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ORIGINAL ARTICLE

Male Fertility

The role of vasoepididymostomy for treatment of obstructive azoospermia in the era of *in vitro* fertilization: a systematic review and meta-analysis

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This study comprises a systematic review and meta-analysis of microsurgical vasoepididymostomy outcomes in epididymal obstructive azoospermia. A comprehensive literature search was performed using Medline, Embase, and the Cochrane library that included all studies related to microsurgical vasoepididymostomy. Keywords included "vasoepididymostomy," "epididymovasostomy," "epididymal obstruction," and "epididymis obstruction." Event rate and risk ratio (RR) were estimated. Patency rate and pregnancy rate were investigated. The analysis comprised 1422 articles, including 42 observational studies with 2298 enrolled patients performed from November 1978 to January 2017. The overall mean patency rate was 64.1% (95% confidence interval [CI]: 58.5%–69.3%; I^2=83.0%), and the overall mean pregnancy rate was 31.1% (95% CI: 26.9%–35.7%; I^2=73.0%). We performed a meta-analysis comparing the patency rate of bilateral microsurgical vasoepididymostomy and unilateral microsurgical vasoepididymostomy and found an RR of 1.38% (95% CI: 1.21%–1.57%; $P < 0.00001$). A comparison of the site of microsurgical vasoepididymostomy showed that caudal or corpus area was favorable for patency rate (RR = 1.17%; 95% CI: 1.01%–1.35%; $P = 0.04$). Patients with motile sperm in epididymal fluid exhibited an RR of 1.53% (95% CI: 1.11%–2.13%; $P = 0.01$) with respect to patency rate. Microsurgical vasoepididymostomy is an effective treatment for epididymal obstructive azoospermia that can improve male fertility. We find that performing microsurgical vasoepididymostomy bilaterally, anastomosing a larger caudal area, and containing motile sperm in epididymis fluid can potentially achieve a superior patency rate.

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Keywords: azoospermia; meta-analysis; vasoepididymostomy

INTRODUCTION

Obstructive azoospermia is associated with obstruction of the vas deferens, epididymis, or ejaculatory duct system. Epididymal obstruction is the second most common cause of obstructive azoospermia behind epididymal infection, which is considered to be the most frequent cause of the acquired forms.[1]

Surgery, specifically microsurgical vasoepididymostomy (MVE), is the treatment of choice for epididymal obstructive azoospermia (EOA) patients. Because of rapid developments in assisted reproductive technology (ART), especially *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) in combination with sperm extraction from testis or epididymis, patients with azoospermia who were previously untreatable can now achieve fertility. However, it is important to comprehensively evaluate the cause of male infertility prior to IVF-ICSI. Without careful evaluation, IVF-ICSI may result in increased medical costs for patients and involve additional risks for the female partner, such as ovarian hyperstimulation syndrome (OHSS), and for the fetus, including multiple gestations, prematurity, and genetic abnormalities.[2,3]

MVE is technically the most challenging procedure of all urological microsurgeries, and in many fertility centers it is also highly dependent on ART. Therefore, a comprehensive evaluation is required to assess the effectiveness of MVE.

The objective of this study is to systematically review the evidence supporting MVE in treating EOA and to provide a meta-analysis of its effectiveness. To the best of our knowledge, this is the first systematic review and meta-analysis of MVE in patients with EOA.

MATERIALS AND METHODS

Literature search

We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses recommendations) and MOOSE Guidelines for Meta-analyses and Systematic Reviews of Observational studies.

We performed a comprehensive literature search using Medline, Embase, and the Cochrane library that included all studies related to MVE from November 1978 to January 2017. The search term was ("vasoepididymostomy" [All Fields]) OR ("epididymovasostomy" [All

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Fields]) OR ("epididymal obstruction" [All Fields]) OR ("epididymis obstruction" [All Fields]). Event rate and risk ratio (RR) were estimated using a random-effects model. Heterogeneity was investigated using the Q statistic and I^2 values.

Inclusion and exclusion criteria and outcome measures

We included articles that evaluated the effects of MVE on patency rate or pregnancy rate, as well as those that compared different surgical techniques and different intraoperative methods during MVE. We excluded articles not written in English, animal studies, review articles, letters, and one article including a majority of vasovasostomy cases.

Included studies were independently selected by two investigators (DK Kim and YE Yoon). Any disagreements were discussed by the two investigators and resolved by consensus with HH Lee. We extracted the following data from the retrieved studies: author's name, publication year, country, sample size, follow-up period, diagnostic criteria for patency, surgical technique, patency rate, and pregnancy rate. We also extracted intraoperative findings, which included bilateral *vs* unilateral anastomosis, anastomosis location in the epididymis, and presence or absence of motile sperm in the epididymis.

Quality assessment

Inclusion of studies in the meta-analysis comparing patency rate and pregnancy rate after MVE was determined using the Quality Assessment Tool for Before-After (Pre-Post) Studies with no Control Group (available at https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular risk-reduction/tools/before-after), which considers 11 "yes/no" items and gives 1 point for each affirmative answer. The total scores of each study were converted into a quality rank between 0 and 1 by dividing each score by the score of the highest scoring study in the group. The quality of each noncontrol study, based on study characteristics of "no control group" obstructive azoospermia patients who underwent MVE, was also assessed using the same tool.

Statistical analyses

The meta-analysis was performed using RevMan 5.3 (Cochrane Community, London, UK) and Comprehensive Meta-Analysis 3.0 (CMA; Biostat, Englewood, NJ, USA). Event rates or RR and 95% confidence interval (CI) for dichotomous variables were investigated. The Mantel–Haenszel random-effects model was used due to heterogeneity of included studies. All *P* values are two-sided, and $P < 0.05$ was considered statistically significant.

The Q statistic was used to test between-study homogeneity. Homogeneity was rejected in cases where the Q statistic *P* value was <0.10.

