Editorial
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Management of Non-Obstructive Azoospermia: Practical Answers to Key Clinical Questions

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INTRODUCTION

Managing non-obstructive azoospermia (NOA) remains among the most challenging areas in reproductive medicine. Despite advances in surgical techniques, genetic diagnostics, and laboratory methodologies, no single strategy guarantees success. Clinicians must navigate a landscape of incomplete predictors, variable responses to hormonal or surgical interventions, and often limited evidence guiding their decisions.

Although NOA is most commonly due to primary testicular failure, potentially reversible factors may occasionally be identified, such as varicocele or hypogonadotropic hypogonadism, which may benefit from targeted treatment [1,2]. Nevertheless, most NOA cases are related to primary testicular insufficiency, most commonly idiopathic in nature, while genetic abnormalities are also identified in a substantial subset of patients; these conditions are not amenable to medical therapy. In such situations, the only available option is testicular sperm extraction followed by assisted reproductive techniques [3,4].

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Despite advances in microsurgical techniques and laboratory handling, managing NOA remains highly challenging. Questions persist regarding the best approach to performing preoperative evaluation, selecting appropriate candidates, and enhancing sperm retrieval rates (SRR), recognizing that proper optimization will only be possible once supported by clinically relevant evidence. New technologies and research continue to emerge, including new genetic markers for surgical sperm retrieval (SSR) [5] as well as artificial intelligence-assisted predictive models and enhanced surgical modifications for SSR [6], raising more debates on their real-world impact and clinical utility. This editorial aims to address the current controversies and advancements in managing men with NOA through utilizing the most recent evidence and expert opinions to reach evidence-based decisions in daily practice to manage such complex cases.

GENETIC TESTING IN NOA: WHAT SHOULD BE INVESTIGATED TODAY?

Genetic anomalies account for up to 27% of the etiological factors in NOA [7]. Identifying these genetic causes, including karyotype abnormalities and azoospermia factor (AZF) deletions, is crucial because they directly influence *SRR* and patient management and counseling. Karyotyping allows the detection of numerical and significant structural chromosomal abnormalities. For example, patients with 46, XX testicular disorder of sex development (XX male syndrome) generally have no chance of sperm retrieval due to complete germ cell aplasia. In contrast, men with Klinefelter syndrome (KS syndrome) may achieve SRR in up to 44% of cases, particularly using microdissection testicular sperm extraction (micro-TESE) [8]. Structural chromosomal anomalies may reduce blastocyst formation, compromise preimplantation genetic screening, and decrease intracytoplasmic sperm injection (ICSI) pregnancy rate [9,10].

The screening of the entire AZF region is mandatory for NOA cases according to the American Urological Association/American Society for Reproductive Medicine (AUA/ASRM) [11], the European Academy of Andrology/European Molecular Quality Network [12], and the European Association of Urology (EAU) Guidelines on Male Infertility [13] since the presence and type of deletion directly impact the likelihood of sperm retrieval and guide clinical management [14]. Complete AZFa or AZFb deletions are associated with zero chance of sperm retrieval [13]. Other deletions or combinations are reported with a more favorable prognosis, including AZFc, partial AZFb, and AZFbc with SSR up to 50% [15]. All of these deletions will be transmitted to male offspring, requiring careful counseling of the couple, including discussion of embryo sex selection if appropriate.

The use of whole-exome sequencing (WES) recently allowed the detection of potential novel monogenic variants associated with NOA, but it remains a research tool without routine clinical application [16,17]. A recent multicenter study on 571 patients identified new gene mutations associated with NOA and significantly related to SSR. Nineteen genes are strongly associated with negative SSR, and nine with positive SSR. They also identified seven new potential genes related to NOA, but their association still needs to be validated [18]. These findings are an important step towards personalized-precision medicine for NOA. Current guidelines recommend karyotyping and Y-chromosome microdeletion testing for all NOA patients, whereas broader genetic tests such as WES are not yet recommended for routine clinical use [11,13,19].

ARE THERE RELIABLE PREDICTORS OF SPERM RETRIEVAL SUCCESS IN MEN WITH NOA?

