Nomograms to Predict Patency After Microsurgical Vasectomy Reversal

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Purpose: After undergoing vasectomy up to 6% of men will elect to undergo vasectomy reversal. For these men paternity can be achieved with vasectomy reversal or surgical sperm retrieval coupled with assisted reproduction. Nevertheless, it remains difficult for surgeons to accurately counsel men on the chance of patency after vasectomy reversal.

Materials and Methods: A retrospective review was conducted of 548 patients who underwent microsurgical vasectomy reversal. Surgery was considered successful if sperm concentration was 100,000 or more sperm per ml, total count was 100,000 or more sperm per ejaculate, motile sperm were present and there was no evidence of subsequent failure. A multivariate logistic regression model was constructed to calculate the probability of having a successful vasectomy reversal and nomograms for patency were generated from this model.

Results: A total of 548 patients met the inclusion criteria for this study. Mean followup was 1.8 ± 0.10 years. Mean patient age was 43.4 ± 0.3 years and mean duration of obstruction was 10.4 ± 0.2 years. Two nomograms to predict patency were generated, one for preoperative counseling and a second for postoperative counseling. The factors with the largest effect on patency were average testicular volume and obstruction duration. The factor with the least effect was the presence of sperm granuloma. The concordance index for the preoperative and the postoperative nomograms was 0.64 and 0.66, respectively.

Conclusions: To our knowledge this represents the first use of nomograms to predict the likelihood of patency after microsurgical vasectomy reversal. These nomograms may prove useful to guide further treatment decisions.

Key Words: vasovasostomy; vasectomy; infertility, male

Abbreviations and Acronyms

ART = assisted reproductive technology

IVF = in vitro fertilization

VE = vasoepididymostomy

VV = vasovasostomy

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INFERTILITY affects 15% of couples, with up to 60% of cases having an abnormal male factor.[1] Vasectomy is the most common cause of obstructive azoospermia and it is estimated that more than 500,000 men undergo vasectomy in the United States each year.[2] Up to 6% of these men will later elect to have more children and will undergo vasectomy reversal.[3] Vasectomy reversal outcomes vary considerably with reported patency ranging from 71% to 99% for VV and from 43% to 80% for VE.[4–7] It is well established that the type of reconstruction, duration of obstruction, presence of sperm granuloma, prior fertility, prior inguinal surgery, prior vasectomy reversal, type of fluid found in the vas deferens and presence of sperm during reconstruction can impact the success of the procedure.[4,8]

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Still it remains difficult for surgeons to accurately counsel men on the chance of achieving long-term patency after vasectomy reversal. We are not aware of any efforts to create nomograms to predict patency after vasectomy reversal. To address this issue we incorporated significant preoperative and intraoperative factors into nomograms to predict patency after microsurgical vasectomy reversal.

METHODS AND MATERIALS

Patients and Evaluation

After institutional review board approval was obtained we reviewed the records of 792 men who underwent microsurgical VV or microsurgical VE for the treatment of infertility by a single reproductive surgeon (MG). Our inclusion criteria were previous vasectomy, bilateral reconstruction and 1 or more evaluable postoperative semen analysis. Men in whom a crossed reconstruction was performed were excluded from this study, as were those who reported pregnancy but never had a postoperative semen analysis. For patients with multiple reproductive surgeries at our institution only the results of the first surgery were considered for analysis. A total of 548 patients (69.2%) met the inclusion criteria and were considered in this analysis.

Demographics as well as operative records, clinical charts, laboratory tests and semen analyses were reviewed. A full history and physical examination was performed by the primary surgeon (MG) in all cases. Physical examination included a full general and urological examination with a particular emphasis on testicular volume, the presence of varicocele and the presence of sperm granuloma. All testicular volumes were determined on physical examination by the use of a Prader orchidometer.

