



Association Between the Presence of Sperm in the Vasal Fluid During Vasectomy Reversal and Postoperative Patency: A Systematic Review and Meta-analysis

Jason M. Scovell, Douglas A. Mata, Ranjith Ramasamy, Lindsey A. Herrel, Wayland Hsiao, and Larry I. Lipshultz

OBJECTIVE	To investigate the association between the presence of sperm in the vasal fluid during vasectomy reversal (VR) and postoperative patency.
METHODS	We performed a systematic review and meta-analysis of the English-language literature reporting on the association between the presence of sperm in the intraoperative vasal fluid (ie, whole or parts vs none) and patency (ie, patent or not) after microsurgical vasovasostomy for men with obstructive azoospermia due to vasectomy. Odds ratios (OR) and 95% confidence intervals were calculated to quantify the strength of the association reported by each study. Meta-analysis was performed using a random-effects model.
RESULTS	Four case series and 2 retrospective cohort studies of a total of 1293 eligible patients were identified. The mean age at VR was 37.8 years, and the mean obstructive interval was 7.1 years. The unadjusted OR of postoperative patency was 4.1 times higher (95% confidence interval, 2.3–7.3) given the presence of intravasal sperm or sperm parts as opposed to their absence at the time of VR ($Q = 3.4$; $df = 5$; $P = .6$; $I^2 = 22\%$). The pooled OR should be interpreted with caution as only the 2 retrospective cohort studies reported meaningful data on this association. Because of inconsistent reporting, analysis of other vasal fluid characteristics (eg, consistency) and outcomes (eg, pregnancy) was not possible.
CONCLUSION	The presence of whole sperm or sperm parts in the vasal fluid during VR is positively associated with postoperative patency. Our review highlights the poor methodological quality of existing evidence and underscores the need for more thorough follow up and higher standards of reporting in future studies. UROLOGY 85: 809–813, 2015. © 2015 Elsevier Inc.

About 175,000 to 354,000 vasectomies are performed in the United States each year,¹ and up to 6% of patients who undergo this procedure later choose to undergo vasectomy reversal (VR).² A landmark multicenter study on the outcomes of 1469 patients who underwent VR was published by the Vasovasostomy Study Group in 1991.³ They demonstrated that a longer obstructive interval and an absence of sperm granuloma on physical examination were associated with

decreased patency after VR. Other factors that appeared to influence success of VR were the character of the vasal fluid and the presence of sperm or sperm parts at the time of reversal.

During surgery, the physician's decision to proceed with vasovasostomy (VV) or epididymovasostomy (EV) depends on the gross quality of fluid expressed from the testicular end of the vas deferens and on the microscopic examination of the fluid for sperm. Findings may include motile or nonmotile whole sperm, sperm parts (ie, sperm heads or tails alone), or no sperm. VV is routinely performed if whole sperm are identified in the vasal fluid or if the fluid appears clear and copious, even in the absence of sperm.⁴ In contrast, when the fluid quality is poor (ie, paste-like) and sperm are absent, EV is generally required. Modern series indicate that patency after VV approaches 99.5% when whole sperm are identified.⁵ Even in cases of bilateral intravasal azoospermia, patency in some series

Jason M. Scovell and Douglas A. Mata contributed equally to this work.

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From the Scott Department of Urology, Baylor College of Medicine, Houston, TX; the Department of Pathology, Brigham and Women's Hospital, Boston, MA; the Department of Urology, Emory University School of Medicine, Atlanta, GA; and the Department of Urology, Kaiser Permanente, Oakland, CA

Address correspondence to: Larry I. Lipshultz, M.D., Department of Urology, Baylor College of Medicine, 6624 Fannin Street, Suite 1700, Houston, TX 77030. E-mail: larryl@bcm.edu

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approaches 80%, and achievement of pregnancy approaches 38% when the obstructive interval is <11 years.⁶ Unfortunately, studies that have carefully evaluated and reported data on vasal fluid quality have generally been small, retrospective, and based on data from single institutions.

A meta-analysis evaluating the outcomes of VV did not assess intraoperative vasal fluid characteristics.⁷ Although 1 other group has reviewed this topic,⁸ the data were not synthesized using a meta-analytic framework. Therefore, we performed a systematic review and meta-analysis of the published literature to evaluate the association between the presence of sperm or sperm parts in the vasal fluid and patency after VV.