Predictive factors for successful sperm retrieval in NOA patients could help avoid unnecessary surgery when the chances of success are essentially zero and would also allow decisions to be based on individualized probabilities rather than a default 50% estimate [13]. Complete deletions of AZFa and AZFb, as well as combinations of microdeletions (AZFbc, AZFabc), are currently regarded as exclusion criteria for sperm retrieval [11,13,19]. In contrast, a history of surgically corrected undescended testes is a favorable predictor of sperm retrieval [20]. However, positive predictive factors remain much less clearly defined.

Hormonal markers such as follicle-stimulating hormone (FSH), luteinizing hormone (LH), inhibin B, and anti-müllerian hormone, as well as testicular volume, have shown variable correlations with sperm retrieval outcomes and cannot be regarded as reliable predictors [21].

Emerging imaging modalities, including high-frequency ultrasound [22] and magnetic resonance imaging [23], along with molecular or proteomic biomarkers such as TEX101 [24] or seminal haploid cells [25], are promising tools for assessing spermatogenic activity. Nevertheless, these methods remain experimental and lack sufficient validation for routine clinical use.

In the context of repeat sperm retrieval surgery, previous favorable histological patterns such as hypospermatogenesis are associated with a higher likelihood of sperm retrieval, whereas maturation arrest or Sertoli-cell-only (SCO) syndrome predict much lower success rates [26,27].

To overcome the limited specificity of the currently studied predictors, multiple predictive models were developed using the interplay of multiple factors to predict SSR in NOA [6,28]. However, these models remain limited by their reliance on retrospective data, which undermines the reliability of their predictive performance. Therefore, it should be acknowledged that no truly reliable markers currently exist to predict sperm retrieval success accurately [13].

HORMONAL THERAPY PRIOR TO SPERM RETRIEVAL: DOES IT REALLY HELP?

Normal spermatogenesis requires both serum FSH and intratesticular testosterone. In hypogonadotropic hypogonadism (hypo-hypo), spermatogenesis is absent due to insufficient gonadotropin stimulation, whereas in hypergonadotropic hypogonadism, spermatogenesis is typically impaired or absent as a result of primary testicular failure. Consequently, hormonal therapy aiming to increase intratesticular testosterone and to a lesser extent serum FSH has been proposed to improve SRR in men with NOA [29]. Moreover, the testosterone-to-estradiol (T/E2) ratio reflects the balance between androgen production and aromatization. In some studies, a disrupted ratio, particularly a low T/E2, has been associated with impaired spermatogenesis, and modulation with aromatase inhibitors has been proposed to improve the intratesticular hormonal milieu [30]. A recent meta-analysis reported higher SRR in eugonadal men who received hormonal therapy prior to micro-TESE (odds ratio [OR] 2.13, p=0.02), while men with hypergonadotropic hypogonadism generally did not benefit. Heterogeneous protocols were used across the included studies, including FSH, human chorionic gonadotropin (hCG), selective estrogen receptor modulators, and aromatase inhibitors [29]. Therefore, due to a lack of proper randomized controlled trials and conflicting data in the literature, current guidelines do not routinely recommend hormonal therapy [11,13,19]

Hormonal therapy has been mainly studied before initial sperm retrieval. However, in selected cases, it may also be considered after a failed micro-TESE as part of an individualized management strategy, with one study showing a 21% SRR after hCG treatment compared to 0% in untreated controls, with hypospermatogenesis on initial biopsy being a key predictor of success [31]. Despite that, these are considered salvage cases of SSR; therefore, every effort should be made to increase SRR. Given the low risk of side effects and having the potential to improve SRR in this subset of complex cases, hormonal therapy may be individually used in men with NOA before ICSI after proper counseling of patients and informing them about the lack or poor evidence of its efficacy [19,32].

Particularly important to emphasize that exogenous testosterone must not be used in hypogonadal men with NOA who are planning testicular sperm retrieval and wish to preserve fertility [19].

SHOULD VARICOCELE REPAIR BE RECOMMENDED IN NOA?