Surgical Procedures

Our surgical techniques of microsurgical VV and VE have been previously described.[5,9] The procedure involves bilateral high scrotal incisions over the testis. After dissecting out the vasectomy site, the testicular end is transected until a patent lumen is identified, and vasal fluid is placed on a slide and inspected at 400× magnification with a bench microscope. If there is evidence of intact spermatozoa, abundant sperm heads, sperm with short tails or copious crystal clear fluid is obtained, a vasovasostomy is performed. The decision to proceed with a VE instead of a VV is made if there is thick, toothpaste-like material devoid of sperm in vasal fluid, or scant or absent vasal fluid with no sperm or sperm heads seen on barbotage.

Outcomes

Patency was defined as a sperm concentration of 100,000 or more sperm per ml, total count 100,000 or more sperm per ejaculate, motile sperm present, 1 ml or more seminal fluid per ejaculate and no evidence of subsequent azoospermia at last known followup. For this study failure to achieve patency was defined as the need for repeat microsurgical reconstruction after a reversal attempt at our institution, the need for further surgical sperm retrieval, 2 consecutive semen analyses showing azoospermia after having achieved success by the previously mentioned criteria, or never achieving 100,000 or more sperm per ml with motile sperm in the ejaculate after vasectomy reversal.

Natural birth rate and overall pregnancy rate (natural birth rate plus assisted reproduction birth rate) were calculated. For calculation of the natural pregnancy rate only patients with complete pregnancy and ART use information were included (ie when a patient had pregnancy information but no information regarding use of ART the patient was excluded from the calculation of natural pregnancy rate). Assisted reproduction was defined as any use of in vitro fertilization (with or without intracytoplasmic sperm injection) and/or intrauterine insemination.

Statistical Analysis

A multivariate logistic regression model was constructed to calculate the probability of a successful vasectomy reversal. This logistic regression model was the basis for the nomograms. Several factors were included in the preoperative nomogram such as duration of obstruction (years), presence of sperm granuloma, history of previous vasectomy reversal at another institution, type of reversal performed (bilateral vasovasostomy, unilateral vasovasostomy with unilateral vasoepididymostomy, or bilateral vasoepididymostomy), average testis volume (cc) and age at surgery (years). The postoperative nomogram included all the factors in the preoperative nomogram, and also included the nature of testicular and vasal fluid (no fluid or scant fluid; thick, creamy toothpaste-like fluid; cloudy, thin, copious fluid; or clear, thin, copious fluid), and the presence of microscopic sperm in the vasal fluid. All decisions regarding the coding of the nomogram variables were made before modeling since changing these variables afterward can hinder the predictive ability of the model.[10]

Internal nomogram validation was performed by bootstrapping with 1,000 re-samples. This method produced a relatively unbiased measure of the ability of the nomogram to discriminate among patients as quantified by the concordance index. The concordance index is similar to measuring the area under the receiver operating characteristic curve,[11] and represents the probability that the model will correctly assign a higher probability to a patient with a successful outcome compared to one with an unsuccessful outcome. A calibration curve was generated to estimate the margin of error of the model. Statistical analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria) and JMP®. Pearson chi-square tests were used to compare categorical variables. The reported values are means ± standard error and $p \leq 0.05$ was considered significant.

RESULTS

Baseline Characteristics

A total of 548 patients met the inclusion criteria for this study. Mean followup was 1.8 ± 0.10 years. Mean patient age was 43.4 ± 0.3 years and mean age of the female partner was 33.6 ± 0.2 years. Mean duration of obstruction was 10.4 ± 0.2 years. The reconstruction was a repeat procedure (with the first being performed elsewhere) in 17.7% of men, and 86.3% of these men had previously proven paternity. Physical examination findings are summarized in table 1.

