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The Kinetics of Sperm Return and Late Failure Following Vasovasostomy or Vasoepididymostomy: A Systematic Review

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All authors have no direct or indirect conflict of interest with any institution or product.

Running head: Sperm Return and Failure Following Vasovasostomy or Vasoepididymostomy

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Key Words: Male infertility, Sperm kinetics; Vasovasostomy; vasoepididymostomy
Abstract:
Purpose: Vasovasostomy (VV) and vasoepididymostomy (VE) are technically challenging microsurgical reconstructive procedures necessary for men with obstructive azoospermia at the level of the vas deferens or epididymis. Patency rates following VV or VE have been widely described in the literature. However, few reports have discussed the timing of sperm return to the ejaculate following reconstruction as well as the proportion of men that develop late failure following VV or VE. Therefore, the objective of this article is to review the rates and predictors associated with late failures and the timing of sperm returning to the ejaculate following VV and VE.

Methods: A literature search was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines via the PubMed®/Medline database. We included relevant articles published in English in peer-reviewed journals from 1960 to 2017 that reported outcomes regarding time to patency, time to late failure, or late failure rates after VV or VE. Macroscopic reconstructions were excluded.

Results: Twenty-four articles were included in the review. Mean time to patency after VV and VE ranged from 1.7-4.3 months and 2.8-6.6 months, respectively. Late failure rates after microsurgical VV and VE ranged from 0-12% and 1-50%, respectively. Mean time to late failure after VV and VE ranged from 9.7-13.6 months and 6-14.2 months, respectively. There was significant heterogeneity in the available data, limiting comparisons between series.

Conclusion: Sperm returns to the ejaculate sooner among men undergoing a VV compared to VE. Late failures are heterogeneously defined in the literature but do occur at non-insignificant rates. As such, clinicians should discuss considerations for sperm cryopreservation.
Introduction:
Vasovasostomy (VV) and vasoepididymostomy (VE) are important reconstructive surgical options for the patient faced with male infertility and obstructive azoospermia. Potential benefits of surgical reconstruction over sperm retrieval/IVF-ICSI include cost effectiveness and the ability for natural conception. Previous analyses have identified patency rates following reconstruction as being the key determinant to cost effectiveness. However, given that achieving a pregnancy may be a time-sensitive endeavor, i.e. limited by the female reproductive window, the timing of return of sperm to the ejaculate is an important consideration. Prolonged time for sperm to return to the ejaculate after reconstruction may potentially obviate the economic benefits and/or influence the decision making process when choosing reconstruction versus sperm retrieval. Thus, the timing of patency after VV/VE is an important clinical metric and of great interest to both patient and provider. Similarly, the durability of patency after VV/VE is another significant factor to consider, as secondary azoospermia (i.e. transient patency or late failure) may occur after an initially patent reconstruction. Early secondary azoospermia may limit clinical utility, thus the rates and timing of failure are important data to consider in patient counseling and making clinical decisions for VV/VE reconstruction versus sperm retrieval/IVF-ICSI.

The kinetics regarding time to patency and time to failure have not been well described or summarized previously. Therefore, we aim to review the literature regarding time to patency and time to failure following VV and VE reconstructions.

Methods

We performed a literature search using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines via PubMed®/Medline database with the following keywords: (“vasectomy reversal” OR “vasovasostomy” OR “vasoepididymostomy”) AND (“temporal” OR “kinetics” OR “failure” OR “delay” OR “secondary azoospermia” OR “patency” OR “outcomes” OR “experience” OR “results” OR “rates” OR “return” OR “fertility”), Figure 1. We included relevant articles published in English in peer-reviewed journals from 1960 to 2017 that reported outcomes regarding time to patency, time to late failure, or late failure rates after VV or VE. Articles were excluded if all VE or VV procedures in the article were performed macroscopically or loupe-assisted. The references section of each identified article was also analyzed for additional pertinent articles.

Results
Twenty-four articles were included in the review. Three studies reported time to patency following VV3-5 and 9 studies reported time to patency following VE2-4, 6-11. Mean time to patency after VV and VE ranged from 1.7-4.3 months and 2.8-6.6 months, respectively. Nine studies reported time to late failures following VV’s3, 12-19 and 6 studies reported time to late failure following VEs2, 3, 6, 8, 10, 19. Late failure rates after microsurgical VV and VE ranged from 0-12% and 1-50%, respectively. Mean time to late failure after VV and VE ranged from 9.7-13.6 months and 6-14.2 months, respectively. There was significant heterogeneity in the available data, limiting comparisons between series.

