003; Hauser *et al.*, 2006; Houwen *et al.*, 2008). In studies comparing cTESE and mTESE, SRR ranges from 17 to 45% in cTESE and 43–63% in mTESE (Schlegel, 1999; Amer *et al.*, 2000; Okada *et al.*, 2002; Tsujimura *et al.*, 2002; Ramasamy *et al.*, 2005; Turunc *et al.*, 2010; Ghalayini *et al.*, 2011). However, although mTESE provides better SRR potential disadvantages include higher cost, longer procedure time, and use of general anesthesia.

Since 1999 we have approached NOA men and azoospermic men where clinical evidence was not completely indicative of either OA or NOA with an initial prognostic TESA in the clinic, and if favorable testing results are seen, we use the same sperm retrieval procedure for subsequent in vitro fertilization (IVF). If either the prognostic- or the therapeutic TESA fail, we offer mTESE. This protocol was established to individualize sperm retrieval for IVF to minimize cost and invasiveness.

The purpose of this study was to retrospectively evaluate this approach. To do so, we describe success rate after prognostic TESA, concordance of prognostic and therapeutic TESA results, success rate of mTESE after failed TESA and complication rates from the two procedures. Furthermore, we describe the effects of the surgical procedures on follicle-stimulating hormone (FSH) and testosterone and the relation between SRR and a number of clinical parameters.

MATERIALS AND METHODS

Patients

We reviewed records of azoospermic patients who underwent TESA at Briarwood Center for Reproductive Medicine, University of Michigan between April 1999 and January 2014.

In patients with normal ejaculation, azoospermia was confirmed in at least two semen analyses (SA). In patients with anejaculation, azoospermia was diagnosed on a SA obtained through either penile vibratory stimulation or electroejaculation when possible. If it was not possible to obtain a SA, patients were considered azoospermic by definition.

The diagnosis of OA/NOA was determined by the same experienced andrologist based on a full medical history, physical examination, hormonal evaluation, karyotype, Y chromosome microdeletion testing, and histopathological diagnosis. The general criteria for NOA were a combination of at least two of the following: testes <4 cm in length, follicle-stimulating hormone (FSH) ≥10 mIU/mL, and histology showing hypospermatogenesis (HS), maturation arrest (MA), or Sertoli cell-only syndrome (SCOS). The definition used for HS was all stages of spermatogenesis seen, but markedly decreased numbers of mature spermatids. Patients with AZF deletions, SCOS, or MA were grouped as NOA without regard to other criteria. If azoospermic patients did not fit our diagnostic requirements for NOA, they were grouped as OA.

Treatable causes of azoospermia were investigated and treatment initiated when deemed appropriate, before attempting sperm retrieval. Patients were excluded from the study when such treatments were successful.

Treatment algorithm

As described above, an initial prognostic TESA was performed in NOA men and azoospermic men where clinical evidence was not completely indicative of either OA or NOA. If the prognostic TESA was successful the procedure was repeated in future IVF cycles. If the prognostic TESA or the therapeutic TESA failed mTESE was offered to retrieve spermatozoa (Fig. 1a). Both TESA and mTESE were deemed successful if at least one spermatozoon was retrieved. All repeat procedures were separated by a time interval of at least 2 months (usually 6 months) to allow recovery of the testicular tissue.

