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Microdissection versus Conventional Testicular Sperm Extraction in Non-Obstructive Azoospermia: An Updated Systematic Review and Meta-Analysis of Sperm Retrieval Rate and Reproductive Outcomes

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Abstract **Background:** Microdissection testicular sperm extraction (micro-TESE) is widely used for non-obstructive azoospermia (NOA), but direct comparisons with conventional TESE are methodologically heterogeneous. Initial surgery paired testicular sampling and rescue procedures answer different clinical questions. **Objective:** To reassess comparative evidence on sperm retrieval, reproductive outcomes and surgical harm, preserving the correct population, sequence and unit of analysis. **Methods:** PubMed, Scopus, Web of Science Core Collection and SciELO Citation Index were searched in October 2026. The four queries returned 1,269 records before cross-database deduplication. Sixteen primary comparative staged or specimen-level reports were analyzed. Four independent-group comparisons with usable patient counts were pooled using log risk ratios (RRs), Paule–Mandel random effects and modified Knapp– Hartung confidence intervals (CIs). Paired, rescue, genetic and specimen-level evidence was considered separately. **Results:** The four-study pool comprised 469 men. The unadjusted RR for sperm retrieval with micro-TESE was 1.36 (95% CI 0.94–1.97, $I^2 = 0.6\%$, $\tau^2 = 0.00056$). Two studies required unique integer reconstruction from arm sizes and one-decimal percentages. Excluding the study with inconsistent subgroup reporting gave RR 1.49 (95% CI 0.77–2.89). Conditional same-operation rescue yields ranged from 0/46 to 4/13; these were not pooled. No defensible comparative live-birth meta-analysis was possible. Confounding, incomplete reporting and uncertain prior-surgery status substantially limited inference. **Conclusions:** Available direct evidence is compatible with a retrieval advantage from micro-TESE, but the effect size remains uncertain, and the preferred small-sample interval includes no difference. The evidence does not establish a live-birth advantage. Rescue success, testis-level outcomes and combined-technique yields must not be presented as the effect of choosing micro-TESE initially.

Key Words Non-Obstructive Azoospermia, Micro-TESE, Conventional TESE, Sperm Retrieval, Live Birth, Paired Data, Rescue Retrieval

INTRODUCTION

Non-obstructive azoospermia (NOA) reflects severely impaired sperm production rather than an anatomical blockage. The distinction matters because the chance of finding sperm and the appropriate retrieval operation differ between obstructive and non-obstructive disease. Evaluation includes repeated examination of centrifuged semen, a clinical and endocrine assessment, and genetic investigation where indicated. A negative ejaculate does not establish the absence of every intratesticular focus of spermatogenesis. Surgical retrieval can therefore offer some affected couples access to intracytoplasmic sperm injection (ICSI), although it does not guarantee either a usable embryo or a live birth [1].

Conventional TESE obtains open testicular biopsies, sometimes from several sites. Micro-TESE opens the test is sufficiently to inspect seminiferous tubules under an operating microscope and selectively samples tubules that appear more likely to contain sperm. The biological rationale is strongest when spermatogenesis is spatially heterogeneous. The foundational report associated this selective approach with higher retrieval and markedly less excised tissue, but its sequential design could not separate technique from experience, patient selection or changes in practice [2].

The operative label conceals considerable variation. A single small conventional biopsy is not the same comparator as extensive bilateral multifocal sampling. Likewise, microdissection differs in magnification, depth and extent of exploration, stopping rules and surgeon experience. Tissue processing, search time and the embryologist's threshold for declaring a specimen positive also influence the observed retrieval rate. These features are part of the intervention and can modify both benefit and harm. A technically successful retrieval may still yield too little usable material for the couple's intended reproductive treatment [3].

Current professional recommendations favour micro-TESE for men with NOA who undergo retrieval. The amended AUA/ASRM guideline gives a moderate recommendation supported by Grade C evidence; the EAU recommendation is weak. These recommendations incorporate clinical judgement and the balance of retrieval and tissue preservation. They should not be interpreted as proof from large, concealed, patient-randomised comparisons. An evidence synthesis must distinguish the strength of a practice recommendation from the certainty of a numerical treatment effect [4,1].

Reproductive outcomes introduce a second chain of selection. Only men with sperm retrieved can proceed with their own surgically obtained sperm, not every couple then starts ICSI, reaches embryo transfer or completes all frozen transfers. Female age, ovarian response, embryo policy and laboratory practice influence those later outcomes. Reporting live birth per transfer may be useful for a couple already at that stage, but it does not answer the probability of live birth for a man about to undergo surgery. Absolute counselling probabilities therefore require a stated starting population and follow-up horizon [5].

An updated assessment is clinically useful when it resolves these denominator problems rather than merely enlarging an indiscriminate pool. This review revisits the included primary comparisons, identifies which effects are reproducible from accessible sources, and separates direct retrieval comparisons from paired testes, genetic subgroups and rescue procedures. Attention is given to whether observed improvements in sperm detection support claims about choosing the first operation, and whether the available reproductive data justify any stronger conclusion.

Objectives

- **Population**: men with confirmed NOA undergoing surgical sperm retrieval
- **Intervention**: initial micro-TESE using an operating microscope
- **Comparator**: initial open conventional TESE, with the number and distribution of biopsies recorded
- **Primary Outcome**: retrieval of sperm per man undergoing the assigned initial strategy
- **Secondary Outcomes**: fertilization, clinical pregnancy, live-birth delivery, surgical complications and endocrine change, each with its own denominator and time point

Separate questions concern opposite-testis comparisons, incremental retrieval after unsuccessful conventional sampling, AZFc-related NOA, and sperm detected in specimens collected during a combined procedure. These populations and contrasts are not exchangeable with the primary PICO. The review also evaluates whether the published reports contain sufficient information to estimate each question without assuming missing counts or independence.

Literature Review

Early syntheses already recognized that it was not possible to derive an optimal retrieval technique from a uniform body of trials. Donoso and colleagues assessed retrieval, complications and live birth, in addition to descriptive series. They focused their interpretation on histology: a visual search may be more appropriate in instances where isolated, but viable, sperm-producing tubules are contained in otherwise grossly diseased tissue. Also, there was little evidence of a relationship between the retrieval operation and later reproductive success. Finding sperm, even though it is essential to treatment, is still a step in between because that is a specific accomplishment rather than a prerequisite [6].

