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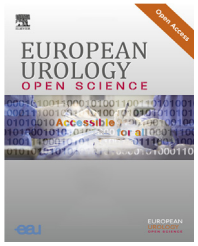

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Prognostic Factors for Pregnancy and Patency Rates After Microsurgery for Obstruction of the Upper Seminal Tract: A Retrospective Single-surgeon Series of 336 Cases

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Abstract

Background and objective: To achieve optimal results in treating vasal obstruction, microsurgery is the standard of care. However, not all vasovasostomy (VV) or vasoepididymostomy (VE) procedures lead to subsequent pregnancy. Identification of parameters that can predict success in restoring fertility is clinically relevant. We evaluated various parameters in relation to patency and pregnancy outcomes in a retrospective single-surgeon series.

Methods: We analysed data for 336 men with azoospermia due to vasal obstruction who underwent microsurgery to restore fertility. Seminal fluid was harvested intraoperatively from the testicular stump for analysis of gross quality. Intraoperative parameters, time to conception, patency rate, age of the female partner, and time from vasectomy to reconstruction were assessed in relation to pregnancy outcomes. Multivariable logistic regression was performed to identify independent prognostic parameters.

Key findings and limitations: The median age at surgery was 42 (range 27–70) yr for the men and 33 (range 19–46) yr for their female partners. The overall patency rate after surgery was 86.8% (236/272). Secondary obstruction occurred in 14/272 men (5.1%). Pregnancy was achieved in 127/258 couples (49.2%). The most significant predictor of successful treatment was the obstruction time ($p < 0.01$), with significantly lower success rates for longer times since vasectomy. None of the intraoperative parameters we analysed was associated with subsequent pregnancy. The primary limitation of our study is its retrospective design.

Conclusions and clinical implications: Patency and pregnancy rates in our series are similar to rates reported in the literature. Pregnancy success after vasectomy reversal mainly depends on the time since vasectomy. Additional biomarkers are needed to predict postoperative pregnancy outcomes.

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Patient summary: In our study, nearly 87% of men were fertile again after surgery to reverse a vasectomy, and about half of the couples were then able to get pregnant. The key factor for success was the time since vasectomy, with better results for shorter times. More research is needed to find reliable ways to predict if a couple will get pregnant after this surgery.

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1. Introduction

Vasectomy is a common procedure among men seeking permanent infertility, often after completion of their planned family. In the USA, approximately half a million men undergo vasectomy annually [1]. Some 6% of these men later choose to pursue conception after vasectomy [1]. Reasons for reversal may include a new female partner, child loss, and, in rare cases, postvasectomy pain syndrome [2]. Microsurgery is the standard of care for treatment of vasal obstruction in azoospermic men with primary or secondary infertility [3]. Typically, a two-layered vasovasostomy (VV) is performed [3]. Depending on the presence of sperm in the seminal fluid from the testicular stump, anastomosis can be performed in either the straight or the convoluted portion of the vas deferens. If no sperm are found in the testicular stump of the vas deferens, anastomosis must be performed at the epididymis, resulting in a vasoepididymostomy (VE).

However, not all microsurgical VV or VE procedures result in subsequent pregnancy. Rates of vas patency and postoperative pregnancy following vasectomy reversal vary widely in the literature. Reports of vas patency range between 71% and 97%, while postoperative fertility rates are lower, ranging between 26% and 67% [4]. To date, the literature has identified few predictive factors for patency, and some of these remain controversial [5]. No data have been published on VV success rates stratified by the location of the anastomosis. It is presumed that anastomosis in the convoluted portion of the vas deferens, where the diameter varies, may be less successful than suturing of two straight portions of equal diameter. Our objective was to evaluate these and other predictive factors, such as intraoperative seminal fluid quality, and to assess their significance via an extensive follow-up study involving a large group of patients who underwent microsurgery for obstruction of the upper seminal tract over a period of 33 yr.