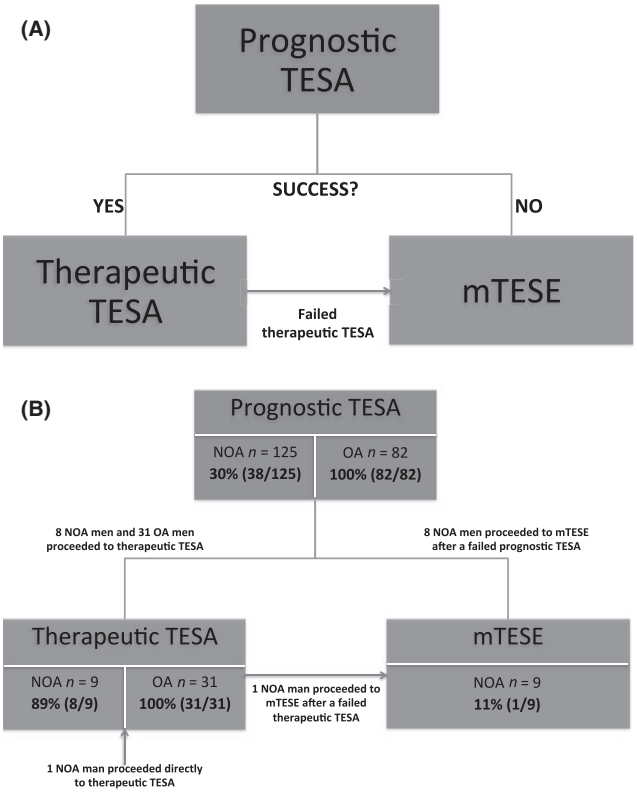
TESA procedure

The patient's scrotum is prepped with alcohol and draped. A spermatic cord block with 0.5% bupivacaine is instilled and a small skin wheal raised overlying the testis.

An 18 gauge needle is then introduced into each testis, and negative pressure applied with a 10 mL syringe. Multiple passes throughout the entire testis, numbering 50–100 passes, are made through a single percutaneous/tunical entry and continued until tissue is visible in the hub of the needle. This is removed by brisk extraction of the needle and pressure held to tamponade bleeding. The specimen is split and sent for standard histology in Bouin's solution, and in media for live sperm analysis by the assisted reproductive technology (ART) laboratory.

The tissue handling in the ART laboratory has previously been described in detail (Morris *et al.*, 2007). This includes microdispersion of the tubule contents, followed by initial examination and subsequent examinations at 24–48 h.

Figure 1 (A) Treatment algorithm. (B) Overall SRR in the prognostic TESA, therapeutic TESA, and mTESE.



mTESE procedure

Microdissection testicular sperm extraction is performed according to Schlegel (Schlegel, 1999). Some patients opted to receive local anesthesia only but in the majority of cases general anesthesia is used. Midline incision of the scrotum is made and carried down to the level of the tunica vaginalis, which is opened to deliver the testis. Equatorial incision is made and the testis bivalved. The operating microscope is used to identify plump-appearing seminiferous tubules, and biopsies are taken from these areas. These samples are examined by an embryologist in the operating room after initial gross dispersion by passing the tissue through a 24 gauge angiocatheter. The procedure is stopped if spermatozoa are found. If no plump tubules are found, random biopsies targeting every area of the testis are taken. If necessary the procedure is carried out on the contralateral testis, as well. Hemostasis is obtained with careful bipolar cautery, and the tunica albuginea and the tunica vaginalis are closed with a running 4-0 Vicryl. Standard scrotal closure is performed and gentle pressure dressing is applied.

Statistics and ethics

In patients with more than one prognostic TESA, only the first TESA was used in data analyses. As the number of therapeutic TESA/mTESE per prognostic TESA varied, only the initial therapeutic procedure was utilized for comparison to avoid skewing results. Descriptive statistics were performed for the majority of outcome parameters. Mann–Whitney *U*-test and Wilcoxon signed-rank test were used to compare baseline characteristics of NOA- and OA men, to compare clinical parameters of men with a successful- or failed TESA and to compare hormonal values before and after treatment attempts with TESA and mTESE. Institutional review board approval was obtained for this study.

RESULTS

A total of 208 azoospermic patients, including 126 NOA men and 82 OA men were included in the study. In 16 cases of anejaculation, azoospermia was diagnosed on at least one SA obtained through either penile vibratory stimulation or electroejaculation. In 21 cases, no SA could be obtained and 19 of these were diagnosed as OA whereas two were diagnosed as NOA based on the described criteria. Baseline characteristics of all men are shown in Table 1 together with etiologies of NOA and OA.