Forest plots were used to show the effects of MVE on patency rates and pregnancy rates. Forest plots contain a pooled estimate of the effect (event rate or RR) as a dashed vertical line with a diamond at the bottom representing the 95% CI, and individual studies are represented as squares with their CIs such that the surface of the square is proportional to the weight of the study.

RESULTS

Eligible studies

Figure 1 shows the PRISMA flow chart depicting the identification of studies according to their inclusion in the meta-analysis. We initially identified a total of 1422 articles; after deleting duplications, we analyzed abstracts of 895 articles. Subsequently, we excluded 143 abstracts, 106 review articles, 51 letters or editorials, 144 animal studies, and 4 nonEnglish studies. After review of 447 abstracts that matched our inclusion and exclusion criteria, we then assessed the full text and each of the remaining 62 articles for eligibility. Of these, 20 articles were excluded: 13 studies in which the main text was not English; 6 that focused mainly on vasovasostomy, and 1 that reported neither patency rate nor pregnancy rate. Ultimately, we included 42 observational studies (9 prospective cohort studies and 33 retrospective cohort studies) with 2298 patients in qualitative as well as quantitative synthesis in the meta-analysis (**Figure 1** and **Supplementary Table 1**). The publication interval was from 1978 to 2017, and cohort sizes ranged from 6 to 249 patients. The study participants were from various countries, including the United States (14 studies), China (11 studies), Japan (4 studies), India (2 studies), Sweden (2 studies), Korea (2 studies), Canada (1 study), Italy (1 study), Belgium (1 study), Saudi Arabia (1 study), Romania (1 study), Slovenia (1 study), and Egypt (1 study).

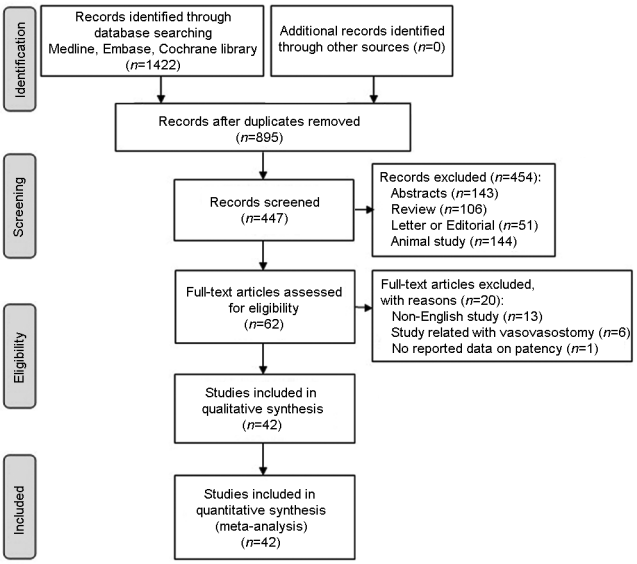

Figure 1: Flow diagram of articles included in the systematic review and meta-analysis.

Quality assessment and publication bias

Supplementary Table 1 presents the quality of each article, as measured by The Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group final results. The median quality score was 7 (interquartile range 6–8) out of a total possible score of 11.

We investigated the possibility of publication bias. As shown in **Figure 2**, funnel plots showed no publication bias with respect to overall patency rate ($P = 0.26$, Egger's test) or overall pregnancy rate ($P = 0.2$, Egger's test).

Overall patency rate after MVE

We included all 42 observational studies in analyses of patency rate after MVE. As shown in **Figure 3**, which presents forest plots of patency rate after MVE, the overall mean patency rate, calculated as the mean weighted by sample size, was 64.1% (95% [CI]: 58.5%–69.3%; $I^2 = 83.0\%$).

Mean time to reach patency was from 2.8 months to 9.6 months (**Supplementary Table 1**). However, the definition of patency varied among studies. Fifteen studies did not specifically define patency; 10 defined it as the presence of spermatozoa; and 4 defined it as the presence of motile spermatozoa. Other studies defined patency in terms of the following threshold spermatozoa concentrations: $>10^4$ spermatozoa per ml (5 studies); $>10^5$ spermatozoa per ml (3 studies); $>10^6$ spermatozoa per ml (1 study); $>10^7$ spermatozoa per ml (3 studies); and $>10^8$ spermatozoa per ml (1 study).

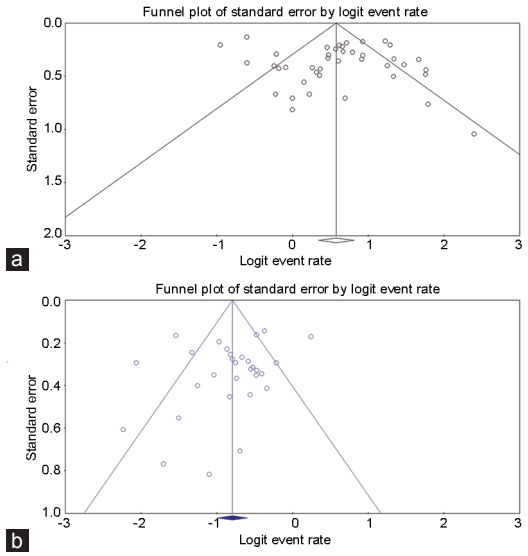

Figure 2: Funnel plots for patency group and pregnancy group. (**a**) Patency group; (**b**) pregnancy group.

Pregnancy rate after MVE

A total of 31 observational studies (7 prospective cohort studies and 24 retrospective cohort studies) were included in analysis of pregnancy rate after MVE. As shown in **Figure 4**, which presents forest plots of pregnancy rate after MVE, the overall mean pregnancy rate, calculated as the mean weighted by sample size, was 31.1% (95% CI, 26.9%–35.7%; I^2 = 73.0%). Mean time to reach pregnancy was from 6.9 months to 9.9 months (**Supplementary Table 1**). However, not all studies clearly indicated whether the definition of pregnancy was biochemical pregnancy or clinical pregnancy detected by ultrasonography.

Outcomes related to MVE surgical technique

Details of surgical techniques were clearly described in all studies included in the analysis. From 1978 to 2005, majority of EOA surgeries utilized the end-to-end or end-to-side technique. After 2005, the majority of studies employed the intussusception technique.

