Testicular Mapping
A Roadmap to Sperm Retrieval in Nonobstructive Azoospermia?

Akash A. Kapadia, MD*, Thomas J. Walsh, MD, MS

KEYWORDS

• Testicular mapping • MicroTESE • Azoospermia • FNA mapping • Testis biopsy • Sperm retrieval

KEY POINTS

- Men with nonobstructive azoospermia (NOA) should undergo complete genetic testing before discussion of surgical sperm retrieval.
- Offered treatment pathways may involve testicular mapping followed by sperm retrieval or upfront sperm retrieval and should include discussion of both advantages and disadvantages.
- The couple should be encouraged to help guide the decision.

SETTING THE STAGE

The diagnosis of azoospermia must be confirmed with 2 separate semen analyses demonstrating complete absence of sperm using high-powered microscopy. Once the diagnosis of nonobstructive azoospermia (NOA) has been confirmed with thorough history, physical examination, and hormonal testing, important considerations must then be made in order to guide a couple through their journey to parenthood. The couple should be made aware that assisted reproduction, whether through partner or donor sperm, traditional adoption, and embryo adoption, is the pathway forward. Foremost, genetic testing in the form of karyotype and Y-chromosome microdeletion (YCMD) should be obtained for the purposes of counseling and prognostication. Both Klinefelter syndrome (KS) and YCMD have a prevalence of approximately 10% in men with NOA.[1–3] Guiding the couple on the probability of finding sperm may start with a discussion of genetic evaluation in patients who accept this testing. In patients without an identifiable cause of NOA, the natural follow-up questions are: *what are my chances of finding sperm?* and *what is the best approach to finding sperm?*

Several studies have investigated noninvasive predictors of sperm retrieval. Colpi and colleagues[4] and Ghalayini and colleagues[5] have shown that increased follicle stimulating hormone (FSH) levels are associated with decreased retrieval success regardless of the type of retrieval procedure. In the same studies, Colpi could not show a significant relation between testicular volume and sperm retrieval; however, Ghalayini demonstrated a positive correlation between testicular volume and retrieval success. On the contrary, Ramasamy and colleagues[6] in their large cohort did not show a correlation between high FSH levels and sperm-retrieval failure via microdissection testicular sperm extraction (microTESE). A composite analysis of sperm-retrieval data suggests that testicular volume and hormonal values alone do not exhibit reliable predictive value in retrieval success.

Testicular histology is the most reliable predictor of sperm-retrieval success. Men with the least severe form of spermatogenic dysfunction (ie, hypospermatogenesis) demonstrate a retrieval rate of 80% to 98%, whereas those with the most severe form of spermatogenic dysfunction (ie, sertoli cell only syndrome [SCOS] or germ

Department of Urology, University of Washington, 1959 Northeast Pacific Street, Box 356510, Seattle, WA 98195, USA
* Corresponding author.
E-mail address: kapadiaa@uw.edu

Urol Clin N Am 47 (2020) 157–164
https://doi.org/10.1016/j.ucl.2019.12.013

cell aplasia) have a success rate of 5% to 24%. Most notably, those with less severe forms of spermatogenic dysfunction demonstrate a high retrieval rate even with the least invasive techniques of sperm retrieval.[7–9] There are several limitations of testicular histology, however. First, the performance of biopsy introduces the risk associated with a diagnostic procedure. As it is known, an open biopsy may then lead to a second invasive procedure for sperm retrieval. Second, and perhaps even more important, there is evidence of high discordance in histologic diagnosis among pathologists. In 2003, Cooperberg and colleagues[10] reported significant intraobserver variability between initial histologic diagnosis and subsequent review diagnosis from 1 institution to another that resulted in clinically significant changes to management of 27% of patients. Last, it is well established that spermatogenesis can be focal and sporadic, and therefore, limited sampling via a single or multiple "random" biopsies may still lead to incomplete information on spermatogenesis while introducing additional risk to patients.[11]

Sousa and colleagues[8] reported significant histologic variability in patients with previously diagnosed "sertoli cell only syndrome," because nearly 40% of the men had a combination of maturation arrest, early, or late spermiogenesis in the study cohort. As a result, sperm retrieval in their patients ranged from 5% to 98% via conventional testicular sperm extraction (cTESE). Thus, it has been suggested that focal spermatogenesis in patients with histologically diagnosed "SCOS" cannot be reliably predicted even in the setting of multiple random biopsies. Ramasamy and Schlegel[12] have described sperm-retrieval rates (SRR) as high as 51% with microTESE in patients with prior biopsies, albeit demonstrating lower retrieval rates and poorer outcomes in cases with increasing negative prior biopsies. Furthermore, the same group reported a retrieval rate of 37% in patients with "SCOS" and at least 1 prior negative biopsy. Therefore, when evaluating predictive factors for sperm retrieval, it is apparent that although histology can guide sperm retrieval in many patients with less severe forms of spermatogenic failure, it does not reliably predict absence of spermatogenesis in those with "SCOS" diagnosed from a traditional, focal or multifocal, biopsy.