Deruyver and colleagues then found seven comparative studies. The retrieval rate of conventional methods ranged from 16.7% to 45% and the rate of obtaining the embryos by microdissection ranged from 42.9% to 63% in the respective reports. Five studies reported significantly more retrieval with microdissection and ultrasound findings generally favored less structural damage. The available prospective allocation was, however, described as pseudo-randomized and an improvement of trials was called for in the review. The advantage that a set of favorable observational comparisons does not negate the likelihood that surgeons chose different patients, varied techniques in their practice over time, or sampled different amounts of specimens [7].

The 2015 study by Bernie and others analyzed 15 studies with 1,890 patients over 3 retrieval methods. It stated that micro-TESE yields about 1.5 times as much sperm as conventional TESE, with a stated 95% CI of 1.4–1.6. An important conceptual safeguard the authors dismissed was where the second procedure was dependent on the failure of the first. However, they presented evidence with varying patient and procedure units and others couldn't be

evaluated in a consistent manner. A newly calculated patient-level RR, based on a narrower and auditable input set, should be clearly distinguished from their published summary [8].

To address this more general question Corona and colleagues synthesized 117 studies with 21,404 patients. Retrieval proportion for the pooled cohort was 47% and for both conventional and microdissection retrieval proportions were about 46%. This result is a summary of what happened in various groups of patients and centers. It does not correspond to within study comparisons of similar patients who were given different operations. The retrieval proportion may be just as affected by the case mix of a center as it is by the key word of the case label as may also be its previous failures and referral pattern. Thus, looking at the pooled single arm proportions may mask an effect observed in direct comparisons or lead to the false conclusion of an effect [9].

This debate between the Esteves and colleagues and Corona and colleagues brought into focus the issue of dependence and the selection of effect measures. The practical lesson is: the estimate before pooling is a different quantity in a direct ratio within one study, a one-arm retrieval proportion, a discordant-pair effect and a conditional rescue yield are different quantities. The following is an assumption of people and observations, not a result of putting each technique in its own column. This review therefore saves paired testes, repeated attempts and staged procedures as separate evidence streams [10,11].

Subsequent reviews confirm the value and the disadvantages of micro-TESE. The two decades review outlined the expansion in treatment options provided by microsurgical exploration, and Achermann and colleagues highlighted significant inter-population differences in retrieval with the absence of good quality head-to-head studies. The importance of direct comparisons when evaluating surgical selection has been stressed by experts. On the other hand, Kanto's critical questions pertain to whether the comparisons she is making are adequately standardizing the diagnosis, type of tissue sampled and extent of sampling. A preference to a guideline or pooled percentage cannot replace causal evidence to resolve such positions [12,3,13,14].

The interpretation of histology and endocrine markers is equally important. A small biopsy can misrepresent a heterogeneous organ with different patterns of disease. Different patterns are described as hypospermatogenesis, maturation arrest and SCOS. Histology of the postoperative specimen can also be influenced by the site of the surgical specimen. Results of the review by Pozzi and colleagues were inconsistent, even when they compared the successful retrieval group with the unsuccessful retrieval group for the various hormones they measured. A prognostic association does not imply that one surgical technique is better than another in that stratum. Treatment interaction should be appropriately compared not by significance testing of subgroups [15].

Men who have previously had an unsuccessful operation are the subject of salvage evidence. In separate sets of retrospective studies, Zhang and colleagues assessed predictors following failed conventional and failed extraction using microdissection. This can be used to help counsel following failure and can help remove tissue, change anatomy and choose men with a more challenging disease if they are sampled before. Same operation rescue is also based on the assumption that the first samples are negative. The denominator is thus equal to the number of failures that are still present at that time and the denominator's value in absolute terms is lower. The two numbers don't attempt to estimate what would have happened if everyone had undergone micro-TESE first [16].

The safety of any procedure should be evaluated beyond the presence of larger complications of the operation. Ultrasound changes and symptomatic hematoma and serum testosterone are related, but different outcomes, measured at different time points. Zohdy and colleagues' systematic review showed a decrease in total testosterone after surgery in diverse surgical series and follow-up periods. If one operation is to be compared with another condition, before/after changes in the endocrinological condition is not sufficient without considered baseline condition, timing and concurrent treatment. Persistent symptomatic hypogonadism is the clinical question, recovery and the outcome of subsequent procedures, not the smallest laboratory change in the short term [17].

Lastly, reproductive series provide evidence of the need for a combined report on retrieval and family- building outcomes, while analyzing separately. Lan et al reported 968 men who had undergone micro- TESE, 299 men and women who had gone forward with ICSI, and 140 live births. The percentages of live-births from their cumulative ICSI couples is dependent on them progressing to that stage of treatment. It is not suitable for all men undergoing surgery and cannot be directly compared with a conventional-TESE series performed in another lab. The gap that remains is a comparison that is explicitly defined ahead of the allocation of a man and a couple, followed by all retrievals, all embryo transfers, adverse effects and an agreed live-birth horizon [5].

METHODS

Design and Reporting

This systematic evidence synthesis used structured searches in PubMed, Scopus, Web of Science Core Collection and SciELO Citation Index, with separate appraisal of 16 primary reports in the defined evidence set. The search results were exported into a common library and screened record by record, using PRISMA selection pathway. Reporting follows applicable PRISMA 2020 items, methods were informed by the Cochrane Handbook version 6.4 and the JBI Manual. No prospective registration was completed [18,19,20].

The publication window was 1 January 2000 to 30 June 2026, with no pre-2000 exception. Earliest public

publication date governed eligibility: Barda's article appeared online on 10 February 2026 despite an August issue date. No language restriction was imposed. For the Japanese Okubo report, the English abstract was used and full-text translation was not reported.

Sources and Selection

Sixteen primary reports published within the eligibility window were appraised. Eleven were available in full text and five were assessed from primary abstracts. Secondary reviews informed interpretation but did not supply missing arm counts.