Table 1 Baseline data, histology and etiology of NOA and OA patients

Baseline characteristics			
	NOA (n = 126)	OA (n = 82)	*p*
Age at time of biopsy (years)	34.4 ± 7.2	38.4 ± 8.8	<0.001
Infertility time (months)	*n* = 58 30 ± 25	*n* = 29 34 ± 27	0.5
BMI (kg/m^2)	*n* = 90 30.2 ± 8.7	*n* = 58 28.3 ± 5.8	0.4
Testicular long axis (cm)	*n* = 102 3.16 ± 0.97	*n* = 52 4.56 ± 0.84	<0.001
FSH (mlU/mL)	*n* = 117 18.51 ± 11.60	*n* = 59 4.60 ± 3.06	<0.001
Testosterone (ng/mL)	*n* = 111 3.75 ± 1.68	*n* = 55 3.92 ± 1.96	0.7
LH (mlU/mL)	*n* = 102 7.93 ± 4.52	*n* = 46 3.68 ± 2.29	<0.001
PRL (ng/mL)	*n* = 35 9.27 ± 4.73	*n* = 13 11.02 ± 8.91	0.6

Histology		
	NOA (*n* = 79)	OA (*n* = 42)
# MA (%)	18 (23)	–
# SCOS (%)	31 (39)	–
# HS (%)	29 (37)	12 (29)
# Normal (%)	–	30 (71)
# Globally necrotic (%)	1 (1)	–

Etiology	
NOA (*n* = 126)	OA (*n* = 82)
58 Idiopathic (46%)	19 Iatrogenic (23%)
20 Cancer therapy (16%)[a]	19 Anejaeulation (23%)[b]
13 Cryptorchidism (10%)	14 Vasectomy (17%)
10 Spinal cord injury (8%)	13 CBAVD(16%)
7 AZFc del (6%)	11 Idiopathic (13%)
5 Karyotype[c] (4%)	4 Ejaculatory duct obstruct (5%)
3 Orchitis (2%)	2 Trauma (3%)
3 Anabolic steroid use (2%)	–
3 Klinefelter (2%)	–
2 Trauma[d] (2%)	–
1 AZFa+b del (1%)	–
1 Kallmanns (1%)	–

Values are mean ± SD unless stated otherwise. [a]Including chemotherapy, bone-marrow-transplant and radiation. [b]For practical reasons men with anejaculation due to spinal cord injury, diabetic neuropathy and spina bifida were grouped as OA if they did not fit the described general criteria for NOA. [c]Including 1 *46XY,15 ps+*, 1 *46XY,22pstk-ps*, 1 *46XY translocation 9qh+*, 1 *45XY,der(13;14)(q10;q10)* and 1 *46XY,t(3;21)*. [d]Direct scrotal trauma.

The overall SRR for OA and NOA men on prognostic TESA was 100% (82/82) and 30% (38/125), respectively (Fig. 1B). Thirty-one OA men proceeded to a therapeutic TESA and spermatozoa were found in all patients. Eight of the 38 NOA men with a successful prognostic TESA chose to proceed to a therapeutic TESA. One additional NOA man had an initial successful therapeutic TESA without having a prior prognostic TESA. On a later intracytoplasmic sperm injection (ICSI) cycle a second therapeutic TESA was unsuccessful and he therefore proceeded to subsequent mTESE cycles with successful outcomes. When including this additional patient as a success according to the study methods, the SRR for the therapeutic TESA in NOA men was 89% (8/9).

Altogether nine NOA men had mTESE after a failed prior TESA and spermatozoa were found in a single man making the SRR 11% for mTESE. In addition to these nine men, two men decided not to follow the presented treatment algorithm before having mTESE; one NOA man underwent a successful mTESE after a successful prognostic TESA and one OA man opted for a mTESE after a successful therapeutic TESA with a subsequent failed ICSI attempt. Table 2 shows SRR in NOA men related to different clinical parameters. There was no statistical significant difference in age, pre-TESA testosterone, pre-TESA FSH, testis size, and BMI (p = 0.5, 0.5, 0.7, 0.7, and 0.3, respectively) between the NOA men with a successful prognostic TESA and the NOA men with an unsuccessful prognostic TESA (data now shown). However, the histological patterns between the NOA men with a successful prognostic TESA and the NOA men with an unsuccessful prognostic TESA was statistically significant different ($p < 0.001$). Among NOA men with a successful prognostic TESA 82% had HS, 9% had SCOS, and 9% had MA. Among NOA men with an unsuccessful prognostic TESA 51% had SCOS, 28% had