2. Patients and methods

2.1. Patient population

For this analysis, we included 336 consecutive men with azoospermia due to vasal obstruction (mostly postvasectomy) who underwent two-layer VV or VE performed by a single surgeon between 1989 and December 2022. Intraoperatively, seminal fluid was harvested from the testicular stump. If sperm were absent, no anastomosis was performed. For the 323 cases with sperm present, intraoperative and patient-related parameters were documented and correlated with the pregnancy outcome as the primary endpoint. To gather information on pregnancy rates, patients were contacted by phone. However, follow-up information regarding pregnancy was unavailable for 67/323 patients (20.7%). Patients who underwent VV or VE in the past 2 yr of the study period were excluded from the primary endpoint analysis owing to the short follow-up (11/323 patients, 3.4%). Postoperative patency of the seminal tract was a secondary outcome and was assessed via spermiogram analysis. Some patients underwent multiple spermiograms, so the results were categorised according to the postoperative interval (2, 4, 6, 9, and >12 mo after surgery, and overall patency). Postoperative spermiogram information was not available for 64/323 patients (19.8%).

2.2. Surgical technique

The surgical technique used in this series was a two-layer bilateral VV performed under general anesthesia. From a scrotal bilateral incision, both stumps of the vas were prepared and freshly cut. For cases with sperm in the fluid from the testicular stump and free run-off through the proximal stump, a two-layer anastomosis was performed with four intraluminal 10-0 Prolene sutures and six to eight 9-0 Prolene sutures in the muscular layer to achieve a watertight anastomosis [3]. For VE, three to four intraluminal 10-0 Prolene sutures were used and the muscular layer was sutured to the tunica epididymis accordingly. Tension-free suturing was used for all anastomoses.

2.3. Assessed parameters

The following parameters related to the primary and secondary endpoints were assessed:

Patient age: the age of the patient in years at the time of VV or VE surgery.
Obstruction time: the time in months between vasectomy and VV or VE surgery.
Anastomosis location: for VV, the vas deferens can be sutured between two straight portions or between a straight portion and a convoluted portion. If VV was not feasible, VE was performed. Anastomosis location was documented for the left and right sides, with suturing between two straight portions considered favourable, and suturing between a straight portion and a convoluted portion or VE considered unfavourable.
Intraoperative fluid quality: the appearance of testicular fluid from the testicular stump was observed and documented as clear or opaque.

Time from surgery to pregnancy: the time between VV or VE surgery and pregnancy was recorded.
Partner age: the age of the patient's female partner in years at the time of VV or VE surgery.
Previous proven fertility: Whether the female partner had a previous pregnancy or not.

Different descriptions of testicular fluid quality are available in the literature [4], typically described as clear, opalescent, opaque, thick, or creamy. For this study, we categorised fluid as "clear" (favourable) or "opaque" (unfavourable). Microscopic analysis of testicular fluid was performed bilaterally; however, we did not use the modified Silber score [4] to describe microscopic sperm morphology and motility in testicular fluid. Instead, anastomosis was performed in all cases for which at least sperm heads were present (Silber score 1–4). In cases with absent sperm (Silber score 5), no anastomosis was performed.

2.4. Statistical analysis

Statistical analysis was conducted using R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) and RStudio, with reproducibility ensured via R markdown. Descriptive statistics were computed for the cohort to summarise baseline characteristics. Univariate logistic regression models were fitted to predict intervention outcomes according to variables that included patient age, partner age, intraoperative fluid quality, anastomosis location, obstruction time, arterial hypertension, and smoking. A multivariable logistic regression model was then fitted using the same variables. Missing values were assessed for a multivariable model via calculations for the number of patients in relation to complete cases. A multivariable logistic regression model for prediction of successful pregnancy was chosen from all the variables of interest because it offers the highest degree of interpretability. A Kaplan-Meier plot was generated for follow-up time, with censoring for cases with no successful pregnancy. The mean value of 8 yr was used as the cutoff for categorisation of the obstruction time. The term "significant" should be understood in an exploratory sense, as no correction for multiple comparisons was applied.