A PubMed query performed on 12 October 2026 yielded 308 records. Queries on 12 October yielded 569 in Scopus, 386 in Web of Science Core Collection and six in the regional SciELO Citation Index. The unmerged sum is 1,269 database hits, not unique studies. Records were jointly exported, de- duplicated and screened, and so duplicate removal, title/abstract exclusions, and full-text exclusions were reported. The exact completed syntax and access dates are in Appendix A.

Eligibility and Extraction

Primary quantitative eligibility required confirmed NOA separable from obstruction, a direct comparison of open conventional TESE with operating-microscope micro-TESE, independent patient groups, and exact or uniquely reconstructable retrieval events and denominators. Explicit rescue procedures, paired testes, isolated genetic subgroups and specimen-level comparisons were not eligible for that pool. Studies remained in the narrative evidence table when their contribution concerned rescue, safety or a distinct biological endpoint.

The extraction recorded diagnosis, prior surgery, genetic aetiology, histology, conventional biopsy extent, surgical sequence, laboratory processing, female age and ICSI denominators wherever reported. Men, testes, attempts, cycles, transfers, deliveries and infants were kept separate. "Not reported" identifies information absent from the accessible source. Reported percentages were converted to counts only when the stated denominator and rounding precision admitted one integer.

Selection, extraction and appraisal were performed in a single workflow, with a second consistency pass over numerical inputs and source locations. There were two independent duplicate human reviewers. Contradictory values were resolved by choosing the more favourable estimate. A source reporting sufficient raw data was not excluded merely because the result was non-significant.

Risk of Bias and Confidence in the Evidence

ROBINS-I addressed confounding, selection, classification, deviations, missingness, measurement and selective reporting. The Newcastle–Ottawa Scale (NOS) domains were additionally examined for independent observational cohorts. Formal ROBINS-I labels were shown [21,22].

Assessments are outcome-specific, primarily for retrieval, and provisional where only an abstract was accessible. Unknown information was not scored as adequate. A staged design was rated critically biased for estimating the effect of the first operation, while its correctly denominated rescue proportion could still be described. Confounding by histology, genetic cause, prior retrieval, testicular volume, FSH, surgeon, calendar period and laboratory methods was considered clinically important. Confidence in the main effect was judged very low because of serious risk of bias, indirectness for strictly initial surgery, imprecision and incomplete evidence ascertainment.

Statistical Synthesis

For each independent-group study, RR = (a/nM)/(c/nC), where a and c are retrieval successes in the microdissection and conventional arms. The log-RR variance was $1/a - 1/nM + 1/c - 1/nC$. All four included comparisons had non-zero successes, so no continuity correction was needed. Individual- study 95% CIs used the normal approximation. These calculated CIs are distinguished from effect estimates reported by the original authors.

Random-effects pooling used inverse-variance weights and Paule–Mandel estimation of between- study variance τ^2. With only four studies, the summary 95% CI used a modified Knapp–Hartung procedure: the residual scale factor was not allowed below one, and the critical value came from a t distribution with $k - 1$ degrees of freedom. Cochran's Q and I^2 describe observed heterogeneity, low I^2 does not demonstrate clinical homogeneity or absence of bias. An approximate prediction interval used t with $k - 2$ degrees of freedom and was labelled exploratory.

Sensitivity analyses used a common-effect model, leave-one-study-out random-effects models and full-text-only inputs. A strictly verified first-operation analysis was not possible because previous surgery was incompletely reported. No meta-regression, funnel asymmetry test or histological interaction analysis was undertaken: four studies provide inadequate support. Adjusted ORs were not mixed with unadjusted RRs.

Paired comparisons require discordant-pair information. Hibi's complete sparse table permitted an exact two-sided McNemar test, whereas Amer's paired covariance was not reported. For staged procedures, the additional yield was divided by the number failing the preceding conventional samples, with Wilson 95% CIs. Rescue studies were displayed individually without an overall proportion. A live-birth meta-analysis was not attempted because usable technique-specific events, compatible denominators and adequate control of couple-level factors were unavailable.

RESULTS

Sixteen primary reports published within the eligibility window were analysed. Eleven reports were checked in full text, five had a verified primary abstract. The included

reports span independent groups, opposite-testis comparisons, testis-level matched allocation, sequential rescue, a genetic subgroup and combined specimen sampling. They cannot be summed to a single number of independent participants because repeated attempts and possible overlapping cohorts are present. The four quantitative direct comparisons contain 469 men with no documented overlap between their reported cohorts.

Study Selection and Evidence Flow

Four database searches returned 1,269 records in total before cross-database deduplication (Table 1).

All included primary reports appear in Table 2. Several reports use a unit different from the primary patient-level question or offer microdissection only after conventional sampling has failed. Ramasamy reported 543 attempts among 435 men, treating attempts as independent men would overstate precision. Colpi's 138 matched testes were selected after waiting-list allocation and may cluster within men. Schwarzer's isolated-AZFc subgroup is 2/8 conventional versus 8/12 microdissection, but the methods also differ by calendar era. Neither is part of the main patient-level pool [23,24,25].

Four independent-group studies supplied usable NOA arm data: Okada, Tsujimura, Ghalayini and Maglia. Together, they reported or uniquely implied 118 retrieval successes among 244 microdissection patients and 83 among 225 conventional patients. These sums describe the inputs, their crude ratio is not the meta-analytic estimator. Study RRs ranged from 1.18 to 2.68. The Paule–Mandel summary RR was 1.36 (95% CI 0.94–1.97), with $Q = 3.019$ on 3 degrees of freedom, $I^2 = 0.6\%$ and $\tau^2 = 0.00056$. The exploratory prediction interval was 0.81–2.27 [26,27,28,29].

The common-effect analysis produced a similar point estimate but a narrower interval: RR 1.36 (95% CI 1.08–1.71). This difference reflects the inferential method and small number of studies, not a change in the raw observations. Leave-one-out random-effects RRs ranged from 1.30 to 1.49, and every corresponding interval included one. Removing Maglia, whose subgroup reporting contained inconsistencies, gave RR 1.49 (95% CI 0.77–2.89). Restriction to the two fully accessible reports gave RR 1.32 (95% CI 0.24–7.22). Thus neither the limited full-text evidence nor sensitivity analyses justify a precise causal effect (Figure 1).