The patency rate for end-to-end/end-to-side and intussusception techniques were 61.1% (95% CI, 52.4%–69.2%; I^2 = 86.3%) and 69.1% (95% CI, 64.1%–73.8%; I^2 = 54.5%), respectively (**Supplementary Figure 1**). The pregnancy rates for end-to-end/end-to-side and intussusception techniques were 26.9% (95% CI, 20.1%–35.1%;

Study name	Event rate	Lower limit	Upper limit	Z value	P value	Relative weight
	Statistics for each study					Event rate and 95% CI
Silber *et al.*[10] 1978	0.857	0.573	0.964	2.346	0.019	1.41
Fogdestam *et al.*[11] 1983	0.440	0.263	0.634	-0.599	0.549	2.38
Dubin *et al.*[12] 1984	0.278	0.204	0.367	-4.580	0.000	2.95
Fogdestam *et al.*[13] 1986	0.854	0.710	0.933	3.991	0.000	2.26
Lee *et al.*[14] 1987	0.353	0.297	0.415	-4.557	0.000	3.12
Silber *et al.*[15] 1989	0.784	0.708	0.845	6.258	0.000	2.96
Marmar *et al.*[16] 1990	0.500	0.200	0.800	0.000	1.000	1.53
Schlegel *et al.*[17] 1993	0.659	0.556	0.749	2.985	0.003	2.92
Niederberger *et al.*[18] 1993	0.455	0.265	0.659	-0.426	0.670	2.30
Grasso *et al.*[19] 1994	0.500	0.168	0.832	0.000	1.000	1.30
Matsuda *et al.*[20] 1994	0.792	0.587	0.911	2.656	0.008	2.07
Matthews *et al.*[21] 1995	0.650	0.552	0.737	2.953	0.003	2.95
Marmar *et al.*[22] 1995	0.579	0.356	0.774	0.685	0.493	2.19
Jarow *et al.*[23] 1995	0.613	0.502	0.713	1.995	0.046	2.90
Boeckx *et al.*[24] 1996	0.355	0.209	0.534	-1.593	0.111	2.46
Jarow *et al.*[25] 1997	0.672	0.587	0.747	3.849	0.000	3.01
Kim *et al.*[26] 1998	0.814	0.670	0.904	3.766	0.000	2.41
Berger *et al.*[27] 1998	0.917	0.587	0.988	2.296	0.022	0.94
Berardinucci *et al.*[28] 1998	0.617	0.472	0.744	1.589	0.112	2.70
Inaba *et al.*[29] 1999	0.444	0.177	0.749	-0.333	0.739	1.62
Eguchi *et al.*[30] 1999	0.556	0.251	0.823	0.333	0.739	1.62
Paick *et al.*[31] 2000	0.689	0.63	0.792	2.869	0.004	2.77
Hibi *et al.*[32] 2000	0.538	0.282	0.776	0.277	0.782	1.92
Chan *et al.*[33] 2005	0.841	0.729	0.912	4.837	0.000	2.56
Schiff *et al.*[9] 2005	0.447	0.312	0.589	-0.728	0.467	2.72
Kumar *et al.*[34] 2006	0.478	0.288	0.675	-0.208	0.835	2.33
Zhang *et al.*[35] 2009	0.714	0.561	0.830	2.683	0.007	2.57
Ho *et al.*[36] 2009	0.565	0.363	0.748	0.624	0.533	2.32
Kumar *et al.*[37] 2010	0.478	0.288	0.675	-0.208	0.835	2.33
Smrkoji *et al.*[38] 2010	0.647	0.476	0.787	1.689	0.091	2.52
Peng *et al.*[39] 2012	0.717	0.582	0.822	3.048	0.002	2.68
Peng *et al.*[40] 2012	0.639	0.522	0.741	2.325	0.020	2.85
Zhao *et al.*[41] 2013	0.588	0.352	0.790	0.724	0.469	2.10
Harza *et al.*[42] 2014	0.778	0.516	0.885	3.125	0.002	2.38
Jiang *et al.*[43] 2014	0.853	0.692	0.937	3.630	0.000	2.13
Peng *et al.*[8] 2014	0.792	0.663	0.881	3.956	0.000	2.58
Binsaleh *et al.*[44] 2014	0.591	0.382	0.772	0.848	0.396	2.28
Zhao *et al.*[45] 2015	0.615	0.456	0.753	1.428	0.153	2.61
Hong *et al.*[46] 2016	0.661	0.536	0.768	2.493	0.013	2.79
Hussein *et al.*[47] 2015	0.667	0.333	0.889	0.980	0.327	1.53
Chen *et al.*[48] 2016	0.717	0.642	0.782	5.280	0.000	3.03
Peng *et al.*[49] 2017	0.773	0.709	0.826	7.216	0.000	3.04
Overall mean patency	0.641	0.585	0.693	4.796	0.000	

Figure 3: Forest plots of overall patency rate after MVE. MVE: microsurgical vasoepididymostomy; CI: confidence interval.

