Comparison of microdissection testicular sperm extraction, conventional testicular sperm extraction, and testicular sperm aspiration for nonobstructive azoospermia: a systematic review and meta-analysis

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Objective: To investigate the relative differences in outcomes among microdissection testicular sperm extraction (micro-TESE), conventional testicular sperm extraction (cTESE), and testicular sperm aspiration (TESA) in men with nonobstructive azoospermia.
Design: Systematic review and meta-analysis.
Setting: Outpatient academic and private urology clinics.
Patients(s): Men with nonobstructive azoospermia.
Intervention(s): Micro-TESE, cTESE, or TESA.
Main Outcome Measure(s): Sperm retrieval (SR).
Result(s): Fifteen studies with a total of 1,890 patients were identified. The weighted average age of the patients was 34.4 years, the follicular stimulating hormone level was 20.5 mIU/mL, the T was 373 ng/dL, and the testicular volume was 13.5 mL. In a direct comparison, performance of micro-TESE was 1.5 times more likely (95% confidence interval 1.4–1.6) to result in successful SR as compared with cTESE. Similarly, in a direct comparison, performance of cTESE was 2.0 times more likely (95% confidence interval 1.8–2.2) to result in successful SR as compared with TESA. Because of inconsistent reporting, evaluation of other procedural characteristics and pregnancy outcomes was not possible.
Conclusion(s): Sperm retrieval was higher for micro-TESE compared with cTESE and for cTESE compared with TESA. Standardization of reported outcomes as well as combining all available SR data would help to further elucidate the SRs of these procedures. (Fertil Steril® 2015;104:1099–103. ©2015 by American Society for Reproductive Medicine.)
Key Words: Meta-analysis, microdissection testicular sperm extraction, nonobstructive azoospermia, sperm retrieval, testicular sperm aspiration

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Testicular sperm retrieval (SR) is performed for men with nonobstructive azoospermia (NOA) and is combined with intracytoplasmic sperm injection (ICSI) to allow them to father biological children. Testicular sperm aspiration (TESA) (1, 2),

conventional testicular sperm extraction (cTESE) (3–5), and microdissection-TESE (micro-TESE) (6, 7) are techniques used to retrieve sperm in men with NOA. Sperm retrieval "rates" (i.e., the percentages of postprocedural SR) vary according to the technique used, the patient population, and the skill of the surgeon. Micro-TESE has become popular because spermatogenesis in men with NOA is often only found in small foci (8, 9).

A previously published systematic review compared the outcomes of cTESE with those of micro-TESE but was limited in that it did not include TESA (10). Similarly, many of the other available studies that compared SR techniques often included patients who only underwent a retrieval technique if they had failed a previous attempt with a different technique, thus biasing the data. Although there does exist great heterogeneity in both the patient population that comprises men with NOA as well as in the processing techniques used after SR is performed, to our knowledge no meta-analysis comparing all three of these SR techniques has been performed. To address the shortcomings in the literature, we performed a comprehensive systematic review and meta-analysis comparing all three SR techniques for NOA: TESA, cTESE, and micro-TESE.

MATERIALS AND METHODS

Study Design

This study was a systematic review and meta-analysis. An a priori protocol was written and agreed to by the authors to include study design, search strategy, inclusion and exclusion criteria, primary outcomes, statistical methods, and assessment for bias in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Literature Search

English-language studies reporting on outcomes of TESA or TESE for SR in men with NOA published between 1988 and 2015 were sought by electronic search of MEDLINE, scanning the reference lists of identified articles, and correspondence with study investigators. The computer-based search terms are shown in Supplemental Table 1 (available online).

Study Selection

Studies were eligible for inclusion if they involved SR from men with NOA, performed multiple methods of SR on the same patient as long as the performance of one method was not dependent on the outcome of another, and compared at least two of the three retrieval methods being studied (TESA, cTESE, or micro-TESE). Studies were excluded if they did not compare more than one technique, included men with obstructive azoospermia (OA) who could not be removed from the analysis to only examine the outcomes of men with NOA, or preformed two comparative techniques sequentially (i.e., a man would only get a second procedure if sperm was not retrieved in the first procedure). If multiple publications reporting on the same patient population were identified, only the latest study was included.

Data Collection

The following information was independently extracted by two reviewers from each article using a standardized form: study population (including population source, sampling method used, sample size, and demographic characteristics); geographic location; publication year; mean patient age at the time of surgery; FSH level; total T; testicular volume; definition of SR; and number of patients from whom sperm was retrieved. Of note, these variables were not required for inclusion in the meta-analysis.

Data Synthesis

All analyses were performed using only within-study comparisons to limit possible biases. The mean ages at TESA or TESE reported by each study were combined and summarized using an arithmetic mean weighted by study sample size. Sperm retrievals and 95% confidence intervals (CIs) for the use of TESA, cTESE, or micro-TESE were calculated to summarize the results of each study. Meta-analysis was performed using a random effects model. The consistency of findings across studies was assessed using Cochrane's Q test and the I^2 statistic. Publication bias was assessed by funnel plot. Statistical significance was defined as a two-tailed P value of $<.05$. Analyses were performed using R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Studies Included in the Systematic Review and Meta-analysis

Fifteen studies of 1,890 total patients were identified (Supplemental Fig. 1). The studies were published between 1997 and 2012. Six took place in Asia, four in Europe, three in North America, and two in Africa (Table 1). Reported sample sizes ranged from 14 to 543 patients undergoing TESA, cTESE, or micro-TESE. The weighted average age of the patients was 34.4 years, the FSH level was 20.5 mIU/mL, the T was 373 ng/dL, and the testicular volume was 13.5 mL. When described, a majority of the studies used immediate microscopic examination of the extracted testicular tissue, followed by further analysis to assess for the presence of sperm. The definition of successful SR used by the studies was not explicitly defined in the articles, although on the basis of the language of most studies, a single sperm that could be either preserved or used for IVF/ICSI constituted success.

Meta-analysis

In a direct comparison of cTESE to micro-TESE, the unadjusted SR was 35% for cTESE (95% CI 30%–40%; $\tau^2 = 0.02$; $P=.28$; $I^2 = 19\%$) and 52% for micro-TESE (95% CI 47%–58%; $\tau^2 = 0.04$; $P=.07$; $I^2 = 48\%$) (Fig. 1A). Therefore, performance of micro-TESE was 1.5 times more likely (95% CI 1.4–1.6) to result in successful SR as compared with cTESE. In a direct comparison of cTESE to TESA, the unadjusted SR was 56% for cTESE (95% CI 50%–61%; $\tau^2 = 0.02$; $P=.20$;