A provider may then ask: *How do I guide my patients with NOA toward their treatment goals?* Because of the historically poor predictive tools for successful sperm retrieval, 2 care pathways have emerged: *Upfront testicular sperm retrieval versus testicular mapping guided sperm retrieval.*

UPFRONT TESTICULAR SPERM RETRIEVAL

There are 2 accepted forms of sperm-retrieval techniques: percutaneous and open.

Percutaneous Retrieval

During a percutaneous procedure for NOA, sperm is aspirated with a moderately large-gauge needle or angiocatheter that is inserted percutaneously after an adequate spermatic cord block. It may also be performed with adjunctive sedation. Using a standard Luer-Lock or Cameco piston syringe to generate suction, the needle is oscillated in the same plane to release a substantial conglomerate of testicular tubules. These tubules are released at the skin and transferred into buffer media for morcellation, analysis, and storage.[13] Patients with NOA are generally reported to have lower success rates with upfront percutaneous techniques (11%–47%) compared with open techniques (16%–63%).[14–17] Mercan and colleagues[15] reported an SRR of 14% with percutaneous aspiration in their cohort of 452 men with NOA. Those who had a failed aspiration (testicular sperm aspiration [TESA]) went on to have a cTESE in the same setting with an overall SRR of 64.4%. Men with a successful aspiration in their cohort had a much higher likelihood of hypospermatogenesis as the predominant histopathology and were much less likely to have maturation arrest or germ cell aplasia. Vicari and colleagues[14] described a much higher rate of SRR with aspiration at 47.3%, albeit with a smaller cohort of NOA. Similar to the prior study, their results showed that aspiration was successful in 100% of men who had diagnostic biopsies demonstrating hypospermatogenesis or maturation arrest with focal spermatogenesis, but the success rates with this technique were lower in complete maturation arrest (42.3%), SCOS (14.3%), and SCOS with focal spermatogenesis (0%).

Table 1 outlines outcomes observed through percutaneous procedures.

Open Retrieval

Open testicular sperm extraction (TESE) can be accomplished using 2 main methods: conventional TESE (via single or multiple random/directed biopsies) and microTESE.

Conventional testicular sperm extraction

cTESE is distinct from a percutaneous procedure in that it involves incision of the tunica albuginea in order to obtain tissue. It is distinct from microTESE in that it does not involve the use of high-powered microscopy and testicular bivalving (see later discussion) in order to guide retrieval. As a result, testicular tissue is retrieved via a single

Table 1
Sperm-retrieval outcomes from percutaneous procedures (testicular sperm aspiration)

Author, Year	Case (n)	SRR (%)
Friedler et al,[17] 1997	37	11
Ezeh et al,[16] 1998	35	14
Mercan et al,[15] 2000	452	14
Vicari et al,[14] 2001	55	47.3

Data from Refs. [14–16]

incision or multiple incisions based on surgeon preference. Tubular characteristics are not factored in tissue retrieval, as is the case with microTESE. SRRs from various studies are outlined in **Table 2**. In a 2006 study, Vernaeve and colleagues[18] reported an overall SRR of 49% with 41% success on first attempt. This study showed high SRR in those men who underwent repeat cTESE with a second attempt resulting in 75% SRR (n = 77), third attempt resulting in 82% SRR (n = 28), and fourth attempt resulting in 100% SRR (n = 11). On pathology review, they found a 98.9% SRR in men with hypospermatogenesis, of which all 57 men undergoing their first cTESE had successful retrieval. On the contrary, in men with "SCOS," the SSR was 38.7% on first attempt and 77.6% on second attempt.[18] As before, SCOS is placed in quotes, because clearly, if sperm are retrieved, this is not the true diagnosis. From this study, and across all studies with available pathology, it is once again clear that men with hypospermatogenesis have reliably and reproducibly high SRRs using conventional methods of retrieval. However, the efficacy of these methods decreases substantially in cases of severe spermatogenic dysfunction.