Discussion

Defining Patency and Failure

The definition of patency following VV is variably reported and may contribute to discordance in patency outcomes when comparing series. Some authors define patency after VV as the presence of any sperm (i.e. motile or non-motile) in the postoperative ejaculate20-22. Other authors restrict the definition of patency (e.g. motile sperm only, only sperm with tails), thereby decreasing the reported patency rates relative to those series with less restrictive definitions3, 6, 22.

Similarly, late failure (i.e. transient patency or secondary azoospermia) is variably defined across series. For instance, Matthews et al. define late failure as progression to non-motile sperm or azoospermia from previously motile sperm, Jarow et al. use a sperm count of <1 x 10^6, Belker et al. define late failure as severe oligospermia or azoospermia after initially achieving a concentration of 1.5 x 10^7, and several series use azoospermia as their threshold for failure3, 6, 13, 21, 23. Finally, some studies use a clinical pregnancy as a surrogate for patency in the absence of any SA data, while other studies exclude patients entirely if postoperative SAs were not performed4, 19. In short, there is no agreed upon standardized definition of patency and failure, thus comparisons between series is hedged with significant limitations.

Mechanism of Failure

The mechanism of transient patency and late failure is not well elucidated. Potential explanations include anastomotic obstruction resulting from sperm granuloma or suture inflammatory reaction. Other postulated mechanisms are failure to resect back far enough on the vasa to find healthy mucosa and muscularis with good bloody supply as opposed to just a patent lumen, presence of a perivascular scrotal hematoma, secondary epididymal obstruction due to epididymitis, and evacuation of non-motile sperm previously present in the vasa lumen between epididymis and vasectomy site16, 24. Cases of very late failure many months from surgery likely represent slowly progressive cicatricial or mucosal scar occlusion rather than sperm granuloma25.
Patency rate and Time to Patency

The time to patency after reconstruction can be stratified by time to patency after VV (Table 1), VE (Table 2) or mixed VV/VE.

Time to patency after VV has been reported by the Matthews et al. (1995) and Yang et al. The former study analyzed 100 patients undergoing VV and found an overall patency rate of 99%, with mean time to patency of 1.7 and 2.2 months for any and motile-only sperm, respectively. Their cohort included only patients with sperm found intraoperatively in the testicular vasal fluid. Yang et al. reported patency rates of 95% among 90 men with prior vasectomy, and found a mean time to patency (motile sperm only) of 3.2 months after VV. Their patency definition was stricter, however, including only patients with motile sperm in the SA. Marshall et al. also examined time to patency in a cohort of 60 robot-assisted VV, with a mean time to patency of 4.3 months. Of note, Marshall et al. began collecting semen analyses at 3 months, potentially delaying their true time to patency. By comparison, the other two studies began collection of semen analyses at 6 weeks.

Nine series have reported time to patency following VE, with rates ranging from 2.8 to 6.6 months. For return of motile sperm, time to patency ranged from 5.8 to 6.3 months. Binsaleh reported a median time to patency of 3 months using a two-suture single armed longitudinal intussusception VE technique. They compared SA parameters in those who had initially positive SA (N=31) versus those with a delayed (N=18) appearance of sperm; sperm count and motility did not significantly differ between groups. They reported that the mean time to patency in men with delayed patency was 6.0 ± 3.5 months. No mean time to patency was reported in the early group, though their methodology defined early as sperm within 3 months postoperatively. Kumar et al. had the longest time to patency of any series, with a mean of 6.6 months. A potential explanation for this finding is their inclusion criteria of only idiopathic obstructive azoospermia, although no literature demonstrates this etiology (i.e. idiopathic) of obstructive azoospermia portends worse outcomes. Both Boeckx and Van Helden, and Paick et al. reported a mean time to patency of 4.0 months, though Paick et al. had a more rigorous definition of patency with a threshold of >10^5 sperm/mL of semen compared to Boeckx’s patency definition of any sperm in the ejaculate. Yang et al. published time to patency rates of 6.3 ± 1.5 months following VE in 23 men. Their mean follow-up was 12.5 months, though this was aggregate follow-up data for their entire cohort (all VV/VE/mixed). Schiff et al. compared outcomes between 4 VE techniques (end-to-end (EE), n=66; end-to-side (ES), n=38; 3-suture triangulation intussusception (TIVE), n=38; double-armed 2-suture longitudinal intussusception (LIVE), n=17) in 153 consecutive patients. The primary outcome of the study was patency rates, but they also reported time to patency ranging from 2.8-3.5 months, with no significant
difference between techniques (p=0.94). Matthews et al. (1995) analyzed time to patency in 100 consecutive VE patients and found a patency rate of 65% and mean time to patency of 3.6 ± 0.4 months, and time to patency (motile or non-motile) was more delayed after VE versus VV (p<0.0001). Overall, the time to patency after VE is slightly longer than after VV, with statistically significant differences demonstrated by both the Matthews et al. and Yang et al.