3. Results

3.1. Patient characteristics

The median age at surgery was 42 (range 27–70) yr for the male patients and 33 (range 19–46) yr for their female partners. The median seminal tract obstruction time was 96 mo (range 10–360). Among the 336 men, anastomosis repair was not performed in 13 (3.9%) because of bilateral absence of sperm in the testicular fluid. The overall patency rate after surgery, including both unilateral and bilateral VV and VE, was 236/272 (86.8%). Secondary obstruction occurred in 14/272 men (5.1%), typically within 6 mo after surgery.

A total of 127/258 couples (49.2%) achieved a pregnancy, at a median time of 16 mo (range 1–109) after surgery. The likelihood of achieving pregnancy decreased rapidly after 4 yr postoperatively (Fig. 1). Owing to the long observation period, we divided the success rate into three decades to evaluate potential bias due to learning effects. No increase in pregnancy rate was observed over the three decades of the study period (Supplementary Table 3).

3.2. Association of risk factors with patency and pregnancy rates

In our study, the most important variable for successful microsurgery to restore fertility was the obstruction time. The success rates for both VV and VE appeared to decrease almost linearly with increasing time since vasectomy (Fig. 2).

We analysed other potential risk factors that could impact a successful outcome. However, multivariable anal-

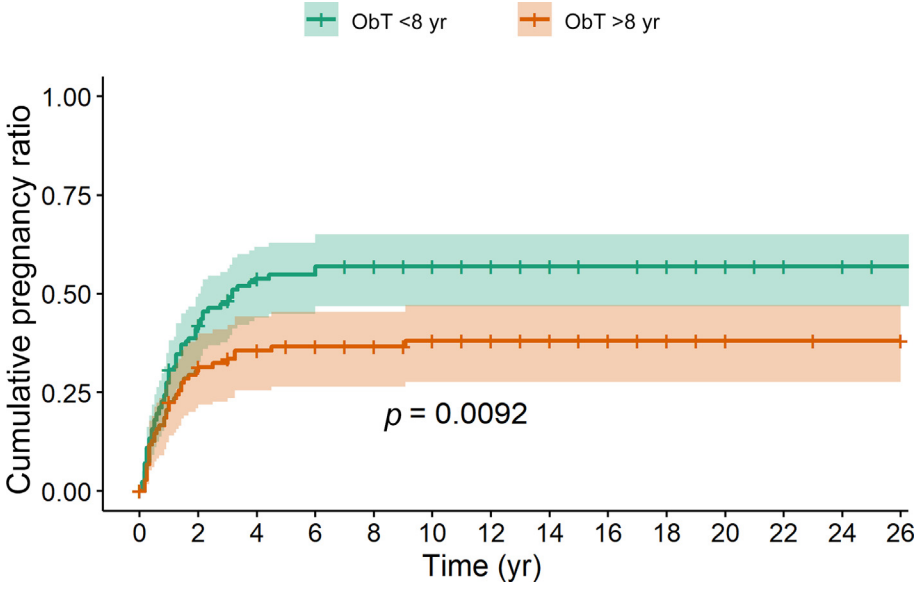

Fig. 1 – Cumulative pregnancy rate by time after vasectomy reversal. ObT = obstruction time.