Microdissection testicular sperm extraction

First described in 1999 by Schlegel,[19] microTESE has suggested promising results in men with NOA when compared with cTESE. In most scenarios, microTESE is performed under general anesthesia. The testes are examined one at a time, with most surgeons preferring to initiate exploration in the larger of the two. After delivery of the testis, the tunica albuginea is incised equatorially toward the mediastinum testis bilaterally, thereby avoiding the traverse of areas rich in vascularity. Upon completing the "bivalving" of the testis, high-powered microscopy enables the systematic examination of the seminiferous tubules in each of the testicular lobules. Dilated opaque tubules are sought in a sea of collapsed or obliterated tubular architecture. Once promising tubules are harvested, they are placed in a buffer,

Table 2
Sperm-retrieval outcomes from conventional testicular sperm extraction

Author, Year	Case (n)	SRR (%)
Schlegel,[19] 1999	22	45
Amer et al,[20] 2000	100	30
Mercan et al,[15] 2000	389	59
Okada et al,[21] 2002	24	16.7
Tsujimura et al,[22] 2002	37	35.1
Ramasamy et al,[23] 2005	83	32
Vernaeve et al,[18] 2006	628	49
Ghalayini et al,[5] 2011	68	38.2

Data from Refs. [5,15,18–23]

morcellated, and examined by an andrologist or embryologist in real time for the presence of sperm. A decision regarding exploration of the contralateral testis is made based on quantity and quality of obtained sperm. Hemostasis is attained with bipolar electrocautery; the tunica albuginea is securely closed, and the testis is returned to the tunica vaginalis (**Fig. 1**).[24]

Several studies over the last 2 decades have shown higher rates of sperm retrieval using microTESE (**Table 3**), and these results have been confirmed in a recent metaanalysis.[25] Another metaanalysis that appraised all 3 techniques (TESA, cTESE, and microTESE) reported that microTESE was 1.5 times more likely to result in successful retrieval compared with cTESE, and in turn, cTESE is 2 times more likely to result in successful retrieval compared with TESA.[26] All indications suggest that microTESE results in SRRs may be clinically significant for patients. When evaluating these data, however, one must also consider an inspection under the microscope. Three studies directly compared SRRs in patients with hypospermatogenesis undergoing cTESE and microTESE. Okada and colleagues[21] and Tsujimura and colleagues[22] did not demonstrate statistical significance in SRRs within their cohorts. Ramasamy and colleagues[23] did show a significant difference in favor of microTESE in their cohort (50% vs 81%). SRRs in hypospermatogenesis across all studies ranged from 81% to 100% with microTESE, and from 50% to 84% with cTESE. Four studies directly compared SRRs in patients previously diagnosed with "SCOS." In their cohorts, Okada and colleagues[21] and Ghalayini and colleagues5 demonstrated statistical and clinical superiority with microTESE. Overall, SRRs in "SCOS" ranged from 22.5% to 41% with microTESE, and from 6.3% to 29% with cTESE. Overall, the results give a sense that

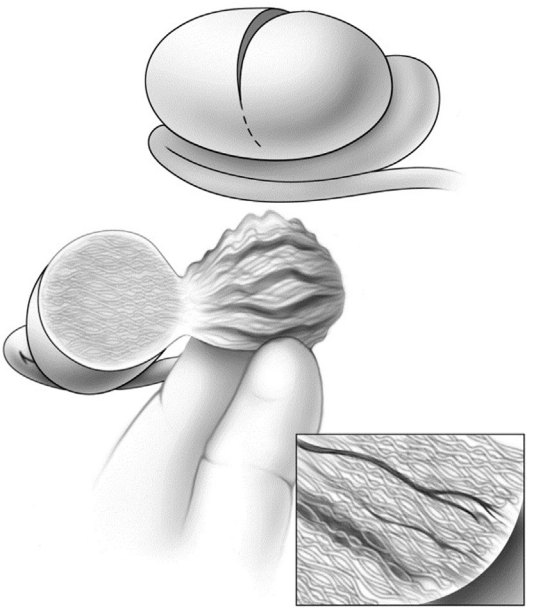

Fig. 1. The testicle is delivered through a scrotal incision. An equatorial incision is made in the tunica albuginea, thus bivalving the testis. The seminiferous tubules are then examined for dilated tubules under an operating microscope. These dilated tubules are more likely to contain sperm and should be harvested to be processed by the embryology/andrology team. The tunica albuginea is then closed with a running suture. The testicle is placed back in the scrotum and the tunica vaginalis, dartos, and skin layers are closed. (*From* Ramasamy R, Yagan N, Schlegel PN. Structural and functional changes to the testis after conventional versus microdissection testicular sperm extraction. Urology. 2005;65(5)1190–1194; with permission.)

men with severe pathologic condition would certainly benefit from a technologically advanced, skill-intensive procedure such as microTESE.