Several authors have also reported time to patency after mixed VV/VE. In the Yang et al. series of 90 patients, 37 underwent mixed VV/VE with mean time to patency of 3.7 ± 1.2 compared to 3.2 ± 0.5 and 6.3 ± 1.5 for VV and VE, respectively. Thus, time to patency appears to lengthen with any vasoepididymal reconstruction. One potential mechanism for longer time to patency with motile sperm, could be shorter functional epididymal length after VE, leading to longer sperm maturation times and ultimately longer time to patency with motile sperm. A second explanation may be that the epididymal anastomosis during reconstruction has a much smaller lumen than the vasal lumen during a VV; any inflammation may functionally obstruct the anastomosis more readily. Thus, longer duration following VEs is required to allow tissue inflammation to subside and allow motile sperm to pass through. A third explanation could be that VEs are typically required in men with long standing obstruction; thus, efficiency of spermatogenesis and transit of sperm may require time to recuperate.

Factors affecting time to patency and patency rate

Yang et al. identified factors predicting faster time to patency. First, the presence of motile sperm compared to non-motile sperm in the vasal fluid intraoperatively was associated with earlier time to patency by 6 months (96% vs. 76% patent, respectively; p=0.04). The obstructive interval is a well-documented factor predicting favorable postoperative patency and in this series it (<8 years vs. 9-16 years) also predicted faster time to patency by 3 months. VV compared to VE was associated with faster time to patency (96% vs. 46% patent by 6 months; p<0.05). This finding is in-line with the kinetics data from the other VV vs. VE series. Age was examined, but was not a statistically significant factor. Matthews et al. also compared unilateral vs. bilateral anastomoses but found that this variable did not affect time to patency. Moreover, the level of the anastomosis (i.e. caput, corpus, or cauda) in VEs did not affect timing of patency. While the level of the anastomosis does not affect the timing of patency, the data is mixed on whether it affects overall patency rates in general. Pregnancy and live birth rates are related to level of anastomosis, with anastomosis to the caput resulting in significantly lower pregnancy rates than to corpus or cauda. With respect to anastomotic technique, it is unclear whether choice of anastomosis affects patency kinetics. For VV cases, Matthews et al. and Yang et al. both performed a multi-layer anastomotic technique while Marshall et al. used a single-layer anastomosis. However, no study has compared VV anastomotic techniques (i.e. single versus multi-layer) for rate of sperm return to the ejaculate.
By comparison, previous literature has consistently demonstrated no difference in overall patency rates between VV anastomoses\cite{30}.

For VE, techniques have evolved considerably over the past several decades. Schiff et al. compared time to patency among the early VE anastomoses (ES and EE) with intussusception techniques (TIVE and double-armed LIVE) but did not find a statistically significant difference\cite{2}. The two-suture LIVE technique is being increasingly employed\cite{28,31,32}. However, no comparative studies have analyzed the kinetics of sperm return using these contemporary anastomoses.

Other factors associated with favorable patency rates in general (e.g. sperm granuloma, history of conception with current partner, length of vasal remnant) have not been analyzed with respect to time to patency\cite{22,33}. Multivariable analysis has yet to be performed and should be a future aim to identify independent predictors of time to patency and reduce the effect of confounding variables.