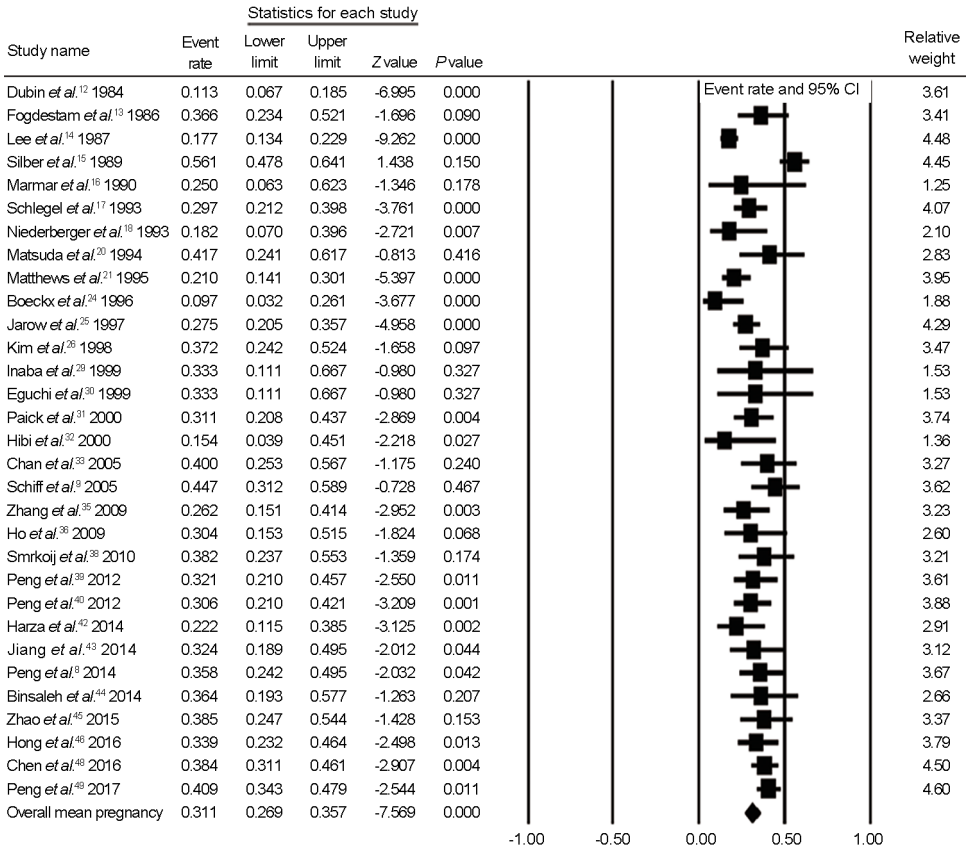

Figure 4: Forest plots of overall pregnancy rate after MVE. MVE: microsurgical vasoepididymostomy; CI: confidence interval.

I^2 = 83.3%) and 35.9% (95% CI, 32.8%–39.2%; I^2 = 54.5%), respectively (**Supplementary Figure 2**). Thus, introduction of the newer intussusception surgical technique improved both patency rate and pregnancy rate after MVE.

Figure 5 presents forest plots of intraoperative findings after MVE. Twelve articles analyzed the patency rate after MVE, according to use of bilateral or unilateral anastomosis techniques. Compared with the unilateral group, the patency rate of patients in the bilateral MVE group exhibited higher RR of 1.38% (95% CI, 1.21%–1.57%; $P < 0.00001$).

Eight studies analyzed the patency rate after MVE according to the location of the operated anastomosis. Compared with the caput anastomosis group, the patency rate of patients in cauda or corpus MVE group exhibited a higher RR of 1.17% (95% CI, 1.01%–1.35%; $P = 0.04$).

Finally, eight studies analyzed the patency rate after MVE according to the intraoperative presence or absence of motile sperm in epididymis fluid. Compared with patients in the non-motile group, patients in the motile-sperm MVE group exhibited higher patency, with RR of 1.53% (95% CI, 1.11%–2.13%; $P = 0.01$).

DISCUSSION

Our research analysis indicates that MVE is capable of achieving an overall patency rate of 64.1% and an overall pregnancy rate of 31.1% in EOA patients. To the best of our knowledge, this is the first systematic review of MVE in EOA. We note that an earlier study investigated the effect of IVF-ICSI with surgically retrieved epididymal sperm in obstructive azoospermia on fertility, reporting a pregnancy rate of 34%.[4]

Before the era of IVF, the primary treatment for infertile men with obstructive azoospermia was vasovasostomy or MVE for reconstructable cases. Using IVF, matured oocytes can be aspirated and fertilized *in vitro*. This effort resulted in the first successful delivery of an IVF child in the United Kingdom in 1978.[5] As the ART field progresses in male infertility, couples who had been previously considered irreversibly infertile, such as those eligible for artificial insemination of donor sperm, may now have the opportunity to parent a genetically related child.[6] ARTs, such as intra-uterine insemination (IUI), *in vitro* fertilization and embryo transfer (IVF-ET), and ICSI, can overcome barriers to fertilization. However, surgical treatment of obstructive azoospermia patients remains an important issue because it retains the natural sperm selection during fertilization.

Surgical techniques of MVE have evolved and advanced over the last 40 years. However, the technique remains among the most technically challenging microsurgical procedures in urology. From 1978 to 2004, MVE was primarily performed using end-to-end or end-to-side techniques and yielded patency and pregnancy rates of 61.1% and 26.9%, respectively. Since that time MVE has been predominantly performed using transverse intussusception vasoepididymostomy (TIVE) or longitudinal intussusception vasoepididymostomy (LIVE) techniques. This change in anastomotic techniques has improved both the overall patency rate (69.1%) and pregnancy rate (35.9%).

The goal of this systematic review was to gather published data on MVE to provide improved counsel for EOA patients. We found that the average incidence of postoperative patency across all publications included in our analysis was 64.1% while the average pregnancy rate