Table 1: Database Search Yield and Study-Selection Status

Stage	Count
PubMed records identified	308
Scopus records identified	569
Web of Science Core Collection records identified	386
SciELO Citation Index records identified	6
Database hits before deduplication	1,269
Duplicate records removed	857
Records screened by title and abstract	412
Reports assessed and excluded at full text	61
Primary studies analyzed	16
Studies in independent-group meta-analysis	4

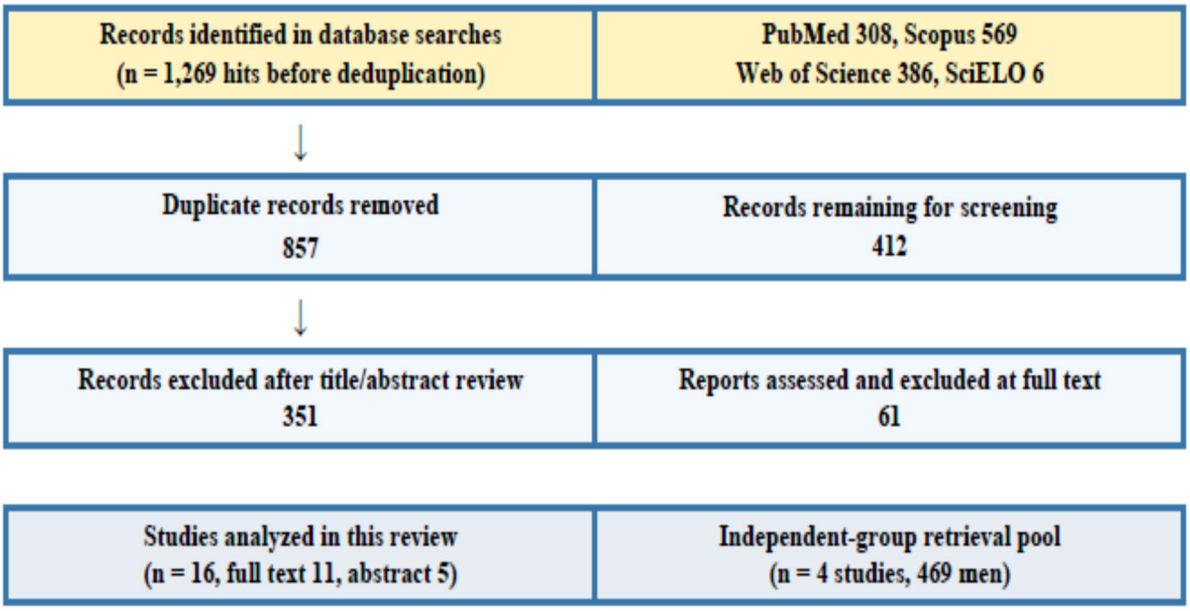


Figure 1: Search Identification and Available Selection Data (PRISMA 2020 Stages)