Varicocele may contribute to the development of azoospermia. As early as the 1950s, there was a report of a patient with NOA in whom bilateral varicocele repair led to the appearance of sperm in the ejaculate and even pregnancy in the partner [33]. More recent studies have demonstrated that up to 43.9% of men may recover sperm in the ejaculate after varicocele treatment [34,35]. Evidence from meta-analyses of controlled studies suggests that varicocelectomy (VR) may improve the probability of successful sperm retrieval in selected NOA patients. Positive predictive factors include hypospermatogenesis, late maturation arrest, and the grading of clinical varicocele [36,37]. However, the quality of these studies remains low, with a high risk of bias, making it impossible to conclude that VR is universally justified for all NOA patients. A recent meta-analysis including only controlled studies found that, in NOA men with clinical varicocele, prior varicocele repair significantly improved outcomes, including

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surgical SRR (OR 2.17, 95% confidence interval [CI] 1.17 to 4.01), sperm appearance in the ejaculate (OR 7.8, 95% CI 3.59 to 16.94), and clinical pregnancy rate after ICSI (OR 2.18, 95% CI 1.03 to 4.60) [2].

While most studies have evaluated VR prior to the first sperm retrieval attempt, this approach may also be considered after a failed micro-TESE in carefully selected patients. These findings strengthen the rationale for offering VR to carefully selected NOA patients after individualized risk–benefit discussion [19]. Notably, in patients with varicocele and prior testicular biopsy, histopathology plays a significant role in predicting outcomes: those with hypospermatogenesis are more likely to benefit from varicocele repair, whereas those with SCO syndrome generally have a poor prognosis [21].

Regarding AUA/ASRM guidelines stated that VR in NOA patients with clinical varicocele is still of limited evidence [11]. Varicocele repair in NOA patients is not recommended for non-palpable varicoceles [19]. It is important to emphasize that VR is not universally justified for all men with NOA, and the potential benefit is limited to carefully selected patients.

FINE NEEDLE ASPIRATION MAPPING: IS THERE A ROLE FOR TARGETED SAMPLING IN NOA?

Fine Needle Aspiration Mapping (FNAM) is a targeted, principally diagnostic technique that systematically samples multiple sites across the testes to localize foci of active spermatogenesis. The aspirated fluid is then spread on a slide, fixed with alcohol, stained by the Papanicolaou stain, and examined for the presence of sperm, thus identifying areas with active spermatogenesis for targeted SSR in further trials. This mapping approach may be helpful in some subsequent sperm retrieval strategies in men with NOA, where spermatogenesis tends to be patchy and focal [38].

The main advantages of FNAM are that it can be performed quickly under local anaesthesia and does not require an operating room [39]. Reported SRR with FNAM varies from 25% to 58%, influenced by the number of aspiration sites (typically 7 to 21), the heterogeneity of spermatogenic activity, and the intrinsic limitations of blind sampling techniques [39]. Although FNAM has shown partial concordance with micro-TESE outcomes, a subsequent TESE procedure remains necessary in approximately 80% of cases to obtain adequate tissue or sperm quantities [40]. A significant limitation of FNAM that was not described before is that the sperm identified on the touch preparation cannot be used for ICSI or cryopreservation, raising the risk of losing valuable sperm in men with severely impaired spermatogenesis.

The procedure is generally well tolerated, with minor complications [39]. Despite being minimally invasive and cost-effective, FNAM is not a common practice and is not recommended by current guidelines [13,19].

IS MICRO-TESE THE ONLY SURGICAL OPTION IN NOA?

Since its introduction by Schlegel in 1999, micro-TESE has become a widely accepted surgical technique among urologists and andrologists [41]. Nevertheless, recent survey data from the Global Andrology Forum (GAF) show that only 32.4% of surgeons routinely proceed directly to micro-TESE in men with NOA. In contrast, others prefer a stepwise approach starting with conventional TESE (c-TESE), testicular sperm aspiration (TESA), or fine-needle aspiration (FNA) before escalating to micro-TESE [42].