**Late failures and time to late failure in Vasovasostomy**

Nine studies reported on late failures and/or time to late failure (Table 3)\cite{3,12-19}. Requeda et al. (1983) and Weinerth (1984) published the first two series of microsurgical VV reconstructions, with a 2.1% and 6% late failure rate, respectively\cite{12,14}. Both authors defined late failure as azoospermia on SA. Belker et al. reported a 3.1% rate of secondary azoospermia in 892 patients after VV\cite{13}. They considered patients initially patent if sperm were motile and the concentration reached $1.5 \times 10^7$; subsequent failure was defined as azoospermia or "severe oligospermia". Limitations to this study include sub-optimal follow-up (67% had follow-up < 1 year) and the failure to report age, obstructive intervals or number of unilateral VVs. A retrospective analysis from Kolettis et al. reported results from 3 surgeons including 242 VV patients and identified the frequency of secondary azoospermia to be 5.3% and 2.9% for any sperm to azoospermia and motile sperm to azoospermia, respectively.\cite{16} Their patient population included 9% repeat procedures and 5% unilateral procedures. The chief limitation to this study is short follow-up. A study by Jee and Hong compares failure rates of loupe-assisted VV with microsurgical VV.\cite{17} They found significant differences in outcomes between the two techniques, with a secondary azoospermia rate of 16% in the loupe VV group compared to 0% in the microsurgical group. An important drawback to this study is that follow-up is not reported, perhaps explaining why they remain the only study with a 0% late failure rate. Schwarz et al. reported on his experience with VV and VE\cite{19,23}. He primarily uses a three-layer technique for VV and in 1,195 VV patients reports a 92% patency rate and 1% late failure rate. The 1% secondary azoospermia rate, however, is the aggregate rate for all cases (VV, VE, and mixed VV/VE); no additional analysis was provided. Other drawbacks include: 30% of patients never provided a SA and mean follow-up is not documented. It is unclear whether men with absent SA data were statistically equal to those with who provided a SA and whether the
mean follow-up compared favorably or unfavorably to other series. Amarin and Obeidat also describe temporal considerations in sperm parameters after VV\textsuperscript{20}. In 68 patients they noted “worse” sperm count (20.5%), motility (22%), and morphology (14.7%) at 12 months follow-up compared to 3 months. They did not report on late failure. A subset of those with “worse” semen parameters may have met the definition for late failure. Overall, late failure rates after microsurgical VV range from 0-12%, with mean time to failure of 9.7-13.6 months\textsuperscript{3,17}.

Late Failures in Vasoepididymostomy

Seven studies reported late failures after VE, (See table 4)\textsuperscript{2, 3, 6, 8, 10, 19, 34}. Matthews et al. (1995) described rates of late failure (defined as progression to non-motile sperm or azoospermia from motile sperm) in their VE group of 100 patients\textsuperscript{3}. At mean follow-up of 17.7± 1.1 months, rates of secondary azoospermia were 21% with occurrence at a mean of 14.2 ± 2.5 months. Jarow et al. in their cohorts of delayed (N=18) versus early return of sperm (N=31) after ES VE, found late failure rates of 10% and 11%, respectively (p=0.76)\textsuperscript{6}. They did not report time to failure. This series had an unusually large proportion of patients (38%) undergoing unilateral VE with a non-functioning contralateral testicle. Schiff et al. in their comparison of 4 VE techniques also documented rates of secondary azoospermia\textsuperscript{2}. They did find differences between techniques for late failure, with late failure developing in 5/10 (50%) and 6/20 (30%) patients in the ES and EE group versus 0/9 (0%) and 1/13 (7.6%) in the LIVE and TIVE groups, respectively (p=0.04), suggesting the intussusception techniques (LIVE and TIVE) have better durability compared to non-intussusception techniques (ES and EE). These results may be due to the longer follow-up in the non-intussusception groups (ES: 116.7, EE: 140.2 months) compared to the intussusception groups (LIVE: 17.2, TIVE 70.8 months); with more follow-up time the failure rates of the intussusception groups may increase. In addition to the Schiff et al. paper, the Cornell group (Chan et al.) also published data from their same institutional cohort of patients looking only at 68 prospectively followed VE patients who underwent an intussusception anastomosis (TIVE or LIVE)\textsuperscript{34}. Among patients with >1 year of follow-up, the late failure rate was 3%. No data was available on late failures for patients with <1 year of follow-up. Kumar et al., had a late failure rate of 18.1% using a longitudinal 2-suture intussusception technique\textsuperscript{10}. They did not calculate a mean time to late failure, but defined its occurrence as happening >1 year after VE. Schwarzer and Steinfatt report a 73% patency rate in 137 VE patients; their late failure rate is 1% among their entire cohort (VV and VE combined)\textsuperscript{19}.

Data on late failure after mixed VV/VE is limited. Matthews et al. in 1997 examined reconstructions after initially failed vasectomy reversal and reported late failure data on mixed VV/VE patients\textsuperscript{35}. Their data included 9 patients with previously failed reversal attempt who then underwent mixed VV/VE reconstruction. Eight were initially patent and one patient developed late failure.
Risk Factors for Late Failure & Secondary Azoospermia after Vasovasostomy or Vasoepididymostomy

Kolettis et al., in a multi-institutional collaboration of three surgeons, identified two risk factors for the development of secondary azoospermia after VV: unilateral reconstruction (25% vs. 4.3%; p=0.0196) and long obstructive interval (13.1 vs. 8.9 years; p=0.0458)\(^1\). Conversely, Matthews et al. did not find rates of secondary azoospermia any higher with unilaterality for VV, but did find late failure was more common with unilateral compared to bilateral VE\(^3\). Kolettis et al., found type of anastomosis was not associated with late failure rates after VV\(^1\). However, when choosing between a microsurgical versus loupe-assisted approach, loupe-assisted VV appears to be a significant risk factor for late failure. For instance, Jee and Hong noted a late failure of 16% for loupe-assisted VV versus 0% for microsurgical VV\(^17\).