Complications of Sperm Retrieval

In addition to improved SRR, microTESE may result in less loss of tissue from the testis. Studies have reported testicular mass reduction ranging from 150 to 720 mg with cTESE. In comparison, mass reduction of approximately 10 to 300 mg has been reported in microTESE.[18,19,28] Harrington and colleagues[29] reported a 29% rate of intratesticular hematoma in cTESE, which may lead to high rates of scarring and additional volume loss. Since then, studies have evaluated patients with serial ultrasound studies to quantify volume loss. In a prospective study of 60 patients, Amer and colleagues[20] described a higher rate of persistent echogenic foci in patients who underwent cTESE compared with microTESE; however, there were no cases of permanent testicular devascularization, as has been previously reported by Schlegel and Su.[28] Subsequently, in a study of 147 men, Okada and colleagues[21] reported higher rates of persistent findings of hematoma, chronic changes, and lower testicular volumes at 6 months with cTESE compared with microTESE, although a decrease in testosterone and need for testosterone replacement were not different between the comparison groups. Ramasamy and colleagues[23] evaluated 435 men with NOA and also found a higher rate of focal hypoechoic changes on ultrasound at 6 months with cTESE. The study also revealed a 20% decline in serum testosterone from baseline at 6 months in both groups with just more than one-third of men returning to 95% of preoperative testosterone levels at 18 months.

Table 3
Sperm-retrieval outcomes from microdissection testicular sperm extraction

Author, Year	Case (n)	SRR (%)
Schlegel,[19] 1999	27	63
Amer et al,[20] 2000	100	47
Tsujimura et al,[22] 2002	56	42.9
Okada et al,[21] 2002	74	44.6
Ramasamy et al,[23] 2005	460	57
Ishikawa et al,[27] 2010	150	42
Ghalayini et al,[5] 2011	65	56.9

Data from Refs. [5,19–23,27]

Similarly, others have evaluated the risk of hypogonadism following sperm-retrieval procedures. Most of the studies find a higher rate of androgen decline in patients with KS who typically start at a lower total testosterone, and return to 50% to 75% of preoperative values.[30] These patients should be monitored closely for symptoms of hypogonadism. In NOA patients without KS, studies show initial significant decline followed by normalization of total testosterone at 12 to 18 months.[21–23,31,32] Although there are measurable ultrasound and hormonal changes in both the short and the long term, it remains to be seen whether these findings correlate with clinical outcomes of hypogonadism.

It is evident that even with the most advanced form of sperm-retrieval techniques, nearly 40% to 50% of men with NOA may undergo an invasive procedure only to return empty-handed. A male infertility specialist must wonder how these men can be identified in order to avoid unnecessary surgery in both the male and in many cases the female partner. By the same principle, can success be maximized with sperm retrieval while minimizing harm to the patient?

TESTICULAR MAPPING

The questions raised above are the guiding principles that led to the conception and development of testicular mapping. In 1997, Turek was the first US urologist to describe testicular fine needle aspiration (FNA) mapping as a way to improve diagnostic accuracy compared with testicular biopsy/histology based on the knowledge that spermatogenesis is focal and sporadic.[11] Testicular FNA mapping is performed with a spermatic cord block using a 23- or 24-gauge needle on a 10-mL syringe and a suctioning syringe holder (Cameco). Aspiration sites are planned depending on the testis size, but typically range between 12 and 18 sites. Given the small needle gauge, only a miniscule number of tubules are extracted and deposited on microscope slides. The seminiferous tubules are smeared onto the microscope slide using standard cytologic principles and fixed with either 95% ethyl alcohol or other suitable fixative. Aspirated seminiferous tubules undergo staining and are examined by a cytopathologist or laboratory andrologist for the presence of sperm. Specimen handling, processing, and interpretation require expertise in cytologic techniques. Patient recovery is rapid, and postprocedural pain is managed with no-narcotic pain medications (**Fig. 2**).[33]