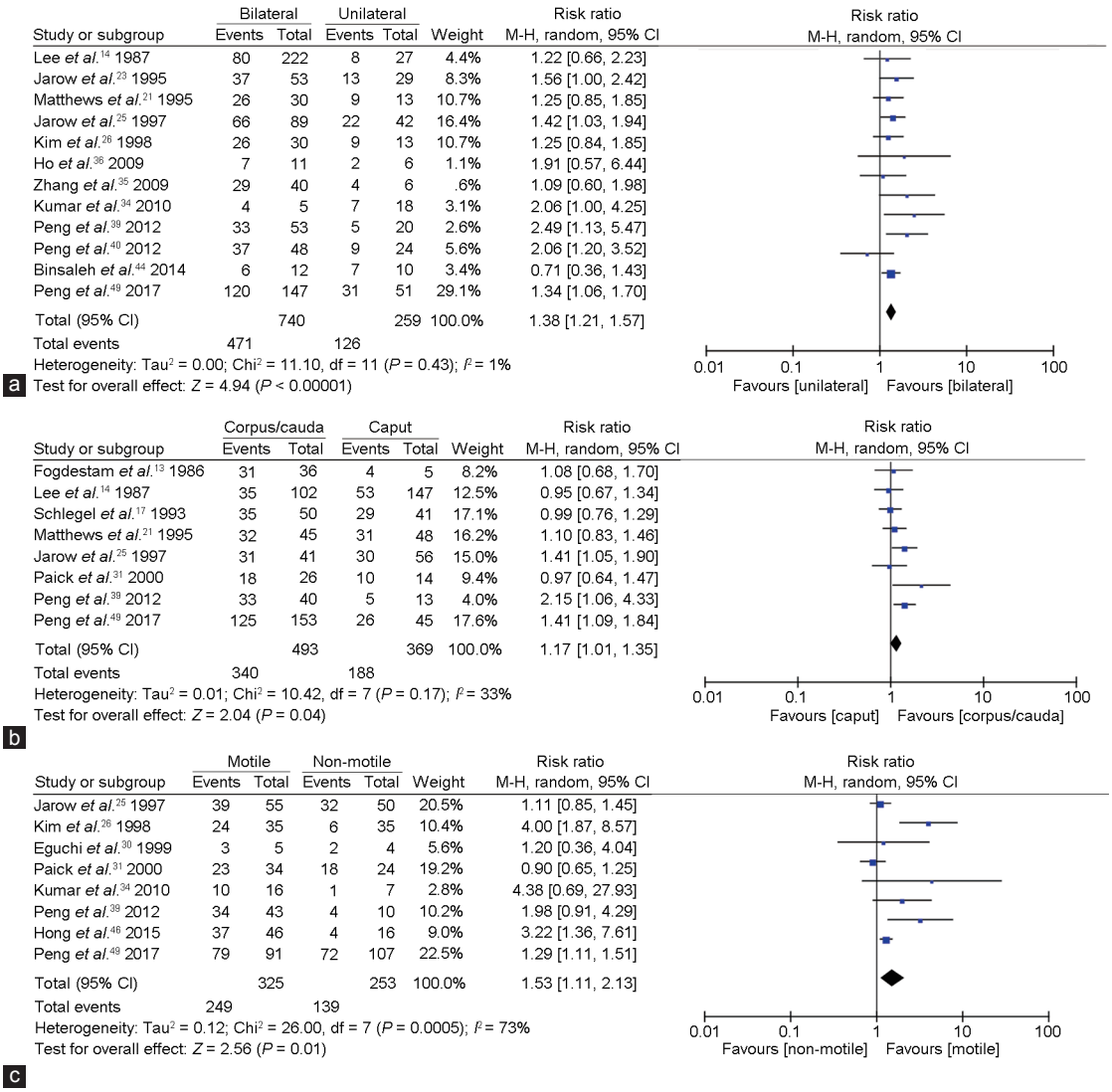

Figure 5: Forest plots of patency rate (**a**) comparing unilateral and bilateral MVE, (**b**) comparing anastomosis location after MVE, and (**c**) comparing motility of epididymal fluid after MVE. MVE: microsurgical vasoepididymostomy; CI: confidence interval.

was 31.1%. However, these results are difficult to interpret because the definition of patency varies among studies. The heterogeneity in definitions and the use of different surgical techniques was a limitation to drawing more definitive conclusions.

Given these interpretative challenges, we investigated improvements in patency rate after MVE by focusing on intraoperative findings. First, in cases of bilateral anastomosis, MVE resulted in significantly higher patency rates compared with unilateral anastomosis cases. Second, anastomoses located to a more caudal area were associated with significantly higher sperm patency rates after MVE. Third, cases in which motile sperm was present in anastomosis areas exhibited significantly higher patency rates. By carefully applying these findings, it should be possible to achieve improved patency and pregnancy rates.

However, even if reconstruction surgery for EOA is carefully performed, it is difficult to compare pregnancy rates following MVE with those for IVF-ICSI for a number of reasons, including female-related fertility issues and the couple's age. Nevertheless, pregnancy through natural intercourse engages physiologic mechanisms that result in natural selection of the best sperm. IVF-ICSI is a complicated technique involving ovarian hyperstimulation, oocyte retrieval, and embryo implantation.[7] Pregnancy after MVE avoids the high cost and associated complications of repeated IVF-ICSI, such as OHSS and multiple gestations.[8] Even patients who do not achieve natural pregnancy after successful MVE will have additional options, such as IUI and IVF-ICSI using freshly ejaculated sperm instead of sperm retrieved surgically from the testis or epididymis. However, in cases of congenital bilateral agenesis of the vas deferens or intratesticular obstruction, IVF-ICSI with testicular sperm extraction remains the only treatment option.

This study has value as the first systematic review of MVE in EOA. MVE is the most challenging microsurgical technique in urology; thus, the resulting patency rate is dependent on the surgeon's microsurgical skill.[9] Continuing efforts on the part of urologists to improve the sperm patency rate and pregnancy rate through MVE are important in managing EOA patients and helping them to achieve natural pregnancy.

We recognize several limitations to the current study. First, only observational studies were included. However, because MVE could create "normozoospermia from azoospermia," it is impossible and

unnecessary to perform a randomized controlled trial to evaluate the effectiveness of MVE. Second, the definition of patency varied among included studies, from the mere presence of spermatozoa to a threshold of more than 10^8 spermatozoa per ml. Third, the surgical method employed changed over time, with initial studies performing end-to-end MVE and a majority of recent studies performing the LIVE technique. Fourth, there have been significant advances in ART over the preceding years, which make it misleading to compare pregnancy rates from the 1980s with those of the present day. Finally, a majority of included studies did not consider female factors in the pregnancy rate, and none of the included studies reported live birth rates.