Moreover, in the general population of patients with NOA, multiple studies and meta-analyses consistently demonstrate that micro-TESE offers the highest SRR among available techniques, 56.9% on average [43]. It is also well established that micro-TESE provides a clear advantage over c-TESE, primarily in SCO syndrome and hypospermatogenesis cases. At the same time, in men with maturation arrest, SRR tend to be similar between the two methods [43].

Nevertheless, not all studies consistently demonstrate higher SRR with micro-TESE, likely reflecting differences in patient selection, lack of randomization, and variability in surgical and laboratory expertise [44,45].

In line with these findings, GAF strongly recommends micro-TESE for men with NOA. AUA/ASRM and EAU guidelines also support it as the preferred method, with moderate and weak recommendations [11,13,19].

Overall, micro-TESE should still be regarded as the preferred technique for sperm retrieval in men with NOA, while c-TESE may be considered in centers lacking microsurgical capability.

HOW CAN WE PERFORM SAFE AND EFFECTIVE MICRO-TESE?

Optimizing outcomes of micro-TESE in patients with NOA requires thorough preoperative planning and meticulous microsurgical technique. Several key intraoperative steps have been proposed to ensure both effectiveness and safety [46]:

1. The standard procedure for micro-TESE involves a large 180°–270° equatorial incision of the testis allowing proper exposure of all testicular compartments. Alternatively, a small para-equatorial incision corresponding to approximately one quarter of the testicular circumference in an avascular albugineal area, extendable, if necessary has been introduced to allow controlled access while facilitating closure.
2. High-power magnification (20–25×) is an essential prerequisite for performing a true micro-TESE to identify seminiferous tubules (STs) with favorable characteristics based on diameter and opacity. Higher magnification (36×) makes it even easier to differentiate tubular sizes. Exploration of superficial and deep STs may be done to increase the possibility of finding dilated tubules.
3. Gentle irrigation with Ringer's solution may help prevent desiccation.
4. In cases of uniform tubule appearance, a piece of suture material or caliper may help compare and differentiate tubule diameters under the microscope.
5. To avoid postoperative bleeding, hemostasis must be performed at normalized blood pressure by gently pressing the testicular tissue using gauze and the least possible cauterization by using the microsurgical bipolar thermal device at low energy power.
6. Tunica albuginea closure should use a water-tight, continuous, absorbable suture, avoiding including everted tubules.
7. Postoperative care includes cold compresses, bed rest for 1–2 days, analgesia, and abstinence from intercourse for 10 days.

It should be noted that many of these practical steps are based on empirical experience and expert opinion and may vary among surgeons.

FRESH *VS.* CRYOPRESERVED TESTICULAR SPERM: DOES IT MATTER FOR ICSI IN NOA?

Although multiple studies and meta-analyses report no significant differences in fertilization, clinical pregnancy, or live birth rates between fresh and cryopreserved testicular sperm in NOA, the question remains clinically relevant for both patients and professionals involved in the ICSI process [46].

Several considerations contribute to this debate. The number of sperm retrieved after micro-TESE may be insufficient for standard cryopreservation, and in such cases, specific freezing protocols have been developed [47]. However, there are no reports on the long-term efficacy of such methods, and these protocols may not be available in all ICSI settings. Moreover, using fresh sperm avoids the risk of complete post-thaw sperm loss, reported at ~6% to 9% in a series of very low/rare sperm, which is particularly critical in NOA, where often only a very low number of sperm can be retrieved [48,49]. Therefore, proper counselling of the couple should be done before choosing to use fresh or cryopreserved sperm.

WHAT ARE THE NEXT STEPS AFTER A FAILED MICRO-TESE?

Micro-TESE in NOA fails to retrieve sperm in 40% to 50% of cases [13]. This raises an important question for both clinicians and patients: what options remain in such cases?

The most apparent approach is to attempt a repeat testicular biopsy (salvage micro-TESE). However, a fundamental issue emerges: on what grounds can we expect success from a second procedure when the first was unsuccessful?