Surgical technique for VE varies considerably among series (Table 2 and Table 4). The majority of VE articles pre-date the intussusception VE. Therefore, it is difficult to compare series directly and ascertain whether contemporary techniques have improved late failure rates. The only series that directly compares VE anastomotic techniques is Schiff et al. They found that ES and EE techniques had significantly higher late failure rates compared to intussusception techniques. Future study should be aimed at comparative effectiveness analysis between the various contemporary VE anastomoses.

Repeat Vasovasostomy/Vasoepididymostomy

Matthews et al. (1997) is the only series to specifically examine time to patency and rates of late failure after repeat reconstruction\(^35\). They identified 57 patients who underwent repeat reconstruction after 1 or more prior failed (i.e. azoospermia on SA) vasectomy reversals (VV or VE). Of these 57 men, 64 vasectomy reversals were available for analysis (52 first and 12 second repeat operations). With patency defined as motile sperm, time to patency was 2.9 ± 0.2 (patency 67%) in men undergoing first repeat reversal, though this was not reported in the second repeat reversal group. Late failure rates were 23% in the first repeat reversal group at a mean 9 months of follow-up and 0% in the smaller second repeat reversal group. When stratified by technique, they reported late failure rates of 27% and 18% for repeat VV and repeat VE, respectively. The comparatively lower rate of late failure in their VE group is likely due to a much lower rate of initial patency in the VE group versus the VV group.

Belker et al. commented in their discussion that of the 28 patients with late failure, 12 of these underwent repeat VV\(^13\). They mention that, at the time of their article, follow-up was not mature but 2/12 patients had normal sperm concentrations at 3 years after the reoperation. Schwarzer et al. also briefly commented on their 8 patients with secondary azoospermia by saying that 6 of
them underwent successful repeat reconstruction\textsuperscript{23}. However, they do not elaborate on the follow-up SA parameters in these patients.

**Limitations**

The studied populations are not uniform between series and it is unknown whether these inter-series differences affect outcomes (See Table 1-4). In the Matthews et al. cohort, the etiology of obstruction included prior vasectomy, infection, iatrogenic, and idiopathic, Belker et al. included reconstructions for chronic pain, Yang et al. included only patients with prior vasectomy, Kumar et al. only idiopathic etiology, and other groups did not specify the etiology at all\textsuperscript{3,4,10,16,21}. As discussed earlier, the definitions used for patency and failure vary widely and are not consistent between series. The interval of semen analysis follow-up was also variable between studies. No studies check semen analyses prior to 6 weeks, suggesting that time to sperm in the ejaculate could be sooner than reported. Technique for VV varied widely from modified one-layer to two-layer or three-layer\textsuperscript{23}. Finally, the series span over several decades, introducing a possible “generational” bias, as many factors (e.g. hospital care, surgical techniques and experience, patient populations) may have changed over time. Holman et al. showed that VV outcomes improved significantly in 1994-1996 compared to 1980-84\textsuperscript{36}.

Follow-up is a critical metric. Most of the included studies are limited by a mean follow-up of <1 year. It is possible that with longer follow-up data the rates of secondary azoospermia could be higher. In the Schiff et al. series of VE patients, the ES and EE techniques had late failures rates of 50% and 30% respectively\textsuperscript{2}. While the authors attribute these high failure rates to an inferior anastomotic technique (i.e. non-intussusception) but follow-up for these patients (EE: 116.7, ES: 140.2) was the lengthiest of any series in the literature, while the intussusception techniques had shorter follow-up. This suggests that late failure rates on a longer time scale may be underappreciated and significantly greater than reported across all series. Conversely, for patients with short follow-up (i.e. 3 months or less) the rates of patency are likely underestimated, as patency may not occur until after 6 months in a significant proportion of cases and may take up to a year or longer. In fact, some authors have shown a small subset of patients with azoospermia have achieved pregnancy, suggesting the late return of sperm to the semen after the last recorded SA and underscoring the need for long follow-up\textsuperscript{21}. These considerations may explain some differences between series. For instance, Matthews et al. (1995) had the highest rate of late failures (12%) after VV but had the longest and most rigorous follow-up of any of the VV series (16.8 months). Kolettis et al., for instance, had a late failure rate of 5.3% but had a mean follow-up of 9.0 months, while Belker et al. had a late failure rate of 3.1% but 57% of patients had <12 months of follow-up (mean follow-up not reported). Similarly, Schwarzer et al. had a very low late failure rate but did not report the follow-up time. Thus, many of these series may have falsely low late failure rates without adequate long-term follow-up.
Another possible factor not reported in most series is anti-sperm antibodies (ASA). The presence of ASAs may exert a deleterious effect on semen parameters, specifically sperm motility. 20 The majority of series did not account for this as a potential etiology of SA parameter changes. However, as Matthews et al. (1997) note in their analysis of repeat VV/VE patients, those who initially experienced a late failure followed by repeat reconstruction had excellent patency rates, suggesting mechanical etiologies leading to late failures and the majority of SA changes rather than ASAs.35