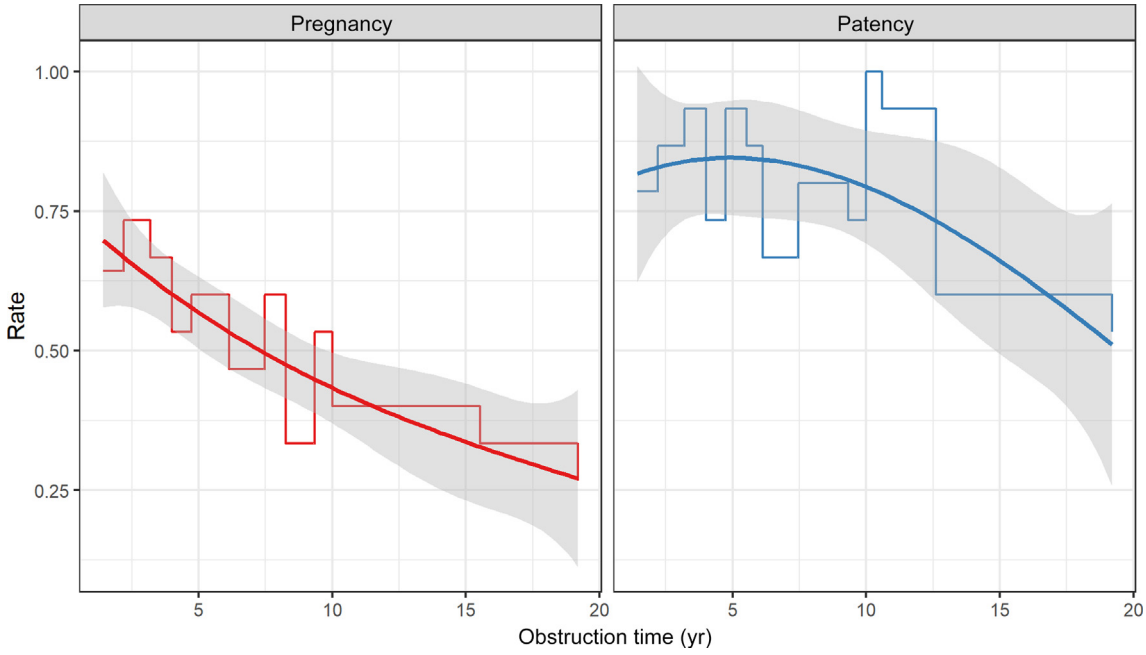

Fig. 2 – Distribution of pregnancy and patency rates according to obstruction time. Rates were calculated for windows that each included 15 data points.

ysis did not identify any significant risk factors apart from the obstruction time (Supplementary Tables 1 and 2).

The age of the female partner was only statistically significant for the primary endpoint in the univariate model, with a trend favouring age <40 yr (Fig. 3; $p = 0.047$).

Regarding the anastomosis location, there was no difference in outcome between straight and convoluted portions of the vas deferens. In addition, we did not observe a lower success rate for VE than for VV. The equal success rate of VV and VE could not have been influenced by a contralateral VV, as no patient received a VE on one side and a VV on the other. Success rates for different anastomosis locations are listed in Table 1.

No parameters for testicular fluid quality were significantly associated with favourable patency or pregnancy rates (Table 2).

Table 1 – Pregnancy and patency rates according to anastomosis location

Location	Successful surgery, *n*/*N* (%)	
	Pregnancy	Patency
Bilateral favourable	54/113 (47)	90/107 (84)
Unilateral favourable	35/67 (52)	52/62 (83)
Bilateral unfavourable	23/52 (44)	37/51 (72)
Vasoepididymostomy	9/13 (69)	11/13 (84)

4. Discussion

We collected retrospective data over a period of 33 yr for 336 men with vasal obstruction who underwent microsurgery performed by a single surgeon to restore fertility. We analysed several parameters in relation to postoperative pregnancy and vasal patency rates. The patency and preg-