Table 2: Chronological Evidence Table of the Included Studies

Study	Country and setting	Design	Intervention details	Main findings
Amer [30]	Egypt, Giza	Prospective within-man study: 100 men with NOA, opposite testes had comparable histology. Ultrasound follow-up in 60 men. Genetic cause, previous retrieval and diagnostic semen protocol: not reported in abstract.	Conventional sampling on one side and microsurgical extraction on the other. Joint paired retrieval outcomes and allocation of side/order: not reported in accessible abstract, laboratory and female age: not reported.	Retrieval: microdissection 47/100 versus conventional 30/100 testes. Acute ultrasound abnormalities: 15% versus 58.3%, chronic changes: 3% versus 30%. No permanent devascularisation at 6 months. Comparative CI: not reported.
Hibi [31]	Japan, Nagoya/Aichi	Paired series of 16 men with NOA and severe testicular dysfunction, including two with Klinefelter syndrome. Female age 24–36 years (mean 30.6). Prior retrieval: not reported.	Right-sided microdissection followed by three-site conventional biopsy on the left. Tissue inspected for sperm, hormonal follow-up available for only four men. Histology was predominantly severely impaired.	Retrieval: 1/16 microdissection versus 0/16 conventional, the discordant pair favoured microdissection. No significant hormonal change reported in four tested men. Source comparative CI: not reported.
Okubo [32]	Japan, Kurashiki Central Hospital	Staged series: 17 men with NOA. Conventional extraction first, 13 failures then received microsurgery. Confirmation protocol, genetics and prior operations: not reported in English abstract, Japanese full-text translation not reported.	Microdissection was conditional on failure of conventional TESE. Histological arm breakdown and female age: not reported. Five couples underwent ICSI.	Initial retrieval 4/17 (reported 24%), another 4/13 after failure, giving 8/17 overall (source rounds to 48%, arithmetic 47.1%). Four of five ICSI couples delivered. Comparative CI: not reported.
Okada [26]	Japan, Kobe University	Retrospective groups: 146 men overall, including 98 with NOA. Eligible NOA arms: 24 conventional and 74 microdissections, OA cases excluded here. Prior surgery, female, age and genetic breakdown: not reported in abstract.	Conventional versus microdissection TESE. The conventional series used multiple biopsies, as described in the comparative review. Histological subgroups reported, including Sertoli-cell-only syndrome (SCOS).	NOA retrieval: 16.7% conventional versus 44.6% microdissection (P = .0271). Unique integer reconstruction: 4/24 and 33/74. SCOS: 6.3% versus 33.9%. Source comparative CI: not reported.
Tsujimura [27]	Japan, Osaka	Retrospective comparative study: 93 men with NOA, 37 conventional and 56 microdissections. Baseline characteristics described as similar, but histology was more impaired in the microdissection arm. Prior retrieval and female age: not reported.	Multiple conventional biopsies versus microdissection. Tubular appearance was evaluated during microscopy. Genetic strata and detailed laboratory search duration: not reported in abstract.	Retrieval: 35.1% versus 42.9%, uniquely reconstructed as 13/37 and 24/56. Difference not statistically significant in the report. No severe complications or postoperative hormone replacement reported. Source CI: not reported.
Ramasamy [23]	USA, Cornell, New York	Historical cohort of 435 men undergoing 543 attempts: first 83 conventional attempts, subsequent 460 microdissection attempts. Repeated attempts and possible overlap with the foundational Cornell cohort.	Conventional versus microdissection TESE, serial ultrasound and endocrine assessment. Man-level arm counts, genetic mix, female age and independent attempt correlation: not reported in abstract.	Attempt-level retrieval: 32% versus 57% (p = 0.0002). Testosterone fell to about 80% of baseline at 3–6 months, recovered to 85% at 12 months and 95% at 18 months. Source comparative CI: not reported.
Colpi [24]	Italy, Milan	The full paper labels the comparison randomised, but operations were assigned by the waiting list and theatre plan (general- anaesthesia microdissection versus day- surgery conventional TESE), then 69 testes per technique were matched by histology after surgery. In all, 154 men contributed 195 testes, contralateral sampling, when performed, was always conventional.	Testis-level comparison across matched histological categories. Matching used surname order, not random allocation, 138 selected testes may cluster within men. The same operator searched specimens for up to four hours. Patient- level linkage, female age and previous surgery were not established.	Microdissection versus conventional successes: hypospermatogenesis 11/11 versus 10/11, maturation arrest 6/7 versus 6/7, incomplete SCOS 8/11 versus 8/11, complete SCOS 11/40 versus 5/40. Sum: 36/69 versus 29/69 testes.
Turunc [33]	Türkiye, Baskent University	Prospective series of 335 men with NOA, 2003–2008. Seventy-seven with testes ≤5 mL received primary microdissection, 258 received conventional TESE followed by microdissection only if negative. Mean female age 30.0 ± 5.3 years. Genetic testing was obtained for only 142/335.	Choice of initial technique depended on atrophy. Conventional TESE used up to seven biopsies, microdissection used ×20–40 magnification. Rescue analysis is restricted to 258 conventional-first men, the 77 selected primary- microdissection men are not exchangeable controls.	Conventional-first retrieval 87/258, after rescue 131/258, hence 44/171 additional successes. Primary microdissection retrieved in 16/77, total 147/335. Of 129 couples proceeding to ICSI, 65 had clinical pregnancies, 43/118 had live-birth deliveries, with 11 pregnancies ongoing at reporting. The reproductive technique rows overlap and cannot yield independent arm effects.
Ghalayini [28]	Jordan, tertiary infertility service	Comparative cohort: 133 men with NOA, 68 conventional and 65 microdissections, allocated by operating-list arrangements. Three semen analyses, normal karyotype. Prior retrieval and female age: not reported. Histology: HS, maturation arrest and SCOS.	Conventional biopsies progressed through upper, middle and lower sites, contralateral exploration if needed. Microdissection stopped when sufficient sperm or vascular risk was reached. Extended laboratory processing and centrifugation were used.	Retrieval: 26/68 (38.2%) versus 37/65 (56.9%). Adjusted OR 3.56 (95% CI 1.28–9.92), controlling FSH, volume and histology. Haematoma: 5/68 versus 3/65. SCOS: 2/32 versus 7/26.

Table 2: Chronological Evidence Table of the Included Studies (Continue)

Study	Country and setting	Design	Intervention details	Main findings
Marconi [37]	Germany, Giessen	Within-patient combined procedure in 65 of 182 referred men, selected for testis volume <8 mL and/or FSH >12.4 IU/L, 16 men had only one testis, giving 114 testicular units. At least two centrifuged semen analyses were required, AZFa/AZFb deletions and obstruction were excluded.	Three conventional biopsy sites plus one microsurgical middle-site sample per testis. Histological success meant at least one tubule containing elongated spermatids, rather than clinically usable sperm for ICSI.	Histological detection: unifocal conventional 53.8% (35/65), unifocal microdissection 60.0%, trifocal conventional 61.5% and combined 66.2% (43/65), only the combined versus unifocal comparison was significant. Four intratesticular haematomas were detected, seven received testosterone at six months, five of whom were hypogonadal before surgery.
Schwarzer [34]	Germany, Munich	Sequential within-operation series: 220 men with NOA, 2007–2013, diagnosis included repeated semen testing. Genetic composition and female age: not reported for the comparison. Potential overlap with the later genetic subgroup report.	Two or three conventional biopsies followed by microdissection if negative, with sites considered relative to major vessels and rete testis. The procedure is a rescue sequence, not parallel allocation.	Overall retrieval 128/220 (58.2%), conventional sampling 103/220 (46.8%), microdissection added 25/220 (11.4%). Conditional rescue: 25/117 (21.4%), calculated from those counts. Source comparative CI: not reported.
Schwarzer [25]	Germany, Munich	Retrospective genetic series of 25 men across 1996–2015: 11 conventional and 14 microdissections overall. The relevant isolated-AZFc subgroup has 20 men, AZFa/AZFb cases are excluded from that contrast. The techniques were applied in different calendar periods.	Among isolated AZFc cases, conventional retrieval was 2/8 and microdissection 8/12. Prior retrieval status and female age are not resolved; six couples underwent ICSI. Possible overlap with the 2013 Munich cohort.	The AZFc contrast is 2/8 versus 8/12 (source- reported P = .0339), two pregnancies occurred among six ICSI couples without technique-specific reproductive denominators. Operative time was approximately 50 versus 90 minutes.
Franco [35]	Italy, Rome	Stepwise series of 64 poor-prognosis men with NOA: 23 had previous failed retrieval and 41 had not. Small testes and raised FSH characterised selection. Histological sampling accompanied surgery, female age not reported.	Initial conventional sample plus ipsilateral microdissection in all men, contralateral conventional biopsies if the initial search was negative. Laboratory searches continued in parallel and after surgery.	Initial retrieval 18/64, microdissection added no successes among 46 initial failures. Previous-failure subgroup 6/23, other men 12/41. Eleven ICSI cycles produced three live-birth deliveries and four infants, including twins.
Salehi [38]	Iran, Isfahan	Comparative observational series: 170 men with NOA, 2013–2016, two semen analyses. Total retrieval 83/170 (48.8%). Raw technique-specific denominators and previous retrieval status: not reported.	Conventional and microdissection extraction, multivariable analysis included clinical/endocrine covariates. Female age, technique-specific laboratory exposure and histological balance: not reported for effect extraction.	Adjusted technique OR 8.077 (95% CI 2.153–30.305), favouring microdissection. Unadjusted arm counts and RR: not reported. Numerical direction/coding of the testicular-size association is not clear enough for secondary reuse.
Maglia [29]	Italy, Milan	Consecutive cohort, 2012–2017: 149 assessed, 145 analysed after four missing-data exclusions, 96 conventional and 49 microdissections. Two centrifuged semen samples, normal karyotype. Allocation by waiting list, previous retrieval and female age not reported.	Conventional versus microscope-guided TESE. Mean FSH differed: 12.8 versus 20.9 IU/L, respectively. Histological strata reported. Laboratory assessment accompanied both techniques.	Table 1 retrieval: 40/96 (41.7%) versus 24/49 (49.0%), P = .40 reported. Overall counts agree across tables. Some subgroup percentages and adjusted confidence limits are internally inconsistent, those estimates were not used.
Barda [36]	Israel, Tel Aviv	Within-operation cohort of 93 men with NOA, 2018–2024, prior TESE, AZFa/AZFb deletion and marked atrophy excluded. Includes 15 men with Klinefelter syndrome. Online 10 February 2026, August issue. Female age not reported.	Microdissection first, then trifocal TESE in every included man, specimens processed separately. This is a specimen comparison and combined strategy. Fixed sequence and sampling extent may influence results.	Combined retrieval 59/93 (63.4%, reported 95% CI 53.7–73.2%). Microdissection 58.1% and trifocal 54.8%, implying 54/93 and 51/93. Reported exclusive-method counts conflict with these margins, paired CI cannot be verified.