CONCLUSIONS

Even in the IVF-ICSI era, MVE remains an effective treatment for EOA that achieves improved male fertility from an azoospermia status, thereby allowing natural selection of healthy sperm. In addition, performing MVE bilaterally, anastomosing a more caudal area, and containing motile sperm in epididymis fluid potentially achieves a superior patency rate.

AUTHOR CONTRIBUTIONS

DKK designed the study. YEY coordinated the study and performed data acquisition. HHL, DKK, YEY, HSM, and SYP participated in collecting and interpreting the data, drafted and critically revised the paper. SHS and DSK reviewed the paper. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declare no competing interests.

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Supplementary information is linked to the online version of the paper on the *Asian Journal of Andrology* website.

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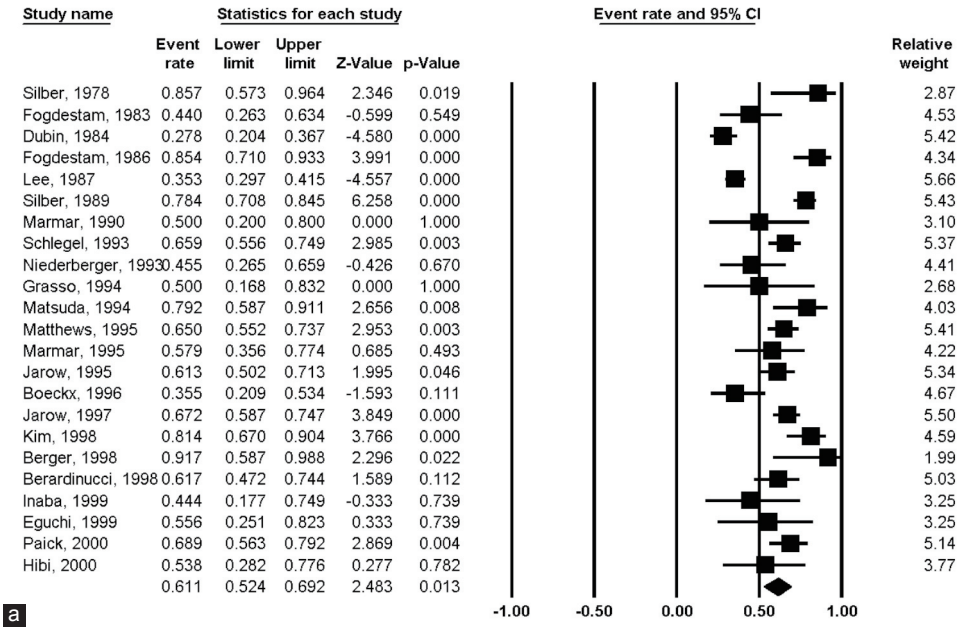
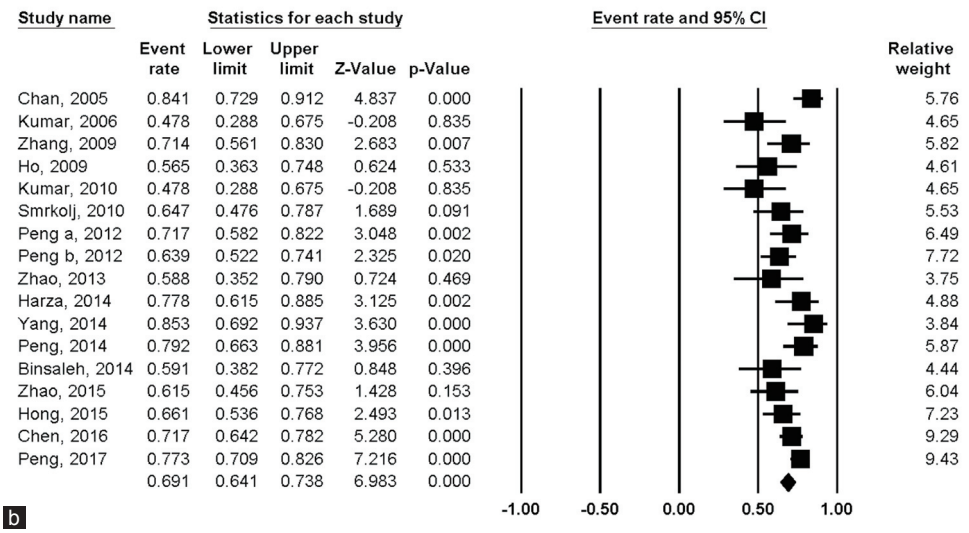
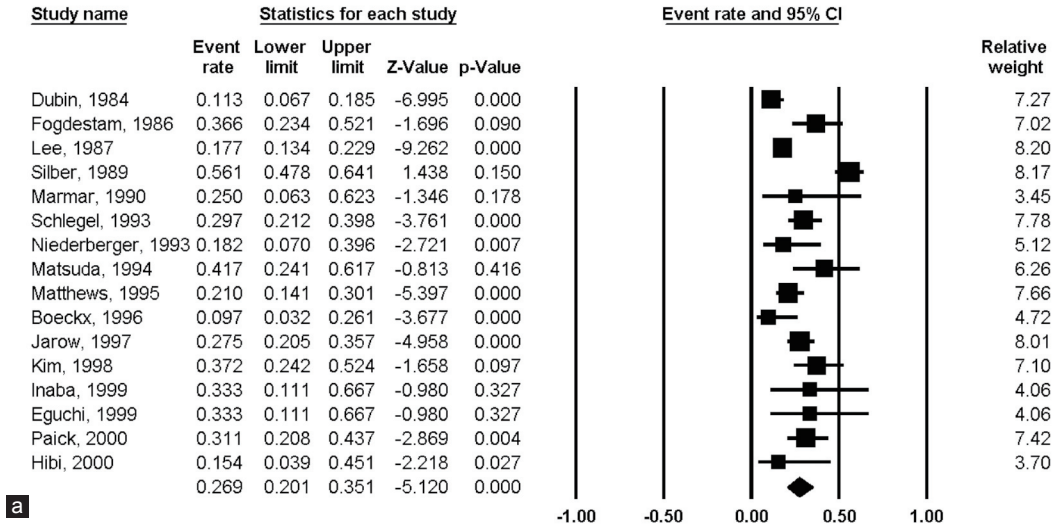
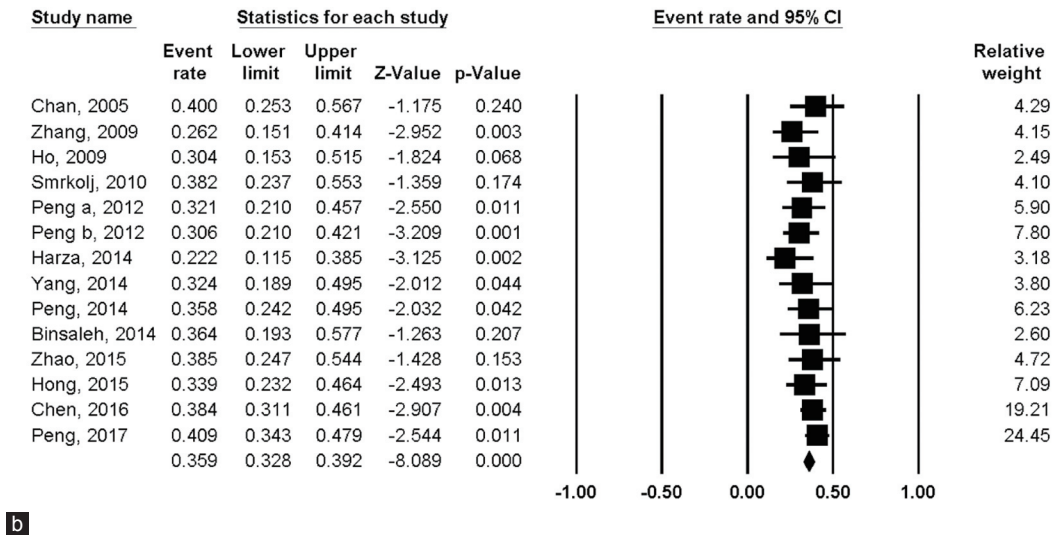