METHODS

Study Design

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

Literature Search

English-language studies reporting on outcomes of microscopic VV for VR between November 1977 (the first report of microsurgical VV⁹) and March 2014 were sought by electronic search of MEDLINE, scanning the reference lists of identified articles, and correspondence with study investigators. The computer-based search included variations of the terms “vasectomy reversal” and “vasovasostomy.”

Study Selection

Studies were eligible for inclusion if they used a microscopic VV approach and reported on outcomes for ≥ 10 patients. Studies of patients undergoing VR for reasons other than a desire for fertility such as a history of epididymitis, hernia repair, idiopathic obstruction, or trauma were excluded. 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 2 reviewers from each article using a standardized form: study population (including population source, sampling method used, sample size, and patient demographic characteristics); geographic location; publication year; mean patient age and obstructive interval at the time of VR; number of patients with sperm or sperm parts in intraoperative vasal fluid; definition of postoperative patency; and number of patients achieving patency.

Data Synthesis

All analyses were performed using only within-study comparisons to limit possible biases. The mean age and obstructive interval at VR reported by each study were combined and summarized using an arithmetic mean weighted by study sample size. An odds ratio (OR) and corresponding 95% confidence interval (CI) for the association between the presence of

intravasal sperm or sperm parts and postoperative patency were calculated for each study. To include the results of case series reporting incomplete data, 0.5 was added to each count in 2-by-2 contingency tables that contained a value of 0 in any cell.¹⁰ Meta-analysis was performed using a random-effects model. The consistency of findings across studies was assessed using the Cochran Q test¹¹ and the I^2 statistic.¹² Publication bias was assessed by the funnel plot and Egger et al¹³ regression asymmetry analysis. Statistical significance was defined as a 2-tailed P value <.05. Analyses were performed using R version 3.0.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Studies Included for Systematic Review and Meta-analysis

Four case series^{6,14-16} and 2 retrospective cohort studies^{3,17} of 1293 eligible patients were identified (Fig. 1). The studies were published between 1977 and 2014 and took place in Asia, Australia, and the United States (Table 1). Reported sample sizes ranged from 11 to 605 patients undergoing microsurgical VV. The weighted mean patient age was 37.8 years and obstructive interval was 7.1 years at the time of VR. The studies used wet-mount light microscopy to assess for the presence of sperm in the vasal fluid.

The definition of patency used by the studies varied markedly. The Vasovasostomy Study Group³ and Sigman¹⁵ defined patency as the presence of whole sperm or sperm parts in the postoperative semen analysis; Sheynkin et al¹⁴ defined it as the presence of whole sperm but not sperm parts; and Bolduc et al,¹⁷ Kolettis et al,⁶ and Smith et al¹⁶ defined it as the presence of motile sperm. Three of the 6 studies^{3,16,17} defined whole sperm as being “mostly normal and motile” or “mostly normal and nonmotile.” In these 3 studies, sperm parts were defined as “mostly heads without tails” or “only heads without tails” on intraoperative examination. Sigman¹⁵ defined sperm parts as “short tails” or “sperm heads.” Kolettis et al⁶ and Sheynkin et al¹⁶ did not differentiate between whole sperm and sperm parts.

Meta-analysis

The unadjusted OR of postoperative patency was 4.1 times higher (95% CI, 2.3-7.3) given the presence of intravasal sperm or sperm parts as opposed to their absence at the time of VR (Fig. 2). The pooled OR should be interpreted with caution as only the 2 retrospective cohort studies reported meaningful data on this association. Although surrogate statistical techniques were used to include case series in this meta-analysis,¹⁰ their data did not contribute significantly to the pooled OR. There was no evidence of statistically significant heterogeneity among the 6 studies ($Q = 3.4$; $df = 5$; $P = .6$; $I^2 = 22\%$) nor was there obvious publication bias by the funnel plot (Fig. 3) or Egger et al¹³ regression analysis ($z = -0.4$; $P = .7$).

Sensitivity Analysis

A sensitivity analysis in which case series were excluded yielded an unadjusted OR of 4.3 (95% CI, 2.2-8.3) and

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