Conclusions
Mean time to patency after VV and VE ranged from 1.7-4.3 months and 2.8-6.6 months, respectively. Late failure after microsurgical VV and VE ranged from 0-12% and 1-50%, respectively. Mean time to late failure after VV and VE ranged from 9.7-13.6 months and 6-14.2 months, respectively. Given that a significant number of patients will develop late failures, it is important for the clinician to discuss sperm cryopreservation. This can be performed intraoperatively at the time of VV/VE and upon return of motile sperm to the ejaculate post-operatively.

Author contributions
NF and RF drafted the manuscript and PL, PSL and MG critically revised it. All authors read and approved the final manuscript.

Competing Interests
All authors declare no competing financial interests.

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Table 1. Time to Patency: Vasovasostomy

<table>
<thead>
<tr>
<th>Series</th>
<th>Sample size (N)</th>
<th>Overall patency rate (%)</th>
<th>Time from surgery to patency (mos)</th>
<th>Time from surgery to motile sperm (mos)</th>
<th>Mean Follow-up (mos)</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Matthews et al. (1995)  | 100             | 99                       | 1.7 ± 0.1                          | 2.2 ± 0.1                              | 16.8                 | **Inclusion**: All microsurgical VV patients with sperm found intraoperatively.  
**Patency**: any sperm (motile or non-motile) with tails.  
**SA Interval**: Serial SAs beginning at 6 weeks |
| Yang et al. (2007)      | 90              | 95                       | 3.2 ± 0.5                          | 3.2 ± 0.5                              | 12.5                 | **Inclusion**: All microsurgical VV patients with vasectomy as etiology of obstruction; 2 or more post-op SAs available (1 if motile sperm)  
**Patency**: motile sperm  
**SA Interval**: 6 weeks, 3 months, 6 months and 1 year |
| Marshall et al. (2017)  | 60              | 88                       | 4.3 ± 3.4                          | NR                                     | NR                   | **Inclusion**: Robot-assisted VV; obstructive interval <10 years  
**Patency**: any sperm  
**SA Interval**: 3 months postoperatively and as indicated |
Table 2. Time to Patency: Vasoepididymostomy