One reasonable justification is a concern about the quality of the initial procedure. Technical shortcomings, such as unilateral exploration, insufficient microdissection, or suboptimal tissue processing, can limit the likelihood of identifying rare spermatozoa. The expertise of both the surgeon and the embryologist plays a pivotal role in this process [50,51]. Histology from previous micro-TESE also plays an important role, as salvage procedures are more likely to succeed in cases of KS syndrome or hypospermatogenesis. In contrast, success is much less likely in SCO syndrome [27]. Two

recent studies illustrate how these factors might influence outcomes. Özman et al (2021) [52] reported a salvage micro-TESE success rate of 18.4% in 125 patients with a failed initial procedure, many of whom had undergone their first micro-TESE in other institutions. In addition, some patients received hormonal therapy before the repeat procedure, but no statistically significant improvement in SRR was observed. In contrast, Yücel et al (2018) [53] documented a 42.8% SRR specifically in salvage (second) micro-TESE procedures among 49 men whose first and second attempts were both performed in the same clinic, using the same protocol and without hormonal preparation. This striking difference supports the notion that operator experience and procedural consistency may be decisive in salvage outcomes.

Several interventions have been proposed to improve salvage micro-TESE results, such as varicocele repair [36], hormonal optimization [31], or even platelet-rich plasma injection into testicular tissue [54]. A recent SRMA on redo-micro-TESE has concluded that hypospermatogenesis and KS syndrome are associated with a better prognosis for successful SRR. However, evidence on the use of hormonal stimulation in men with NOA and previous failed SSR remains limited [27]. Therefore, the current evidence base is insufficient to recommend any procedure or predictive factors for routine clinical use or to consider them a standalone indication for repeat surgery.

In summary, current evidence indicates that the skill of the surgical and embryology team largely determines salvage micro-TESE success. No adjunctive therapy has yet demonstrated consistent benefit sufficient for routine recommendation after a failed primary micro-TESE. Until robust, high-quality data emerge, the most impactful decision after an unsuccessful attempt is to ensure the procedure is performed in an experienced, high-volume center. Beyond surgical considerations, it is equally important to provide couples with clear counseling on the emotional impact of an unsuccessful retrieval. Discussion should include alternative family-building options such as the use of donor sperm, adoption, or choosing to live without children. Incorporating structured psychological support into the care pathway can help couples navigate these difficult decisions more resiliently.

CONCLUSION

This editorial has reviewed several key aspects of NOA management, which remains one of the most challenging domains in male infertility, requiring a multidisciplinary and individualized approach. Evidence still supports micro-TESE as the preferred method of sperm retrieval. However, its success depends on surgical expertise, laboratory proficiency, and patient selection. Adjunctive interventions, such as varicocele repair and hormonal therapy, may have a role in carefully selected cases, but their benefit remains limited and subject to ongoing debate. The choice between fresh and cryopreserved sperm requires individualized planning, with clear counseling regarding risks and benefits.

Emerging advances in genetic diagnostics, imaging modalities, molecular biomarkers, and regenerative medicine hold promise, but most remain investigational and lack clinical validation. Until such innovations mature, management should rely on evidence-based strategies, systematic data collection, and proper couple counseling to balance medical, psychological, and ethical dimensions of care.

The field of NOA management is still in need of more properly designed multicenter studies as well as randomized controlled studies to validate proposed predictors for SSR and enhance personalized-precision medicine for NOA.