In their 1997 pilot study, Turek and colleagues[11] described 16 patients who underwent matched open testicular biopsies and FNA mapping. Testis mapping was more sensitive than open biopsy and equally specific in detecting sperm. Numerous studies have now shown a very high concordance rate between FNA cytology and open biopsy histology, allowing for high reliability in prognostication of patients.[33–36] In a subsequent study, Turek and colleagues[33] reported the identification of sperm via FNA in 27.1% of men who had a negative previous biopsy.[37] This finding is further strengthened by findings showing sperm detection rates of 47% in men who underwent FNA at 7 sites per testicle, increasing to 52% with 14 sites per testicle, findings that are similar to rates of sperm retrieval when microTESE is performed.[38]

Of the men who had detectable sperm, FNA-directed TESE were performed under local anesthesia with a mean 3.1 biopsies per patient and 72 mg of tissue removed. Sufficient sperm was obtained for all oocytes in 95% of in vitro fertilization (IVF) cycles (20/21).[39] Using an alternative aspiration technique, Lewin and colleagues[40] demonstrated a 58.8% sperm detection rate with FNA when averaging 15 sites per testicle, indicating that increasing number of sampling per testicle correlates with higher sperm detection rate. Once again, these studies seem to confirm a success rate of sperm identification and subsequent retrieval that may be comparable to that of upfront microTESE.

Importantly, the information obtained via the FNA map may help to tailor sperm retrieval that yields the greatest success while minimizing invasiveness for the patient. In a series of 132 NOA cases with FNA mapping, 45 patients underwent directed TESA or TESE, whereas 14 underwent directed microTESE. Jad and Turek[41] found a retrieval rate of 98% (44/45 cases) in the TESA/TESE cohort, whereas microTESE resulted in 86% success (12/14 cases). In addition, all microdissection cases in this series of previously FNA mapped patients were unilateral and involved sperm retrieval from only 1 testicle. Overall, sufficient sperm was obtained in 95% of cases. As such, the testis map may offer a less invasive

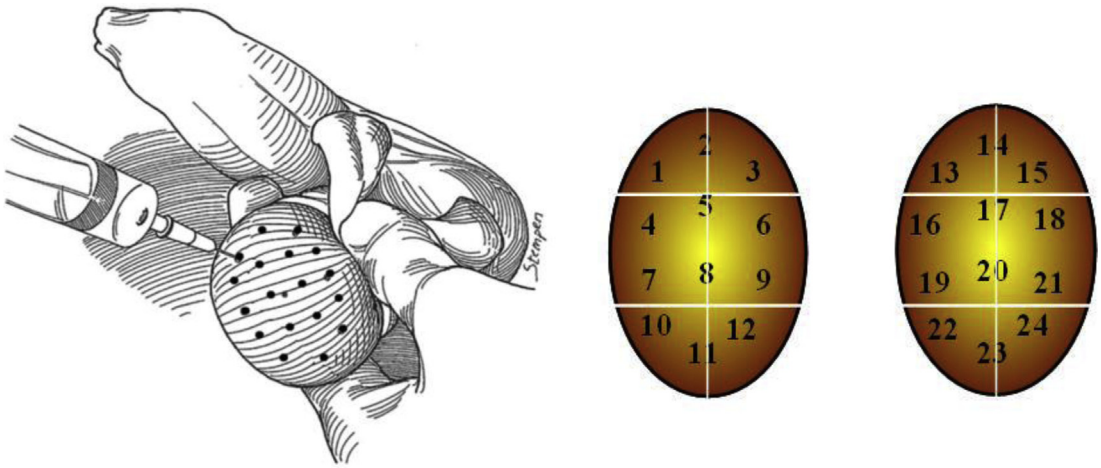

Fig. 2. FNA mapping procedure and mapping template. *From* Beliveau ME, Turek PJ. The value of testicular "mapping" in men with non-obstructive azoospermia. Asian J Androl. 2011; 13(2): 225-230; with permission.

form of identifying areas of spermatogenesis, if present, and a guide for efficient, targeted, and less invasive future sperm-retrieval procedures.

An additional area of testicular mapping utilization is in cases of failed microTESE when a patient desires further investigation. In a recent study, Jarvis and colleagues[42] retrospectively identified 82 patients who had a failed microTESE and subsequently underwent FNA-guided testicular mapping. Of these, 24 (29%) men had at least 1 FNA site that was positive for sperm. Fifteen men then underwent a sperm-retrieval procedure with successful retrieval in all, as well as successful cryopreservation for future use in 10 (67%). Similar studies in patients who undergo repeat microTESE after a failed microTESE revealed success in 30% to 50% of patients. Talas and colleagues[43] described 3 of 5 patients who had a successful repeat microTESE following initial failure, whereas Morris and colleagues[44] reported 3 of 9 patients who had successful repeat microTESE. Clearly, these findings speak to the potential variation with how microTESE is performed. In this setting, testicular mapping may help select patients who could then go on to have a directed microTESE at a higher success rate, while avoiding a second invasive procedure in those with unfavorable findings.