Table 2 Subdivision of SRR following prognostic TESA in NOA men

125 NOA men[a]	
BMI (kg/m^2)	*n* = 89
BMI ≤ 25	14% (4/28)
25 < BMI ≤ 30	36% (8/22)
30 < BMI ≤ 35	23% (5/22)
BMI > 35	35% (6/17)
Testicular long axis (cm)[b]	*n* = 101
Size ≤ 3	29% (17/59)
3 < size ≤ 4	22% (6/27)
Size > 4	40% (6/15)
FSH (mIU/mL)	*n* = 116
FSH ≤ 10	23% (7/30)
I0 < FSH ≤ 20	46% (20/44)
20 < FSH ≤ 30	22% (5/23)
FSH > 30	26% (5/19)
Histology	*n* = 79
MA	11% (2/18)
SCOS	7% (2/31)
HS	60% (18/30)
Etiology of NOA	*n* = 125
Idiopathic	22% (13/58)
Cancer treatment	26% (5/19)
Cryptorchidism	69% (9/13)
Spinal cord injury	30% (3/10)
AZF del	29% (2/7)
Karyotype	40% (2/5)
Orchitis	0% (0/3)
Anabolic steroid use	67% (2/3)
Klinefelter	0% (0/3)
Trauma	100% (2/2)
AZFa+b del	0% (0/1)
Kallmanns	0% (0/1)
Failed prior TESE	*n* = 125
No prior TESE[c]	33% (38/116)
1 prior TESE	0% (0/9)

[a]One NOA man not included since he did not have a prognostic TESA. [b]If not bilaterally equal the largest was used for analysis. [c]Only biopsies with the purpose of retrieving sperm are included.

MA, and 21% had HS (data not shown). Pregnancy outcomes are presented in supplemental Table 1.

Including repeat procedures we performed a total of 267 TESA on 208 men. Following these 267 TESA we experienced no major complications with an overall complication rate of 3% (7/267). Three men experienced a vasovagal syncope during the procedure, three men developed a scrotal hematoma, and one man developed a spermatic cord hematoma. The four hematomas were managed by applying scrotal support and administering NSAID. Following TESA, FSH increased from 24.52 ± 17.52 (mean ± SD) to 31.65 ± 15.90 mIU/mL (p = 0.03, n = 12) measured 29 ± 28 months after TESA, whereas no statistically significant difference was seen in testosterone levels before (3.54 ± 1.79 ng/mL) vs. after (4.52 ± 2.19 ng/mL) TESA (p = 0.24, n = 18) measured 19 ± 25 months after TESA.

Including repeat procedures we performed 14 mTESE with an overall complication rate of 21% (3/14). One man was unable to walk because of pain and was treated with IV pain medicine in the emergency room on day two post-operation. One man developed scrotal infection and was treated with IV antibiotics and scrotal abscess drainage. He also developed de novo androgen deficiency (occurrence of hypogonadism following mTESE that was not present before mTESE). One man experienced desaturation while in the recovery room, possibly because of aspiration, and later developed de novo androgen deficiency. Following mTESE there was a decrease in testosterone from 3.62 ± 1.12 to 2.54 ± 1.29 ng/mL (p = 0.047, n = 7) measured 9 ± 18 months after mTESE. No statistically significant difference was seen in FSH levels before (15.57 ± 11.71 mIU/mL) vs. after (61.23 ± 46.85 mIU/mL) mTESE (p = 0.25, n = 3) measured 18 ± 27 months after mTESE. All patients undergoing TESA or mTESE recovered fully with the exception of two mTESE subjects who have ongoing hypogonadism requiring testosterone supplementation.

DISCUSSION

This study evaluates SRR in a prognostic TESA followed by a decision to proceed with therapeutic TESA or mTESE depending on individual results. It is one of few studies on sperm retrieval techniques that incorporate a diagnostic and prognostic approach before initiating the therapeutic IVF/ICSI cycle with TESA, cTESE, or mTESE.