Conflict of Interest

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REFERENCES

1. Mao JF, Xu HL, Duan J, Chen RR, Li L, Li B, et al. Reversal of idiopathic hypogonadotropic hypogonadism: a cohort study in Chinese patients. Asian J Androl 2015;17:497-502.
2. Çayan S, Pinggera GM, Alipour H, Altay B, Shah R, Giulioni C, et al. The effects of varicocele repair on testicular sperm retrieval, sperm recovery in the ejaculate and clinical pregnancy rates in non-obstructive azoospermic men with clinical varicocele: a systematic review and meta-analysis. World J Mens Health 2025. doi: 10.5534/wjmh.250065 [Epub].
3. Tharakan T, Luo R, Jayasena CN, Minhas S. Non-obstructive azoospermia: current and future perspectives. Fac Rev 2021;10:(7).
4. Chiba K, Enatsu N, Fujisawa M. Management of non-obstructive azoospermia. Reprod Med Biol 2016;15:165-73.
5. Cerván-Martín M, Castilla JA, Palomino-Morales RJ, Carmona FD. Genetic landscape of nonobstructive azoospermia and new perspectives for the clinic. J Clin Med 2020;9:300.
6. Jamalirad H, Jajroudi M, Khajehpour B, Sadighi Gilani MA, Eslami S, Sabbaghian M, et al. Ai predictive models and advancements in microdissection testicular sperm extraction for non-obstructive azoospermia: a systematic scoping review. Hum Reprod Open 2025;2025:hoae070.
7. Cioppi F, Rosta V, Krausz C. Genetics of azoospermia. Int J Mol Sci 2021;22:3264.
8. Momtazi-Mar L, Naelitz BD, Mucci A, Cannarella R, Lundy SD. Surgical sperm retrieval in patients with nonmosaic Klinefelter syndrome (47,XXY) may be safely delayed until adulthood: a systematic review and meta-analysis. Fertil Steril 2025;124:1223-34.
9. Nguyen MH, Morel F, Pennamen P, Parent P, Douet-Guilbert N, Le Bris MJ, et al. Balanced complex chromosome rearrangement in male infertility: case report and literature review. Andrologia 2015;47:178-85.
10. Majzoub A, Viana MC, Achermann APP, Ferreira IT, Laursen RJ, Humaidan P, et al. Non-obstructive azoospermia and intracytoplasmic sperm injection: unveiling the chances of success and possible consequences for offspring. J Clin Med 2024;13:4939.
11. Brannigan RE, Hermanson L, Kaczmarek J, Kim SK, Kirkby E, Tanrikut C. Updates to male infertility: AUA/ASRM guideline (2024). J Urol 2024;212:789-99.
12. Krausz C, Navarro-Costa P, Wilke M, Tüttelmann F. EAA/EMQN best practice guidelines for molecular diagnosis of Y-chromosomal microdeletions: state of the art 2023. Andrology 2024;12:487-504.
13. Minhas S, Boeri L, Capogrosso P, Cocci A, Corona G, Dinkelman-Smit M, et al. European Association of Urology guidelines on male sexual and reproductive health: 2025 update on male infertility. Eur Urol 2025;87:601-16.
14. Abur U, Gunes S, Ascı R, Altundag E, Akar OS, Ayas B, et al. Chromosomal and Y-chromosome microdeletion analysis in 1,300 infertile males and the fertility outcome of patients with AZFc microdeletions. Andrologia 2019;51:e13402.
15. Kleiman SE, Yogev L, Lehavi O, Hauser R, Botchan A, Paz G, et al. The likelihood of finding mature sperm cells in men with AZFb or AZFb-c deletions: six new cases and a review of the literature (1994-2010). Fertil Steril 2011;95:2005-12.e4.
16. Alhathal N, Maddirevula S, Coskun S, Alali H, Assoum M, Morris T, et al. A genomics approach to male infertility. Genet Med 2020;22:1967-75.
17. Fakhro KA, Elbardisi H, Arafa M, Robay A, Rodriguez-Flores JL, Al-Shakaki A, et al. Point-of-care whole-exome sequencing of idiopathic male infertility. Genet Med 2018;20:1365-73.
18. Riera-Escamilla A, Arafa MM, Farnetani G, Xavier MJ, Oud MS, Majzoub AA, et al. Genetic determinants of testicular sperm extraction outcomes: insights from a large multicentre study of men with non-obstructive azoospermia. Hum Reprod Open 2025;2025:hoaf049.
19. Hamoda T, Shah R, Mostafa T, Pinggera GM, Atmoko W, Rambhatla A, et al. Global Andrology Forum (GAF) clinical guidelines on the management of non-obstructive azoospermia: bridging the gap between controversy and consensus. World J Mens Health 2026;44:90-105.
20. Kim SW, Lee J, Lee TH, Kim DS, Song SH, Kim DK. Azoospermic men with a history of cryptorchidism treated by orchiopexy have favorable outcomes after testicular sperm extraction: a systematic review and meta-analysis. World J Mens Health 2023;41:81-93.
21. Cissen M, Meijerink AM, D'Hauwers KW, Meissner A, van der Weide N, Mochtar MH, et al. Prediction model for obtaining spermatozoa with testicular sperm extraction in men with non-obstructive azoospermia. Hum Reprod 2016;31:1934-41.
22. Ohta T, Kojo K, Kurobe M, Numahata D, Tatsuya T, Okada S, et al. Feasibility of high-frequency ultrasound for seminiferous tubule assessment and correlation of B-mode imaging