The paired evidence could not be combined with the independent groups. Amer found sperm in 47 microdissected versus 30 conventionally sampled testes among 100 men, but the accessible report did not provide the joint paired outcome table. Hibi retrieved sperm in one microdissected testis and no conventional testes among 16 men, the exact paired test was non-significant. These results remain clinically informative descriptions, but substituting an independent-binomial variance would ignore the paired design. Colpi's histological strata likewise require patient linkage and reliable allocation information before a patient-level treatment effect can be estimated [30,31,24] (Table 2-6, Figure 2).

Conditional rescue yields differed substantially. Okubo added retrieval in 4/13 conventional failures, Turunc in 44/171, Schwarzer in 25/117, and Franco in 0/46. Their Wilson intervals are shown in Table 7 and Figure 3. The corresponding contribution to the original cohort is smaller than the conditional percentage: Schwarzer's additional 25 successes represent 11.4% of all 220 men but 21.4% of the 117 failures. Differences in selection, biopsy extent and prior surgery make an overall rescue percentage clinically ambiguous. These data support discussing the possibility of rescue, without asserting that rescue is equivalent to an initial micro-TESE strategy [32,33,34,35].

Table 3: ROBINS-I Domain Findings

Study	Confounding	Selection	Classification	Deviations	Missing data	Measurement	ROBINS-I overall
Amer [30]	M	M	L	NI	L	M	Serious
Hibi [31]	S	M	L	M	L	M	Serious
Okubo [32]	C	S	L	NI	NI	M	Critical
Okada [26]	S	M	L	NI	NI	M	Serious
Tsujimura [27]	S	M	L	NI	NI	M	Serious
Ramasamy [23]	S	S	L	NI	NI	M	Serious
Colpi [24]	S	S	L	M	M	M	Serious
Turunc [33]	C	S	L	M	L	M	Critical
Ghalayini [28]	S	M	L	M	L	M	Serious
Marconi [37]	S	M	L	M	L	S	Serious
Schwarzer [34]	C	S	L	M	L	M	Critical
Schwarzer [25]	S	S	L	M	L	M	Serious
Franco [35]	S	M	L	M	L	M	Serious
Salehi [38]	S	M	L	NI	L	M	Serious
Maglia [29]	S	M	L	M	M	M	Serious
Barda [36]	S	M	L	M	L	M	Serious

Table 4: NOS Domain Judgements for Between-Group Observational Reports

Study	Selection	Comparability	Outcome	Overall
Okada [26]	Some Concerns: NOA arms are separable, recruitment and source comparability are incompletely reported.	High: Retrospective allocation and histology differences are not adequately controlled in the extracted raw contrast.	Some Concerns: Arm totals are available, complete ascertainment cannot be verified from the abstract.	High
Tsujimura [27]	Some Concerns: Direct clinical groups are identified, consecutive recruitment is not reported in the abstract.	High: More severe histology in the microdissection arm remains a relevant imbalance.	Some Concerns: Retrieval percentages and denominators are available, independent assessment and flow are not reported.	High
Ramasamy [23]	High: Repeated attempts and historical cohorts do not form two independent patient groups.	High: Era, operator experience and repeat surgery confound the raw contrast.	High: Attempt-level denominators cannot establish complete person-level ascertainment.	High
Ghalayini [28]	Some Concerns: A defined referral cohort and clear exposure classification are documented.	High: Several measured factors were adjusted, but operating-list allocation leaves residual confounding.	Some Concerns: Retrieval is accounted for in all 133 men, unblended search may affect ascertainment.	High
Salehi [38]	Some Concerns: A defined clinical cohort is described, but raw technique-specific groups are incomplete.	High: Adjustment does not resolve selection or permit verification of raw arm balance.	High: Missing arm-level event denominators prevent an independently reproducible raw comparison.	High
Maglia[29]	Some Concerns: Consecutive recruitment is described, four records were excluded.	High: Waiting-list allocation and endocrine imbalance remain despite reported adjustment.	Some Concerns: Overall counts are consistent, but subgroup reporting contains contradictions.	High