Our results indicate that multiple needle-pass TESA is a reliable and sufficient sperm retrieval technique when the cause for azoospermia is obstructive. On other hand, the SRR in the prognostic TESA in NOA men was only 30%. Although this result is in line with the general literature it is difficult to make direct comparisons between studies because of differences in technique and diversity of the study population. This becomes apparent in the only published study comparing mTESE and TESA where TESA was performed with a 23G butterfly needle and 12–18 puncture sites resulting in a SRR of 10% compared with 54% in mTESE (El-Haggar *et al.*, 2008). The low SRR obtained by TESA in this study is likely because of the chosen TESA technique. In general, using a larger needle with multiple passes makes it possible to aspirate more tissue thus increasing the possibility of aspirating the patchy distributed spermatozoa as seen in our study.

The SRR we obtained by mTESE in NOA men, who have failed a prior prognostic TESA, was disappointing. For comparison, few other studies have reported outcomes of mTESE after prior sperm retrieval attempts. In a study by Ramasamy & Schlegel (2007) the SRR of mTESE in NOA men dropped from 53% in patients with no prior cTESE to 51% in 1–2 prior cTESE and to 23% in 3–4 prior cTESE and it was concluded that previous testicular biopsies provide limited or no prognostic value for sperm retrieval with mTESE. In our study mTESE after a failed TESA had a SRR of 11% (1/9). In addition to aspirating more tissue in the method we apply when doing TESA we are also able to sample the entire testis and the SRR we obtain with mTESE after failed TESA suggests that our way of performing TESA may be more predictive of future mTESE results than cTESE. In addition, although spermatozoa are found in some men after a salvage mTESE, the SRR drops meaning that some patients are treatable with less invasive procedures as shown in our study. The challenge is to find these patients. By using the treatment algorithm presented in this study, we select the patients who need mTESE. In this way TESA is an effective first-line treatment and mTESE should be reserved for patients with a failed TESA. This decreases the cost of care, as TESA in our center is 400 USD while the price for mTESE is 6.500 USD.

The use of TESA as a first-line treatment may also have advantages regarding complications after surgical sperm retrieval. Thus, we found a low rate of self-limiting complications only with TESA while there were no adverse effects on hormone

levels. Meanwhile the complication rate with mTESE was unusually high. However, it should be kept in mind, that the results are based on a low number of operations and a learning curve might affect the complication rate. In addition, the complications after mTESE may not only be a result of the operation itself but could stem from repeated procedures on these men as they only had mTESE performed after failed TESA. Finally, it should be mentioned that the use of a large biopsy needle for TESA has previously produced concerns of injury following multiple passes and rare testicular bleeding have been reported (Friedler *et al.*, 1997; Ezeh *et al.*, 1998). However, we did not observe excessive scarring of the testicular tissue when performing mTESE on men with prior TESA attempts. Thus, studies from more centers are needed to draw final conclusions on the issue.

In addition to the benefits with sperm retrieval, the low complication rate and the simplicity of the technique, the amount of tissue we obtain makes our way of performing TESA a good alternative to cTESE when analysis for histopathology is wanted. As illustrated in our study, this can aid in making the correct NOA/OA diagnosis and thereby minimize population bias when reporting SRR. It also confers an additional advantage because of the connection between infertility and carcinoma in situ (CIS) in the testes (Dohle *et al.*, 2012). This connection should be kept in mind and histopathology, including analysis for CIS, should be carried out in patients at increased risk of testicular cancer, that is, patients with cryptorchidism or small atrophic testes (Dohle *et al.*, 2012).

Histopathology is one among many parameters that have been suggested as a method to predict outcomes of sperm retrieval (Glina & Vieira, 2013). However, in a number of studies on mTESE a biopsy for histology is only obtained during the surgical sperm retrieval thereby excluding the prognostic value of histopathological diagnosis (Tsujimura *et al.*, 2002; Ramasamy *et al.*, 2005; Turunc *et al.*, 2010; Ghalayini *et al.*, 2011). For example, in a study by Ramasamy *et al.* (2005) histopathological diagnosis was known from prior biopsies in some patients, whereas the other patients had a biopsy taken during the surgical sperm retrieval. They report an overall SRR following mTESE of 58%. When looking at their patients with known histopathology the SRR is 49% (182/372). The drop in SRR can in theory be because of misdiagnosis of NOA in patients without histopathological diagnosis or the presence of less severe histopathological patterns in these patients. Our criteria for diagnosing NOA were very strict and included histopathology when available.