with pathological findings in the testis in azoospermia. J Med Ultrason (2001) 2024;51:465-75.
23. Wang H, Guan J, Lin J, Zhang Z, Li S, Guo Y, et al. Diffusion-weighted and magnetization transfer imaging in testicular spermatogenic function evaluation: preliminary results. J Magn Reson Imaging 2018;47:186-90.
24. Fietz D, Sgaier R, O'Donnell L, Stanton PG, Dagley LF, Webb AI, et al. Proteomic biomarkers in seminal plasma as predictors of reproductive potential in azoospermic men. Front Endocrinol (Lausanne) 2024;15:1327800.
25. Koscinski I, Wittemer C, Rigot JM, De Almeida M, Hermant E, Defossez A. Seminal haploid cell detection by flow cytometry in non-obstructive azoospermia: a good predictive parameter for testicular sperm extraction. Hum Reprod 2005;20:1915-20.
26. Caroppo E, Colpi EM, Gazzano G, Vaccalluzzo L, Scroppo FI, D'Amato G, et al. Testicular histology may predict the successful sperm retrieval in patients with non-obstructive azoospermia undergoing conventional TESE: a diagnostic accuracy study. J Assist Reprod Genet 2017;34:149-54.
27. Elbardisi H, Bakircioglu E, Liu W, Katz D. Second chance in fertility: a comprehensive narrative review of redo micro-TESE outcomes after initial failure. Asian J Androl 2025;27:409-15.
28. Majzoub A, Arafa M, Khalafalla K, AlSaid S, Burjaq H, Albader M, et al. Predictive model to estimate the chances of successful sperm retrieval by testicular sperm aspiration in patients with nonobstructive azoospermia. Fertil Steril 2021;115:373-81.
29. Tharakan T, Corona G, Foran D, Salonia A, Sofikitis N, Giwercman A, et al. Does hormonal therapy improve sperm retrieval rates in men with non-obstructive azoospermia: a systematic review and meta-analysis. Hum Reprod Update 2022;28:609-28.
30. Raman JD, Schlegel PN. Aromatase inhibitors for male infertility. J Urol 2002;167:624-9.
31. Shiraishi K, Ohmi C, Shimabukuro T, Matsuyama H. Human chorionic gonadotrophin treatment prior to microdissection testicular sperm extraction in non-obstructive azoospermia. Hum Reprod 2012;27:331-9.
32. Pozzi E, Venigalla G, Raymo A, Ila V, Achermann APP, Esteves SC, et al. Eligibility for the medical therapy among men with non-obstructive azoospermia-Findings from a multicentric cross-sectional study. Andrology 2025;13:234-42.
33. Tulloch WS. Varicocele in subfertility; results of treatment. Br Med J 1955;2:356-8.
34. Esteves SC, Miyaoka R, Roque M, Agarwal A. Outcome of varicocele repair in men with nonobstructive azoospermia: systematic review and meta-analysis. Asian J Androl 2016;18:246-53.
35. Sajadi H, Hosseini J, Farrahi F, Dadkhah F, Sepidarkish M, Sabbaghian M, et al. Varicocelectomy may improve results for sperm retrieval and pregnancy rate in non-obstructive azoospermic men. Int J Fertil Steril 2019;12:303-5.
36. Jensen S, Ko EY. Varicocele treatment in non-obstructive azoospermia: a systematic review. Arab J Urol 2021;19:221-6.
37. Kaltsas A, Dimitriadis F, Chrisofos M, Sofikitis N, Zachariou A. Predictive value of varicocele grade and histopathology in simultaneous varicocelectomy and sperm retrieval in non-obstructive azoospermia: a retrospective cohort study. Medicina (Kaunas) 2024;60:2056.
38. Turek PJ, Cha I, Ljung BM. 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.
39. Beliveau ME, Turek PJ. The value of testicular 'mapping' in men with non-obstructive azoospermia. Asian J Androl 2011;13:225-30.
40. Janosek-Albright KJC, Schlegel PN, Dabaja AA. Testis sperm extraction. Asian J Urol 2015;2:79-84.
41. Schlegel PN. Testicular sperm extraction: microdissection improves sperm yield with minimal tissue excision. Hum Reprod 1999;14:131-5.
42. Rambhatla A, Shah R, Ziouziou I, Kothari P, Salvio G, Gul M, et al. Global practice patterns and variations in the medical and surgical management of non-obstructive azoospermia: results of a world-wide survey, guidelines and expert recommendations. World J Mens Health 2025;43:92-122.
43. Ghalayini IF, Al-Ghazo MA, Hani OB, Al-Azab R, Bani-Hani I, Zayed F, et al. Clinical comparison of conventional testicular sperm extraction and microdissection techniques for non-obstructive azoospermia. J Clin Med Res 2011;3:124-31.
44. Corona G, Minhas S, Giwercman A, Bettocchi C, Dinkelman-Smit M, Dohle G, et al. Sperm recovery and ICSI outcomes in men with non-obstructive azoospermia: a systematic review and meta-analysis. Hum Reprod Update 2019;25:733-57.
45. Esteves SC, Ramasamy R, Colpi GM, Carvalho JF, Schlegel PN. Sperm retrieval rates by micro-TESE versus conventional TESE in men with non-obstructive azoospermia-the assumption of independence in effect sizes might lead to misleading conclusions. Hum Reprod Update 2020;26:603-5.
46. Amer M, Fakhry E. Fresh vs frozen testicular sperm for assisted reproductive technology in patients with non-obstructive azoospermia: a systematic review. Arab J Urol 2021;19:247-54.
47. Mangoli V, Evgeni E, Wyns C. Sperm cryopreservation