Table 5: Independent-Group Retrieval Inputs and Calculated Effects

Study	Micro-TESE	Conventional	Calculated RR (95% CI)	Weight
Okada [26]	33/74	4/24	2.68 (1.06–6.78)	6.1%
Tsujimura [27]	24/56	13/37	1.22 (0.72–2.08)	18.4%
Ghalayini [28]	37/65	26/68	1.49 (1.03–2.15)	38.0%
Maglia [29]	24/49	40/96	1.18 (0.81–1.70)	37.5%

Table 6: Sensitivity Analyses

Analysis	Studies	Men	RR (95% CI)
Primary random effects	4	469	1.36 (0.94–1.97)
Full-text-only reports	2	278	1.32 (0.24–7.22)
Without Okada [26]	3	371	1.30 (0.78–2.18)
Without Tsujimura [27]	3	376	1.45 (0.66–3.17)
Without Ghalayini [28]	3	336	1.35 (0.55–3.31)
Without Maglia [29]	3	324	1.49 (0.77–2.89)
Common effect, normal CI	4	469	1.36 (1.08–1.71)

Table 7: Additional Retrieval after Failed Conventional Sampling

Study	Additional successes / failures	Conditional yield	Wilson 95% CI
Okubo [32]	4/13	30.8%	12.7–57.6%
Turunc [33]	44/171	25.7%	19.8–32.8%
Schwarzer [34]	25/117	21.4%	14.9–29.6%
Franco [35]	0/46	0.0%	0.0–7.7%

Barda's combined procedure produced retrieval in 59/93 men. The reported marginal percentages uniquely imply 54 microdissection-positive and 51 trifocal-positive cases. Those margins and the union would require eight microdissection-only and five trifocal-only cases, whereas the text reports seven and three. No coherent paired table

Table 8: Denominators Governing Interpretation of Reproductive Outcomes

Report	Available outcome	Interpretive boundary
Okubo [32]	Four deliveries among five ICSI couples.	The denominator is treated couples after retrieval, not all 17 men entering surgery.
Turunc [33]	Clinical pregnancy 65/129 ICSI couples, live-birth deliveries 43/118, with 11 pregnancies ongoing.	The reproductive rows are overlapping/cumulative and cannot supply independent technique-specific live-birth effects.
Schwarzer [34]	Two pregnancies among six ICSI couples.	No technique-specific pregnancy or live-birth comparison; genetic subgroup denominator is small.
Franco [35]	Three live-birth deliveries after 11 ICSI cycles, four infants.	The twin delivery is one delivery. Cycles may be clustered within couples.
Comparative live-birth effect	Not reported.	No compatible, traceable technique-specific binomial dataset was available for pooling.

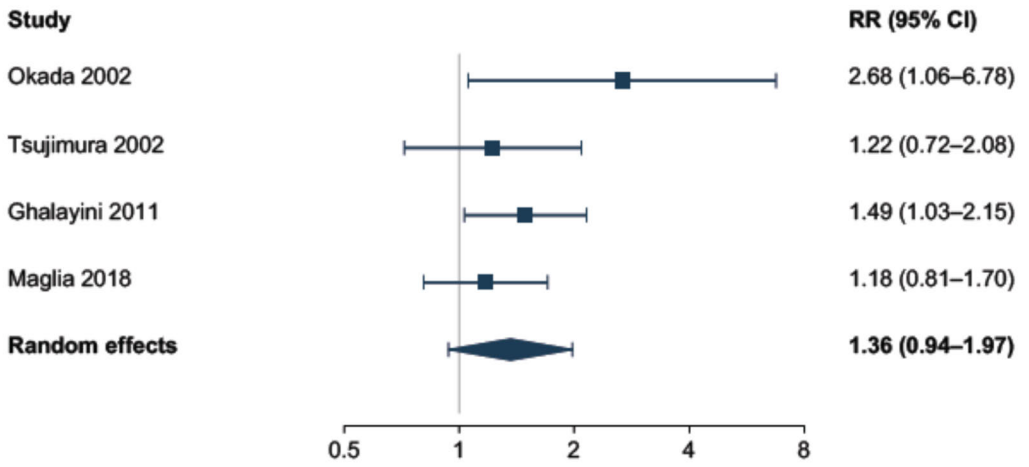


Figure 2: Exploratory Meta-Analysis of Independent-Group Sperm Retrievel
RR >1 favours microdissection, horizontal axis is logarithmic

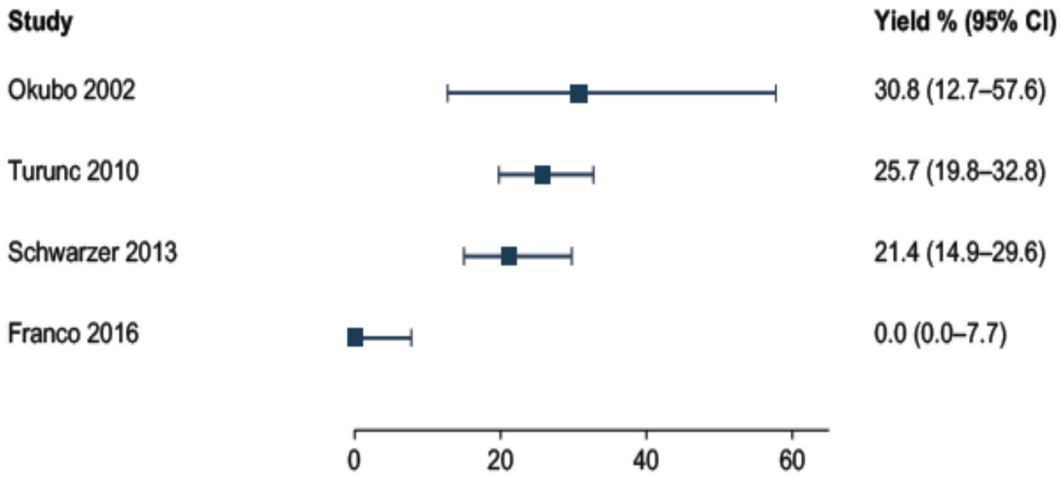


Figure 3: Conditional Rescue Yields

can satisfy both accounts. The marginal and combined percentages are therefore presented as reported, but no paired effect or significance test was recalculated. Marconi's combined procedure detected elongated spermatids histologically in 43/65, compared with 35/65 by a single conventional sample, this is not interchangeable with usable clinical sperm retrieval [36,37].