Other proposed predictors of sperm retrieval success include FSH, testosterone, testis size, and inhibin B and although they provide some prognostic information none of them have been found to safely predict the success of mTESE or other sperm retrieval techniques (Glina & Vieira, 2013). The lack of accurate predictors would encourage the use of a prognostic approach to avoid unavailability of spermatozoa when ICSI is to be performed on collected oocytes. As a result fine-needle aspiration (FNA) mapping has been developed to tailor sperm retrieval in NOA patients (Turek *et al.*, 1997). The technique is performed with a fine needle and systematically puncturing the testis and aspirating the tissue in a grid to create a map of where spermatozoa are present in the testis. Depending on the number of sites where spermatozoa are present, the next step is to perform TESA, cTESE, or mTESE (Beliveau & Turek, 2011). Thus, it is important to note that FNA mapping is not a sperm retrieval technique in itself.

Despite the lack of predictors a prognostic approach is rarely used, as it is argued that the patchy distributed spermatozoa are hard to find and it would therefore require multiple biopsies thus increasing the risk of complications (Dabaja & Schlegel, 2013). As a result and because of the relatively high SRR and low reported complication rates (Schlegel, 1999; Amer *et al.*, 2000; Okada *et al.*, 2002; Tsujimura *et al.*, 2002; Ramasamy *et al.*, 2005; Turunc *et al.*, 2010; Ghalayini *et al.*, 2011) many centers use mTESE as the first choice of retrieving spermatozoa in NOA. However, this global approach does not allow for individualized treatment based on the patients needs. The treatment algorithm presented in this study offers an alternative to mTESE as a first-line treatment.

To further optimize the algorithm a cryopreservation step after the prognostic TESA may be implemented. This could be a method of avoiding cancelled future IVF cycles but the cryosurvival of testicular spermatozoa has been questioned (Schlegel, 2009). However, recently the success of freezing testicular spermatozoa is increasing (Ohlander *et al.*, 2014) thereby making it feasible to freeze the sperm retrieved after the prognostic TESA and use the therapeutic TESA as a backup in case of low post-thaw cryosurvival.

The main limitation of our study is the low number of patients proceeding to therapeutic TESA and mTESE, which is mainly because of the fact that many patients are required to pay the entire treatment themselves, and therefore choose not to continue after the prognostic TESA. This observation further highlights the need for financial consideration when treating azoospermic men. Furthermore, our SRR in salvage mTESE lacks comparison to SRR in mTESE as an initial approach. Thus, further studies are needed to investigate this. Regardless we found a low SRR in salvage mTESE and a good concordance between prognostic and therapeutic TESA thereby limiting the number of invasive testicular procedures and cases where spermatozoa are unavailable for ICSI.

CONCLUSIONS

TESA performed under local anesthesia, in a clinic setting, is a safe procedure providing reasonable SRR. The success rate of mTESE drops after a failed TESA indicating that TESA has a role as a first-line treatment before proceeding to mTESE. Using our protocol, we are able to give patients more accurate information on the outcome of their future therapeutic treatment cycle and design an individual treatment algorithm ensuring that we use the least invasive sperm retrieval technique possible for any given patient.

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None.

DISCLOSURE

No conflict of interest, financial, or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

CFSJ and DAO did the conception and design of the research; DAO performed the procedures; MRH, GDS, and TS were responsible for the laboratory work; CFSJ and DAO created the

database and analyzed the data; CFSJ, DAO, MF, TS, and JS interpreted the results of the experiments; CFSJ, DAO, and MF drafted the manuscript; CFSJ, DAO, MF, and JS edited and revised the manuscript; all authors approved the final version of the manuscript.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Fertilization rates, pregnancy rates, and live birth rates following therapeutic TESA and mTESE.