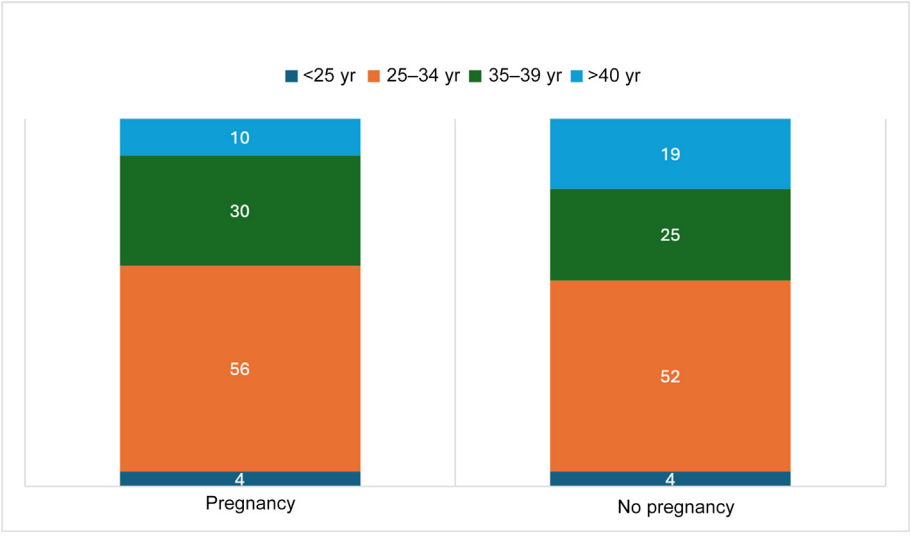

Fig. 3 – Age distribution among female partners in relation to pregnancy outcome.

Table 2 – Pregnancy and patency rates according to intraoperative gross fluid quality

Fluid quality	Successful surgery, *n*/*N* (%)	
	Pregnancy	Patency
Bilateral favourable	26/51 (51)	43/49 (87)
Unilateral favourable	23/46 (50)	38/43 (88)
Bilateral unfavourable	56/116 (48)	86/106 (81)
p value	0.94	0.41

nancy rates in our series are consistent with rates reported over a 10-yr period as reviewed by Namekawa et al [5], for which the mean patency rate was 87% (range 80–98%) and the mean pregnancy rate was 49% (range 22–68%). Chen et al [6] investigated patency and pregnancy rates following VV in patients with a history of childhood inguinal herniorrhaphy and seminal tract obstruction. The authors reported much lower patency (57%) and pregnancy (25%) rates in comparison to our findings, which can be attributed to differences in the patient populations and their preconditions. Studies indicate that the inferior outcomes after herniorrhaphy are because of more challenging surgical conditions and diminished spermatogenesis in these patients [6,7]. Li et al [8] explored a microsurgical two-layer anastomosis technique in patients with failed vasectomy reversal, and reported higher patency (94%) and pregnancy (69%) rates in comparison to our results. These superior outcomes are probably because of the study focus on revision surgeries in a small patient cohort (n = 34).

The most significant predictor for successful treatment was the obstruction time ($p < 0.01$). Similar to the findings by Bolduc et al. [9], we observed an almost linear decrease in both patency and pregnancy rates with increasing obstruction time (Fig. 2). After an obstruction time of 8 yr, the patency rate exhibited a linear decline. This information can guide urologists in clinical decision-making and patient counselling. However, owing to the linear nature of the curve, there is no apparent cutoff time beyond which microsurgery to restore fertility should not be attempted. In addition, not all VV studies support a significant decrease in vasal patency rate with longer obstruction times. A systematic review by Elzanaty and Dohle [10] suggested that the duration of vasal obstruction may not be a significant factor for vasal patency after surgery.

Most studies support strong correlation between the female partner's age and the pregnancy rate [5]. This correlation was observed in our cohort, particularly on univariate analysis, in which the decrease in pregnancy rate reached statistical significance for partner ages ≥40 yr (Supplementary Table 2).

Patient age was another significant predictor for successful pregnancy on univariate analysis (p = 0.02). The mean age was 42.4 yr in the pregnancy-positive group versus 44.5 yr in the pregnancy-negative group, consistent with age-related decline in pregnancy rates reported in the literature [11–13]. This suggests that both the age of the woman and the age of the man can be predictive of successful pregnancy. With a small age gap of only 2.1 yr between the pregnancy-positive and pregnancy-negative groups, our study supports the notion that VV or VE can be offered to patients of all ages, although success rates may be slightly lower for older patients.