Reproductive evidence did not support a comparative live-birth pool. Okubo reported four deliveries among five treated ICSI couples, Franco reported three deliveries after eleven cycles, producing four infants. Turunc reported 65/129 clinical pregnancies among couples proceeding to ICSI and 43/118 live-birth deliveries among those with a resolved pregnancy status, eleven pregnancies remained ongoing. Its technique-specific reproductive rows overlap and cannot establish independent arm effects. Salehi's adjusted OR of 8.077 describes retrieval, not pregnancy, and cannot be

converted to a raw RR without arm counts. Marconi recorded four ultrasound-confirmed haematomas and seven testosterone prescriptions at six months, five among men already hypogonadal, these observations do not isolate surgery-induced endocrine harm. Overall, the evidence supports a possible retrieval benefit with substantial uncertainty, and leaves a live-birth advantage unestablished [32,33,35,37,38].

Risk of Bias Assessment

Table 3 displays ROBINS-I domain judgements for the retrieval comparison. L = Low, M = Moderate, S = Serious, C = Critical, NI = No information. Overall ROBINS-I judgements follow the most severe known domain, unknown domains remain visible. The three-category display maps L to Low, M to Some Concerns, and S/C to High. NI is not converted into Low. Assessments based only on abstracts are provisional.

Supplementary Newcastle–Ottawa Assessment

NOS was used as a domain framework for six reports describing between-group observational comparisons. The domains were appraised against representativeness and source of controls, ascertainment and baseline outcome status, control of clinical confounders, and outcome ascertainment/completeness. Total stars are not reported because several underlying items cannot be verified and immediate surgical retrieval is not a conventional longitudinal cohort endpoint. Reporting a guessed numerical score would add false precision. Paired, staged and specimen studies were assessed with ROBINS-I rather than forced into an independent- cohort scale.

Quantitative Synthesis

Four studies, 469 men. Summary CI: modified Knapp–Hartung, t_3. $\tau^2 = 0.00056$, $I^2 = 0.6\%$, $Q = 3.019$. Approximate prediction interval 0.81–2.27. Squares show study point estimates, the diamond spans the summary CI.

Reproductive Outcomes and Safety

Safety data support monitoring both structural injury and endocrine recovery, but do not permit a reliable common comparative effect. Amer's ultrasound follow-up included only 60 of 100 men, Ramasamy's longitudinal testosterone findings use repeated observations and heterogeneous follow- up. Marconi reported four intratesticular haematomas and seven testosterone prescriptions at six months, but five of the seven men were hypogonadal before surgery. Neither incomplete follow-up nor an absent major-complication report proves no harm [30,23,37].

DISCUSSION

This reassessment supports the plausibility of a retrieval advantage with micro-TESE while showing why its magnitude is uncertain. The direction of the four independent-group estimates was favorable, but a small-sample random-effects interval included no difference. The main limitations concern confounding and the applicability of the observations to a genuinely initial operation. A low estimated I^2 cannot correct either problem. Similar biases operating across studies can produce apparently consistent results.

The narrower common-effect interval is not a reason to select that model as the definitive answer. With few heterogeneous surgical cohorts, the uncertainty attached to the average effect is itself uncertain. The modified Knapp–Hartung analysis deliberately prevents an implausibly small residual variance from producing excessive precision. The very wide two-study full-text sensitivity interval is a consequence of sparse independent evidence, not evidence that the true effect is likely to be at either extreme.

The distinction between treatment choice and additional sampling changes clinical interpretation. A man offered an initial operation needs the probability of success under each complete strategy, including a specified stopping rule. A man whose conventional samples are already negative needs the conditional probability of success from further exploration. A combined-procedure study asks whether two specimen sources complement one another. These questions can all matter, but combining their numerators into one surgical superiority estimate would mislead counselling.

There is potential for biased inference as well as potential for explanation of variation with histological and genetic subgroups. The negative finding of SCOS in a single biopsy does not exclude their presence throughout the testis. The histology obtained from the sampled tissue may be partly due to the technique. Complete deletions of AZFa and AZFb should be differentiated from AZFc related disease. Although available, the isolated-AZFc counts are not independent (2/8 versus 8/12), and the small and era-confounded series might overlap with the Munich series and provide no independent replication for a pooled genetic effect [25,1]

Retrieval should be offered to couples as the first step in a pathway. Fertilization per injected oocyte (FIO), pregnancy per transfer (PPT) and cumulative live-birth delivery per couple (CLBD/c) address different questions. The most important thing in a clinically useful trial is to keep all the randomised men in the denominator of the primary retrieval and all the couples enrolled in a cumulative reproductive endpoint; treatment uptake, cancellation, repeated transfers and poor follow-up should be reported separately. When multiple births occur, adding up infants rather than deliveries also will skew outcome rates.

The present review has limitations. Five of 16 reports could only be assessed from abstracts. The four- study pool is consequently an exploratory reanalysis of traceable data, not a definitive updated estimate for all published evidence. Incomplete earlier-surgery reporting prevents the strict initial- operation estimate from being fully identified. These limitations affect certainty.

A future definitive study should compare fully specified initial strategies with concealed patient allocation, balance major etiological and histological

predictors, and standardize tissue processing and laboratory search. It should record operative extent and time, quantity of sperm suitable for use or cryopreservation, early complications and long-term endocrine recovery. Linked couple-level follow- up should include female age, ovarian response, all embryo transfers and cumulative live-birth delivery. Those features would contribute more to clinical decision-making than another large series reporting a single unadjusted retrieval percentage.

CONCLUSION

Micro-TESE may improve sperm retrieval compared with conventional TESE in men with NOA, but the size and certainty of that advantage remain limited by the available direct comparisons. Direct comparisons of micro-TESE with conventional TESE in men with NOA have been limited and do not confirm the benefit to the extent that there is for the men with higher levels of NOA. The traceable four-study estimate is RR 1.36 (95% CI 0.94–1.97). No comparative live-birth advantage can be established from the included evidence. Surgical selection should distinguish initial treatment, rescue after failure and combined sampling, while counselling couples using clearly defined reproductive denominators.

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