Testicular mapping has been reported to be well tolerated and with a minimal complication profile. Lewin and colleagues[40] demonstrated a 7% rate of intratesticular bleeding on ultrasound 30 minutes following the procedure, which did not result in clinically measurable changes in postprocedural care. In extrapolating outcomes after large needle aspirations, Westlander and colleagues[45] found no changes in FSH or testosterone levels 3 months following the procedure. These investigators found no change in testicular volumes; however, 4 patients (6%) had focal echogenic intratesticular lesions with 3 of 4 seeing resolution in 6 to 9 months. Similarly, Carpi and colleagues[46] found 11% of patients who underwent an FNA followed by a large-needle biopsy demonstrated a hypoechoic area of 1 cm or less on imaging.

The physical and financial burden on the couple is also of importance. The upfront microTESE approach, as classically described, implies fresh sperm utilization, necessitating simultaneous or prior egg retrieval by the female partner, and thereby resulting in distribution of precious manpower and resources within the practice. The implication is that at least 40% of female partners may undergo an unnecessary procedure if no sperm is found and donor sperm is not acceptable to the couple. Therefore, this approach requires extensive upfront counseling of couples, and detailed discussion of the "what if" scenarios. Finally, from a cost-effectiveness standpoint, preliminary cost analysis models looking at incremental cost-effectiveness ratio have shown that testicular mapping may yield a slightly lower SRR, but is more cost-effective than microTESE.[47]

In summary, FNA-guided testicular mapping may help to avoid several pitfalls encountered with random biopsies. It relies on cytology for sperm detection, hence avoiding problems with histologic variability and markedly increasing sensitivity. Furthermore, it demonstrates concordance to histologic findings, lending credibility to cytologic findings. Importantly, using a grid technique (as described in later discussion) provides direct knowledge of present or absent mature spermatozoa (as well as immature sperm forms) at any given site. In a scenario whereby a patient demonstrates diffuse hypospermatogenesis on the testis map, it arms the provider with options of performing less invasive and less costly retrieval procedures, like TESA or cTESE. On the contrary, when faced with complete absence of spermatogenesis, it allows a provider the confidence and assurance of appropriate patient counseling.

Patient-Centered Approach to Care

Many in andrology will agree that providing the best care means coming to learn about goals and values of the couples for whom they are caring. Various cultural, psychosocial, emotional, financial, and personal factors may become apparent during a patient visit, which may guide the shared decision-making process. Patients should be apprised of not just success and complication rates of the care pathways but also the emotional and economic burdens of what is to come. Men often endure the easier burden of the two, and this should be emphasized. When an upfront microTESE pathway is undertaken, given the uncertainty of spermatogenesis, coordinated treatment requires simultaneous oocyte retrieval or preemptive oocyte retrieval with cryopreservation. In this scenario, the female partner must undergo the full process with IVF, including its attendant medical risk and financial cost, regardless of the fate of the partner's sperm. This endeavor requires significant provider planning, hours of laboratory effort, and notable patient expenses. Testicular mapping may help reduce the "unknown" and simplify care coordination, yet may place a higher burden of care on the man. Regardless of the scenario, couples should be presented with all diagnostic and therapeutic sperm-retrieval options. With the provision of complete information, the couple should be empowered to make informed decisions regarding their care.

DISCLOSURE

The authors of this article have no financial conflict of interest.