<table>
<thead>
<tr>
<th>Series</th>
<th>Sample size (N)</th>
<th>Overall patency rate (%)</th>
<th>Time from surgery to patency (mos)</th>
<th>Time from surgery to motile sperm (mos)</th>
<th>Mean Follow-up (mos)</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Jarow et al. (1995)    | 18              | NR                       | 6.0 ± 3.5                         | NR                                      | 9                    | Inclusion: All microsurgical VE patients  
Patency: > 1 x 10^6 sperm  
SA Interval: 2-3 mos postoperatively, then every ~2 months  
Technique: ES  
Other: Time to patency only calculated in a subgroup of initially azospermic patients with delayed patency |
| Matthews et al. (1995) | 100             | 65                       | 3.6 ± 0.4                         | 5.8 ± 0.8                               | 17.7± 1.1            | Inclusion: All microsurgical VE patients with sperm found intraoperatively.  
Patency: any sperm (motile or nonmotile) with tails.  
SA Interval: Serial SAs beginning at 6 weeks  
Technique: EE and ES |
| Boeckx et al. (1996)   | 24              | 46                       | 4.0 (range: 1-12)                 | NR                                      | NR                   | Inclusion: All microsurgical VE patients with 2 year-follow-up  
Patency: any sperm  
SA Interval: Every 3 months postoperatively  
Technique: ES |
| Berardinucci et al. (1998) | 44        | 61                       | 45, 90 and 96% patent at 3.6 and 12 mos, respectively | NR                                      | 12                   | Inclusion: All patients with suspected obstructive azospermia undergoing scrotal exploration and VE  
Patency: any sperm  
SA Interval: Every 3 months postoperatively  
Technique: ES |
| Paick et al. (2000)    | 61              | 69                       | 4.0                               | 5.8                                     | 30                   | Inclusion: All microsurgical VE patients with >24 months follow-up  
Patency: >10^5 sperm/mL of semen  
SA Interval: 1 month postoperatively then |
<table>
<thead>
<tr>
<th>Study</th>
<th>Total:</th>
<th>LIVE:</th>
<th>TIVE:</th>
<th>NR</th>
<th>Patency:</th>
<th>SA Interval:</th>
<th>Technique:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schiff et al. (2005)</td>
<td>153</td>
<td>80</td>
<td>84</td>
<td>NR</td>
<td>intact whole sperm</td>
<td>3 and 6 months postoperatively and as indicated</td>
<td>ES in 57/61 patients</td>
</tr>
<tr>
<td>Yang et al. (2007)</td>
<td>23</td>
<td>62</td>
<td>6.3 ± 1.5</td>
<td>NR</td>
<td>motile sperm</td>
<td>6 weeks, 3 months, 6 months and 1 year</td>
<td>ES, EE, LIVE, TIVE</td>
</tr>
<tr>
<td>Kumar et al. (2010)</td>
<td>23</td>
<td>48</td>
<td>6.6 (range: 3-26)</td>
<td>NR</td>
<td>any sperm</td>
<td>First SA between 6-12 weeks, then every 3 months</td>
<td>LIVE/TIVE</td>
</tr>
<tr>
<td>Binsaleh (2014)</td>
<td>22</td>
<td>59</td>
<td>3 (range: 1-24)</td>
<td>NR</td>
<td>&gt;10^4 sperm/mL of semen</td>
<td>1, 3, 6, 9, and 12 months postoperatively</td>
<td>Two-suture single-armed LIVE</td>
</tr>
<tr>
<td>Series</td>
<td>Sample size (N)</td>
<td>Overall patency rate (%)</td>
<td>Late Failure Rate (%)</td>
<td>Time to Late Failure</td>
<td>Mean Follow-up (mos)</td>
<td>Comments</td>
<td></td>
</tr>
<tr>
<td>--------</td>
<td>----------------</td>
<td>-------------------------</td>
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<td>---------------------</td>
<td>---------------------</td>
<td>----------</td>
<td></td>
</tr>
</tbody>
</table>
| Requed et al. (1983) | 47 | 80 | 2.1 | 12 | NR | Inclusion: All VV patients 
Definition of Failure: azoospermia 
SA Interval: Not reported 
Other: Microscopic (95%) and macroscopic (15%) technique performed |
| Weinerth (1984) | 34 | 98 | 6 | NR | NR | Inclusion: All microsurgical VV patients 
Definition of Failure: azoospermia 
SA Interval: 3 months postoperatively then as indicated |
| Belker et al. (1985) | 892 | 86 | 3.1 | NR | NR | Inclusion: All VV patients 
Definition of Failure: severe oligospermia or azoospermia after initially >1.5 x 10⁷ and motile. 
SA Interval: 3-4 month intervals for 1 year postoperatively 
Other: 223 (25%), 491(55%), 386(43%) patients had <6, >6, and >12 months of f/u, respectively. |
| Fox et al. (1994) | 103 | 84 | 5.6 | NR | 8-60 (range) | Inclusion: All microsurgical VV patients 
Definition of Failure: azoospermia. 
SA Interval: Every 3 months for 1 year 
Other: 2-layer VV technique. 52% performed with 10-0 suture, 48% with 8-0. |
| Matthews et al. (1995) | 100 | 99 | 12 | 13.6 ± 1.7 | 16.8 | Inclusion: All VV patients with sperm found intraoperatively. 
Definition of Failure: progression to azoospermia or to non-motile from motile sperm. 
SA Interval: Serial SAs beginning at 6 weeks |
| Kolettis et al. (2005) | 242 | 91 (80% motile sperm) | 5.3 | 9.7± 2.3 | 9.0 ± 0.7 | Inclusion: All VV patients 
Definition of Failure: progression to azoospermia or to non-motile from motile sperm. 
SA Interval: 1-3 months postoperatively, then every ~3 months 
Other: 5.3% and 2.9% failure rate for any sperm to azoospermia and motile sperm to azoospermia, respectively |
<table>
<thead>
<tr>
<th>Study</th>
<th>Micro: 25</th>
<th>Micro: 96</th>
<th>Micro: 0</th>
<th>NR</th>
<th>NR</th>
<th>Inclusion: Prior vasectomy</th>
<th>Definition of Failure:</th>
<th>SA Interval:</th>
<th>Other:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jee et al. (2010)</td>
<td>25</td>
<td>96</td>
<td>16</td>
<td>NR</td>
<td>NR</td>
<td>progression from motile to non-motile sperm</td>
<td>1 or 3 months then 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shin et al. (2012)</td>
<td>97</td>
<td>86</td>
<td>9.3</td>
<td>NR</td>
<td>6.0</td>
<td>All VV patients with follow-up data at 1 and 6 months</td>
<td>progression from oligospermia or normospermia to azoospermia</td>
<td>1, 3, and 6 months</td>
<td></td>
</tr>
<tr>
<td>Schwarzer (2012, 2014)</td>
<td>1195</td>
<td>92</td>
<td>1</td>
<td>3-13 months (range)</td>
<td>NR</td>
<td>All VV patients</td>
<td>azoospermia.</td>
<td>3 months postoperatively, then as indicated</td>
<td>VV / VE failure rates combined (no subgroup analysis available).</td>
</tr>
</tbody>
</table>
Table 4. Time to failure: Vasoepididymostomy