Supplementary Figure 1: Forest plots of patency rates compared by surgical techniques. (**a**) patency rates by end-to-end/end-to-side technique; (**b**) patency rates by intussusception technique.





Supplementary Figure 2: Forest plots of pregnancy rates compared by surgical techniques. (**a**) pregnancy rates by end-to-end/end-to-side technique; (**b**) pregnancy rates by intussusception technique.

Supplementary Table 1: Characteristics of the studies included in the systematic review

First author	*Year of publication*	*Country*	*Study design*	*Mean age (range)*	*Causes of obstruction (%)*	*Surgical technique*	*Mean time for patency, months (range)*	*Patency rate (%)*	*Mean time for pregnancy, months, (range)*	*Pregnancy rate (%)*	*Follow-up (months)*	*Quality score*[*]
Silber[10]	1978	USA	Retrospective cohort	N/A	N/A	End to end	N/A	85.7	N/A	N/A	8	6
Fogdestam and Fall[11]	1983	Sweden	Retrospective cohort	32.3 (24–47)	N/A	End to end or side	N/A	44	N/A	N/A	12	5
Dubin and Amelar[12]	1984	USA	Retrospective cohort	N/A	Congenital 65.3 Infection 34.7	Side to side	N/A	27.8	N/A	11.3	N/A	7
Fogdestam *et al.*[13]	1986	Sweden	Retrospective cohort	32.6 (26–47)	N/A	End to side	N/A	85.3	6–36	36.6	36	7
Lee[14]	1987	Korea	Retrospective cohort	33 (20–53)	Nontuberculosis epididymitis 64.3 Tuberculosis epididymitis32.5 Trauma 3.2	Side to side	N/A	35	N/A	17	12	9
Silber[15]	1989	USA	Retrospective cohort	N/A	N/A	End to end	6.4	78	N/A	56	48	8
Marmar *et al.*[16]	1990	USA	Retrospective cohort	27–46	Congenital 100	End to end	N/A	50	N/A	25	N/A	4
Schlegel and Goldstein[17]	1993	USA	Retrospective cohort	N/A	Infection 68.2 Vasectomy 31.8	End to end or side	N/A	74	N/A	27	12	9
Niederberger and Ross[18]	1993	USA	Retrospective cohort	N/A	Congenital 73 Epididymitis 14 Vasectomy 14	End to side	N/A	48	N/A	N/A	N/A	5
Grasso *et al.*[19]	1994	Italy	Retrospective cohort	N/A	Epididymitis 83.4 Iatrogenic 16.6	End to side	N/A	50	N/A	N/A	N/A	3
Matsuda *et al.*[20]	1994	Japan	Retrospective cohort	27–54	Vasectomy 34.7 Epididymitis 26.1 Idiopathic 26.1 Other 13.1	End to end	N/A	80.8	N/A	41.7	17.5	7
Matthews *et al.*[21]	1995	USA	Retrospective cohort	N/A	N/A	End to end or side	3.6	65	N/A	21	17.7	9
Marmar[22]	1995	USA	Retrospective cohort	N/A	N/A	End to side	N/A	58	N/A	16	18	7
Jarow *et al.*[23]	1995	USA	Retrospective cohort	38 (26–57)	Vasectomy 40 Congenital 24 Infection 20 Idiopathic 16	End to side	N/A	60	N/A	N/A	9	8
Boeckx and Van Helden[24]	1996	Belgium	Retrospective cohort	32 (22–59)	Idiopathic 48.4 Infection 35.5 Iatrogenic 16.1	End to side	N/A	35.5	N/A	9.7	24	5
Jarow *et al.*[25]	1997	USA	Retrospective cohort	39	Vasectomy 48 Congenital 20 Infection 19 Unknown 13	End to side	6 (3–15) Delayed	67	N/A	27	32	8
Kim *et al.*[26]	1998	USA	Retrospective cohort	33	Idiopathic 48.8 Infection 44.2 Congenital 4.6 Trauma 2.4	End to side	N/A	81	N/A	37	42	8