REFERENCES

1. Barr ML. The natural history of Klinefelter's syndrome. Fertil Steril 1966;17:429–41.
2. Visootsak J, Graham JM Jr. Klinefelter syndrome and other sex chromosomal aneuploidies. Orphanet J Rare Dis 2006;24:1–42.
3. Stahl PJ, Mielnik A, Schlegel PN, et al. A decade of experience emphasizes that testing for Y chromosome microdeletions (YCM) is essential in men with azoospermia and severe oligospermia. Fertil Steril 2008;90:S319.
4. Colpi GM, Colpi EM, Piediferro G, et al. Microsurgical TESE versus conventional TESE for ICSI in non-obstructive azoospermia: a randomized controlled study. Reprod Biomed Online 2009;18:315–9.
5. Ghalayini IF, Al-Ghazo MA, Hani OB, et al. Clinical comparison of conventional testicular sperm extraction and microdissection techniques for non-obstructive azoospermia. J Clin Med Res 2011;3:123–31.
6. Ramasamy R, Lin K, Gosden LV, et al. High serum FSH levels in men with nonobstructive azoospermia does not affect success of microdissection testicular sperm extraction. Fertil Steril 2009;92:590–3.
7. Seo JT, Ko WJ. Predictive factors of successful testicular sperm recovery in non-obstructive azoospermia patients. Int J Androl 2001;24:306–10.
8. Sousa M, Cremades N, Silva J, et al. Predictive value of testicular histology in secretory azoospermic subgroups and clinical outcome after microinjection of fresh and frozen-thawed sperm and spermatids. Hum Reprod 2002;17:1800–10.
9. Su LM, Palermo GD, Goldstein M, et al. Testicular sperm extraction with intracytoplasmic sperm injection for nonobstructive azoospermia: testicular histology can predict success of sperm retrieval. J Urol 1999;161:112–6.
10. Cooperberg MR, Chi T, Jad A, et al. Variability in testis biopsy interpretation: implications for male infertility care in the era of intracytoplasmic sperm injection. Fertil Steril 2005;84:672–7.
11. Turek PJ, Cha I, Ljung B-M. Systematic fine-needle aspiration of the testis: correlation to biopsy and results of organ "mapping" for mature sperm in azoospermic men. Urology 1997;49:743–8.
12. Ramasamy R, Schlegel PN. Microdissection testicular sperm extraction: effect of prior biopsy on success of sperm retrieval. J Urol 2007;177:1447–9.
13. Gorgy A, Podsiadly BT, Bates S, et al. Testicular sperm aspiration (TESA): the appropriate technique. Hum Reprod 1998;13:1111–3.
14. Vicari E, Graziosos C, Burrello N, et al. Epididymal and testicular sperm retrieval in azoospermic patients and the outcome of intracytoplasmic sperm injection in relation to the etiology of azoospermia. Fertil Steril 2001;75:215–6.
15. Mercan R, Urman B, Alatas C, et al. Outcome of testicular sperm retrieval procedures in non-obstructive azoospermia: percutaneous aspiration versus open biopsy. Hum Reprod 2000;15:1548–51.
16. Ezeh UI, Moore HD, Cooke ID. A prospective study of multiple needle biopsies versus a single open biopsy for testicular sperm extraction in men with non-obstructive azoospermia. Hum Reprod 1998;13:3075–80.
17. Friedler S, Raziel A, Strassburger D, et al. Testicular sperm retrieval by percutaneous fine needle sperm aspiration compared with testicular sperm extraction by open biopsy in men with non-obstructive azoospermia. Hum Reprod 1997;12:1488–93.
18. Vernaeve V, Verheyen G, Goossens A, et al. How successful is repeat testicular sperm extraction in patients with azoospermia? Hum Reprod 2006;21:1551–4.
19. Schlegel PN. Testicular sperm extraction: microdissection improves sperm yield with minimal tissue excision. Hum Reprod 1999;14:131–5.
20. Amer M, Ateyah A, Hany R, et al. Prospective comparative study between microsurgical and conventional testicular sperm extraction in non-obstructive azoospermia: follow-up by serial ultrasound examinations. Hum Reprod 2000;15:653–6.
21. Okada H, Dobashi M, Yamazaki T, et al. Conventional versus microdissection testicular sperm extraction for nonobstructive azoospermia. J Urol 2002;168:1063–7.
22. Tsujimura A, Matsumiya K, Miyagawa Y, et al. Conventional multiple or microdissection testicular sperm extraction: a comparative study. Hum Reprod 2002;17:2924–9.
23. Ramasamy R, Yagan N, Schlegel PN. Structural and functional changes to the testis after conventional versus microdissection testicular sperm extraction. Urology 2005;65:1190–4.
24. Flannigan R, Bach PV, Schlegel PN. Microdissection testicular sperm extraction. Transl Androl Urol 2017;6:745–52.
25. Deruyver Y, Vanderschueren D, Van der Aa F, et al. Outcome of microdissection TESE compared to conventional TESE in non-obstructive azoospermia: a systematic review. Andrology 2014;2:20–4.
26. Bernie AM, Mata DA, Ramasamy R, et al. Comparison of microdissection testicular sperm extraction, conventional testicular sperm extraction, and testicular sperm aspiration for nonobstructive azoospermia: a systematic review and meta-analysis. Fertil Steril 2015;104:1099–103.