Although limited data are available, some studies suggest higher patency and pregnancy rates if the fluid harvested from the testicular stump is clear in appearance. A retrospective single-surgeon analysis of 351 men who underwent microsurgery to restore fertility revealed such a trend, but it did not reach statistical significance [4]. Another single-surgeon series of 1267 patients suggested that gross fluid quality has no predictive value at all [14]. Our aim was to contribute more data on this matter, but our results did not show a significant correlation between fluid quality and successful vasectomy reversal. This conclusion may be limited by the subjective nature of the analysis of fluid quality. The absence of a validated scale for the gross quality of seminal fluid necessitated the description we used for our analysis, in accordance with other studies [4,14].

To date, no studies on VV success rates stratified by the anastomosis location have been published. Owing to the varying diameter in the convoluted portion of the vas deferens, one might assume that anastomosis in this location would be less successful than suturing between two straight portions of equal diameter. However, our results do not support this hypothesis.

A major limitation of our study is its retrospective nature, including the lack of a predefined follow-up protocol. To prevent bias, patient tracking and data recording were carried out by the same individual. This measure ensures consistent and standardised data collection, minimising potential biases arising from varying data collection practices and standards and enhancing the data quality and the reliability of the results. Our single-surgeon consecutive series had a reasonable sample size, which minimises bias, and revealed success rates similar to those in the literature [5]. We also took into consideration the learning curve associated with the procedure by splitting the data set into three decades. No increase in the success rate was observed over the decades, suggesting that a significant learning effect did not influence our results (Supplementary Table 3). This can be attributed to the high experience level of the surgeon, who completed the learning curve for the procedure before the start of the study. Another limitation is the sparse evaluation of female factors, which may affect pregnancy rates independent of other variables.

Regarding clinical implications, our findings suggest the onset of a linear decline in the patency rate at an obstruction time of >8 yr, accompanied by a significantly lower pregnancy rate for women older than 40 yr. Since VV is not covered by health insurance in Switzerland, data on the probability of success are crucial for decision-making, as the willingness to pay is influenced by the anticipated success rate. This highlights the importance of identifying additional predictive factors. A possible approach to achieve this would be a controlled analysis of previous studies, which would expand the patient population and could aid in the development of a more robust predictive model.

5. Conclusions

In our single-surgeon series the patency rate was 86.8% (236/272) and the pregnancy rate was 49.2% (127/258), which are consistent with rates reported in the literature [5], underscoring the reliability of our data set.

Pregnancy after vasectomy reversal primarily depends on the obstruction duration, with a linear decrease in the success rate with increasing obstruction duration. Female partner age appears to be a risk factor, particularly for individuals older than 39 yr. Other intraoperatively determined parameters for seminal fluid and patient- or couple-specific variables were not significant predictors of success in our analyses. Additional reliable prognostic factors are needed for effective prediction of outcomes of microsurgery for vasectomy reversal.

Author contributions: Jan Blaser had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: A. Sieber, M.A. Sieber, Seiler.
Acquisition of data: A. Sieber, Blaser, M.A. Sieber.
Analysis and interpretation of data: M.A. Sieber, Blaser, A. Sieber, Seiler.
Drafting of the manuscript: M.A. Sieber, Blaser.
Critical revision of the manuscript for important intellectual content: Seiler, Abt, Blarer, A. Sieber.
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Administrative, technical, or material support: M.A. Sieber, Blaser, A. Sieber.
Supervision: Seiler, A. Sieber.
Other: None.

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***Data sharing statement*:** Data sets generated and/or analysed for the study are available from the corresponding author on reasonable request. Please note that protected, patient-specific data are excluded from this availability.

***Ethics considerations*:** Ethics clearance was not required for this article as it involves a retrospective analysis of previously performed surgeries and their outcomes and patients cannot be identified from any of the data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.08.010.

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