protocol for micro-TESE-retrieved sperm. Asian J Androl 2025;27:392-8.
48. Huang C, Gan RX, Hu JL, Liu F, Hong Y, Zhu WB, et al. Clinical benefit for cryopreservation of single human spermatozoa for ICSI: a systematic review and meta-analysis. Andrology 2022;10:82-91.
49. Kathrins M, Abhyankar N, Shoshany O, Liebermann J, Uhler M, Prins G, et al. Post-thaw recovery of rare or very low concentrations of cryopreserved human sperm. Fertil Steril 2017;107:1300-4.
50. Ishikawa T, Nose R, Yamaguchi K, Chiba K, Fujisawa M. Learning curves of microdissection testicular sperm extraction for nonobstructive azoospermia. Fertil Steril 2010;94:1008-11.
51. Ramasamy R, Reifsnyder JE, Bryson C, Zaninovic N, Liotta D, Cook CA, et al. Role of tissue digestion and extensive sperm search after microdissection testicular sperm extraction. Fertil Steril 2011;96:299-302.
52. Özman O, Tosun S, Bayazıt N, Cengiz S, Bakırcıoğlu ME. Efficacy of the second micro-testicular sperm extraction after failed first micro-testicular sperm extraction in men with nonobstructive azoospermia. Fertil Steril 2021;115:915-21.
53. Yücel C, Budak S, Keskin MZ, Kisa E, Kozacioglu Z. Predictive factors of successful salvage microdissection testicular sperm extraction (mTESE) after failed mTESE in patients with non-obstructive azoospermia: long-term experience at a single institute. Arch Ital Urol Androl 2018;90:136-40.
54. Gudelci T, Cakiroglu Y, Yuceturk A, Batır S, Karaosmanoglu O, Korun ZEU, et al. The effect of intratesticular autologous platelet-rich plasma injection on sperm retrieval rates and in vitro fertilization outcomes in couples with non-obstructive azoospermia. J Obstet Gynaecol Res 2024;50:1977-84.