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First author	*Year of publication*	*Country*	*Study design*	*Mean age (range)*	*Causes of obstruction (%)*	*Surgical technique*	*Mean time for patency, months (range)*	*Patency rate (%)*	*Mean time for pregnancy, months, (range)*	*Pregnancy rate (%)*	*Follow-up (months)*	*Quality score**
Berger[27]	1998	USA	Retrospective cohort	N/A	N/A	End to side	N/A	92	N/A	N/A	6	5
Berardinucci *et al.*[28]	1998	Canada	Retrospective cohort	N/A	Idiopathic 73.7 Infection 17.5 Iatrogenic 8.8	End to side	N/A	62	N/A	N/A	13	6
Inaba *et al.*[29]	1999	Japan	Retrospective cohort	36.1 (23–55)	Iatrogenic 35.7s Vasectomy 32.1 Unknown 32.2	End to side	N/A	44.4	N/A	33.3	12.7	6
Eguchi *et al.*[30]	1999	Japan	Retrospective cohort	31.9 (25–37)	N/A	End to side	N/A	55.6	N/A	33.3	N/A	6
Paick *et al.*[31]	2000	Korea	Retrospective cohort	32 (25–45)	Infection 52.5 Unknown 47.5	End to side	4 (1–13)	68.9	N/A	31.1	30	9
Hibi *et al.*[32]	2000	Japan	Retrospective cohort	30.8 (24–47)	N/A	End to side	9.6 (2–15)	54	N/A	17	7–72	6
Chan *et al.*[33]	2005	USA	Prospective cohort	39.8 (22–57)	Vasectomy 31 Idiopathic 26.5 Infection 22 Iatrogenic 19 Trauma 1.5	Triangulation longitudinal intussusception	2.1	84	N/A	40	15.2	8
Schiff *et al.*[9]	2005	USA	Retrospective cohort	N/A	Vasectomy 46.4 Infection 44.4 Iatrogenic 6.5 Unknown 2.7	End to end or side TIVE, LIVE	2.9,2.8, 2.8, 3.5	45	N/A	12.8	Various among techniques	9
Kumar *et al.*[34]	2006	India	Prospective cohort	30.7 (24–38)	N/A	2 double arm LIVE	3.2 (1.5–7)	48	N/A	N/A	7.6	5
Zhang *et al.*[35]	2009	China	Retrospective cohort	N/A	N/A	2 double arm LIVE	N/A	71.4	N/A	26.3	6–12	7
Ho *et al.*[36]	2009	Hong Kong	Retrospective cohort	36	N/A	TIVE, LIVE	4 (1–20)	57	N/A	32	15	8
Kumar *et al.*[37]	2010	India	Prospective cohort	31 (23–40)	N/A	2 double arm LIVE	6.6 (3–15)	48	N/A	N/A	11.47	7
Smrkolj *et al.*[38]	2010	Slovenia	Prospective cohort	N/A	N/A	TIVE	N/A	63.6	3–6	38.2	N/A	8
Peng *et al.*[39]	2012	China	Prospective cohort	30.9 (23–48)	N/A	2 double arm LIVE	4.3 (3–9)	71.7	9.9	32.1	13.5	9
Peng *et al.*[40]	2012	China	Retrospective cohort	30.4 (21–57)	Idiopathic 88.9 Infection 9.9 Iatrogenic 1.2	2 double arm LIVE	N/A	63.9	N/A	30.6	24	6
Zhao *et al.*[41]	2013	China	Retrospective cohort	30.4	N/A	Single arm LIVE	N/A	58.8	N/A	N/A	N/A	7
Harza *et al.*[42]	2014	Romania	Prospective cohort	34 (31–37)	N/A	End to side	N/A	77.7	N/A	36	15	7
Jiang *et al.*[43]	2014	China	Prospective cohort	31.6 (22–45)	Idiopathic 68.6 Infection 25.5 Iatrogenic 5.9	2 double arm LIVE	N/A	85.3	N/A	32.4	22	6

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Supplementary Table 1: Contd...

First author	*Year of publication*	*Country*	*Study design*	*Mean age (range)*	*Causes of obstruction (%)*	*Surgical technique*	*Mean time for patency, months (range)*	*Patency rate (%)*	*Mean time for pregnancy, months, (range)*	*Pregnancy rate (%)*	*Follow-up (months)*	*Quality score*[*]
Peng *et al.*[8]	2014	China	Retrospective cohort	30.4 (22–48)	N/A	2 double arm LIVE	3.6 (3–7)	79.2	N/A	35.8	29	9
Binsaleh[44]	2014	Saudi Arabia	Prospective cohort	31 (23–47)	Infection 63.6 Idiopathic 27.3 Iatrogenic 9.1	Single arm LIVE	3 (1–24)	59	N/A	36	18	7
Zhao *et al.*[45]	2015	China	Retrospective cohort	31.4	Idiopathic 64.1 Infection 35.9	Single arm LIVE	6.2 (1.5–12)	61.5	6.9 (2.5–12)	38.5	10.3	7
Hong *et al.*[46]	2015	China	Retrospective cohort	31 (23–45)	N/A	Single arm LIVE	N/A	66.1	N/A	34.1	8.8	8
Hussein[47]	2015	Egypt	Retrospective cohort	N/A	N/A	New one layer	N/A	66.6	N/A	N/A	9	6
Chen *et al.*[48]	2016	China	Prospective cohort	28.5	N/A	Single arm LIVE	N/A	72	N/A	38.7	16.5	8
Peng *et al.*[49]	2017	China	Retrospective cohort	31	N/A	Double arm LIVE	3.8 (2–10)	77.3	9.2 (3-24)	40.9	25.3	9

[*]Quality assessment tool for before-after (pre-post) studies with no control group. LIVE: longitudinal intussusception vasoepididymostomy; TIVE: triangulation intussusception vasoepididymostomy; N/A: Not available