27. Ishikawa T, Nose R, Yamaguchi K, et al. Learning curves of microdissection testicular sperm extraction for non-obstructive azoospermia. Fertil Steril 2010;94:1008–11.
28. Schlegel PN, Su L. Physiological consequences of testicular sperm extraction. Hum Reprod 1997;12:1688–92.
29. Harrington TG, Schauer D, Gilbert BR. Percutaneous testis biopsy: an alternative to open testicular biopsy in the evaluation of the subfertile man. J Urol 1996;156:1647–51.
30. Takada S, Tsujimura A, Ueda T, et al. Androgen decline in patients with nonobstructive azoospemia after microdissection testicular sperm extraction. Urology 2008;72:114–8.
31. Binsaleh S, Alhajeri D, Madbouly K. Microdissection testicular sperm extraction in men with nonobstructive azoospermia: experience of King Saud University Medical City, Riyadh, Saudi Arabia. Urol Ann 2017;9:136–40.
32. Eliveld J, van Wely M, Meibner A, et al. The risk of TESE-induced hypogonadism: a systematic review and meta-analysis. Hum Reprod Update 2018;24:442–54.
33. Arïdoğan IA, Bayazït Y, Yaman M, et al. Comparison of fine-needle aspiration and open biopsy of testis in sperm retrieval and histopathologic diagnosis. Andrologia 2003;35:121–5.
34. Mahajan AD, Ali NI, Walwalkar SJ, et al. The role of fine-needle aspiration cytology of the testis in the diagnostic evaluation of infertility. BJU Int 1999;84:485–8.
35. Qublan HS, Al-Jader KM, Al-Kaisi NS, et al. Fine needle aspiration cytology compared with open biopsy histology for the diagnosis of azoospermia. J Obstet Gynaecol 2002;22:527–31.
36. Meng MV, Cha I, Ljung B-M, et al. Testicular fine-needle aspiration in infertile men: correlation of cytologic pattern with biopsy histology. Am J Surg Pathol 2001;25:71–9.
37. Turek PJ, Ljung B-M, Cha I, et al. Diagnostic findings from testis fine needle aspiration mapping in obstructed and nonobstructed azoospermic men. J Urol 2000;163:1709–16.
38. Meng MV, Cha I, Ljung BM, et al. Relationship between classic histological pattern and sperm findings on fine needle aspiration map in infertile men. Hum Reprod 2000;15:1973–7.
39. Turek PJ, Givens CR, Schriock ED, et al. Testis sperm extraction and intracytoplasmic sperm injection guided by prior fine-needle aspiration mapping in patients with nonobstructive azoospermia. Fertil Steril 1999;71:552–7.
40. Lewin A, Reubinoff B, Porat-Katz A, et al. Testicular fine needle aspiration: the alternative method for sperm retrieval in non-obstructive azoospermia. Hum Reprod 1999;14:1785–90.
41. Jad AM, Turek PJ. Experience with testis FNA mapping and microdissection (M & M) in difficult nonobstructive azoospermia cases. Fertil Steril 2002;78:S71.
42. Jarvis S, Yee HK, Thomas N, et al. Sperm fine-needle aspiration (FNA) mapping after failed microdissection testicular sperm extraction (TESE): location and patterns of found sperm. Asian J Androl 2019;21:50–5.
43. Talas H, Yaman O, Aydos K. Outcome of repeated micro-surgical testicular sperm extraction in patients with non-obstructive azoospermia. Asian J Androl 2007;9:668–73.
44. Morris S, Yap T, Alkematy K, et al. Is there a role for salvage or redo micro-dissection testicular sperm extraction in non-obstructive azoospermia? Proceedings of the American Urologic Association. San Francisco, CA, May 18–21, 2018. Available at: https://www.auajournals.org/doi/10.1016/j.juro.2018.02.221.
45. Westlander G, Ekerhovd E, Granberg S, et al. Serial ultrasonography, hormonal profile and antisperm antibody response after testicular sperm aspiration. Hum Reprod 2001;16:2621–7.
46. Carpi A, Menchini F, Palego P, et al. Fine-needle and large-needle percutaneous aspiration biopsy of testicles in men with nonobstructive azoospermia: safety and diagnostic performance. Fertil Steril 2005;83:1029–33.
47. Chen T, Ahn J, Johnsen N, et al. Cost-effectiveness of initial fine needle aspiration mapping versus microscopic testicular sperm extraction for men with nonobstructive azoospermia. Proceedings of the American Urologic Association. Chicago, IL, May 3–6, 2019. Available at: https://www.auajournals.org/doi/10.1097/01.JU.0000556131.90620.bb.