<table>
<thead>
<tr>
<th>Series</th>
<th>Sample size (N)</th>
<th>Overall patency rate (%)</th>
<th>Late Failure rate (%)</th>
<th>Time to Late Failure (months)</th>
<th>Mean Follow-up (months)</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Jarow et al. (1995)         | 89              | 56                       | 10-11                 | Not reported                 | 9                       | Inclusion: All VE patients  
|                             |                 |                          |                       |                              |                         | Definition of Failure: <1 x 10⁶ sperm.  
|                             |                 |                          |                       |                              |                         | SA Interval: 2-3 mos postoperatively, then every ~2 months  
|                             |                 |                          |                       |                              |                         | Technique: ES                                                             |
| Matthews et al. (1995)      | 100             | 65                       | 21                    | 14.2 ± 2.5                   | 16.8                    | Inclusion: only if sperm found intraoperatively.  
|                             |                 |                          |                       |                              |                         | Definition of Failure: progression to azoospermia or to non-motile sperm.  
|                             |                 |                          |                       |                              |                         | SA Interval: Serial SAs beginning at 6 weeks  
|                             |                 |                          |                       |                              |                         | Technique: EE and ES                                                      |
| Berardinucci et al. (1998)  | 44              | 61                       | 2.3                   | 6.0                          | 12                      | Inclusion: All patients with suspected obstructive azoospermia undergoing scrotal exploration and VE  
|                             |                 |                          |                       |                              |                         | Definition of Failure: azoospermia  
|                             |                 |                          |                       |                              |                         | SA Interval: Every 3 months postoperatively  
|                             |                 |                          |                       |                              |                         | Technique: EE, ES                                                        |
|                             |                 |                          |                       |                              |                         | Definition of Failure: initial return of sperm with azoospermia on 2 subsequent SAs  
|                             |                 |                          |                       |                              |                         | SA Interval: 3 and 6 months postoperatively and as indicated  
|                             |                 |                          |                       |                              |                         | Technique: ES, EE, LIVE, TIVE                                             |
| Kumar et al. (2010)         | 23              | 48                       | 18.1                  | Not reported                 | 11.5                    | Inclusion: All VE patients with idiopathic etiology of obstruction  
|                             |                 |                          |                       |                              |                         | Definition of Failure: azoospermia  
|                             |                 |                          |                       |                              |                         | SA Interval: First SA between 6-12 weeks, then every 3 months  
|                             |                 |                          |                       |                              |                         | Technique: LIVE  
|                             |                 |                          |                       |                              |                         | Other: Late failures occurred “>1 year” after surgery; precise timing     |
Schwarzer (2012, 2014) | 137 | 73 | 1 | 3-13 months (range) | Not reported
Inclusion: All VE patients
Definition of Failure: azoospermia.
SA Interval: 3 months postoperatively, then as indicated
Technique: ES
Other: VV/VE failure rates combined (no subgroup analysis available).
Abbreviations and Acronyms

ASA = anti-sperm antibodies
EE = end-to-end
ES = end-to-side
LIVE = longitudinal intussusception vasoepididymostomy
PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
TIVE = triangulation intussusception vasoepididymostomy
VE = vasoepididymostomy
VV = vasovasostomy