Table 1. *Baseline characteristics from findings on physical examination*

	No. (%)
Lt varicocele grade (526):	
1–3	132 (25.1)
1	47 (8.9)
2	53 (10.1)
3	32 (6.1)
Rt varicocele grade (517):	
1–3	58 (11.2)
1	25 (4.8)
2	24 (4.6)
3	9 (1.7)
Sperm granuloma present (541):	
On either side	222 (41.0)
Lt	136 (25.1)
Rt	154 (28.4)
Av ml testis vol (543):	
Less than 15.0	9 (1.7)
15.0–19.9	74 (13.6)
20.0–24.9	209 (38.5)
25.0–29.9	194 (35.7)
30 or Greater	57 (10.5)

Success Rates

Intraoperative findings and type of reconstruction performed are summarized in table 2. Of the 548 patients available for analysis 411 (75.0%) had durable success while 137 (25.0%) did not achieve patency at last known followup. When stratified by procedure performed the patency rates were 80% (308 of 385) for bilateral VV, 69.5% (66 of 95) for unilateral VV with unilateral VE and 54.4% (37 of 68) for bilateral VE. Of the 137 cases of failure 53 (9.7% of the overall group) had transient return of sperm with more than 100,000 sperm per ml and the presence of motile sperm but azoospermia developed at a median followup of 2.3 years. Of these patients 60% required a second surgical procedure at a median followup of 1.8 years. However, 84 (15.3%) patients never reached the threshold of 100,000 or more sperm per ml and the presence of motile sperm with a median followup of 8.4 months.

Pregnancy Rates

Pregnancy data were available in 240 patients with IVF use information available in 179 (74.6%). In all couples the overall pregnancy rate was 85.8% (206 of 240). The natural pregnancy rate was 52.0% (93 of 179). Only 179 patients were included in the calculation of the natural pregnancy rate since 61 patients lacked information on whether ART was used. Of the 61 pregnancies in our series associated with ART use 15 were achieved with intrauterine insemination while 46 couples achieved pregnancy with IVF or IVF/intracytoplasmic sperm injection.

Nomograms

Two nomograms were developed to predict the likelihood of durable return of sperm to the ejaculate, one to be used for counseling preoperatively and one to be used postoperatively (fig. 1). The preoperative nomogram was constructed using the clinical predictors of duration of obstruction, presence of sperm granuloma, history of previously attempted vasectomy reversal, type of reconstruction performed, testicular volume and age at surgery. The postoperative nomogram included all the factors from the preoperative model but also included gross characteristics of vasal fluid and the presence of sperm on microscopy at the time of reconstruction. The factors with the greatest effect on patency were average testicular volume and duration of obstruction. The factor with the least effect was the presence of sperm granuloma.

To derive an estimate of the expected performance of the nomogram for new patients we performed bootstrapping, a statistical method in which sampling, nomogram building, and nomogram evaluation are repeated many times.[12] This approach simulated the presentation of new patients for assessment via nomogram. Using bootstrapping, the concordance index of the nomogram was estimated to be 0.64 for the preoperative nomogram and 0.66 for the postoperative nomogram. The nomogram calibrations are shown in figure 2.

DISCUSSION

We constructed a pair of nomograms to predict patency after vasectomy reversal. There are several advantages to using nomograms rather than simple cutoffs for a number of different variables in predicting surgical outcomes. Among the advantages of using nomograms is the ability to integrate multiple variables as well as provide a more specific, individualized prediction for patient outcome. With these data in hand, patients and surgeons can make more informed choices about whether to undergo vasectomy reversal (using the preoperative nomogram) as well as how to proceed after vasectomy reversal (using the postoperative model). While not widespread, the use of nomograms in male infertility is not new. Parekattil et al developed and externally validated a

Table 2. *Surgical parameters with intraoperative findings and subsequent reconstruction*

	No. (%)
Gross appearance of vasal fluid (237):	
Thick, creamy or toothpaste-like	18 (7.5)
Scant or no fluid	64 (27.0)
Clear, thin, copious fluid	59 (24.9)
Cloudy, thin, copious fluid	96 (40.5)
Whole sperm (motile or nonmotile) seen at 400× (426)	360 (84.5)
Type of reconstruction performed (548):	
Bilat VV	385 (70.3)
Unilat VV/unilat VE	95 (17.3)
Bilat VE	68 (12.4)

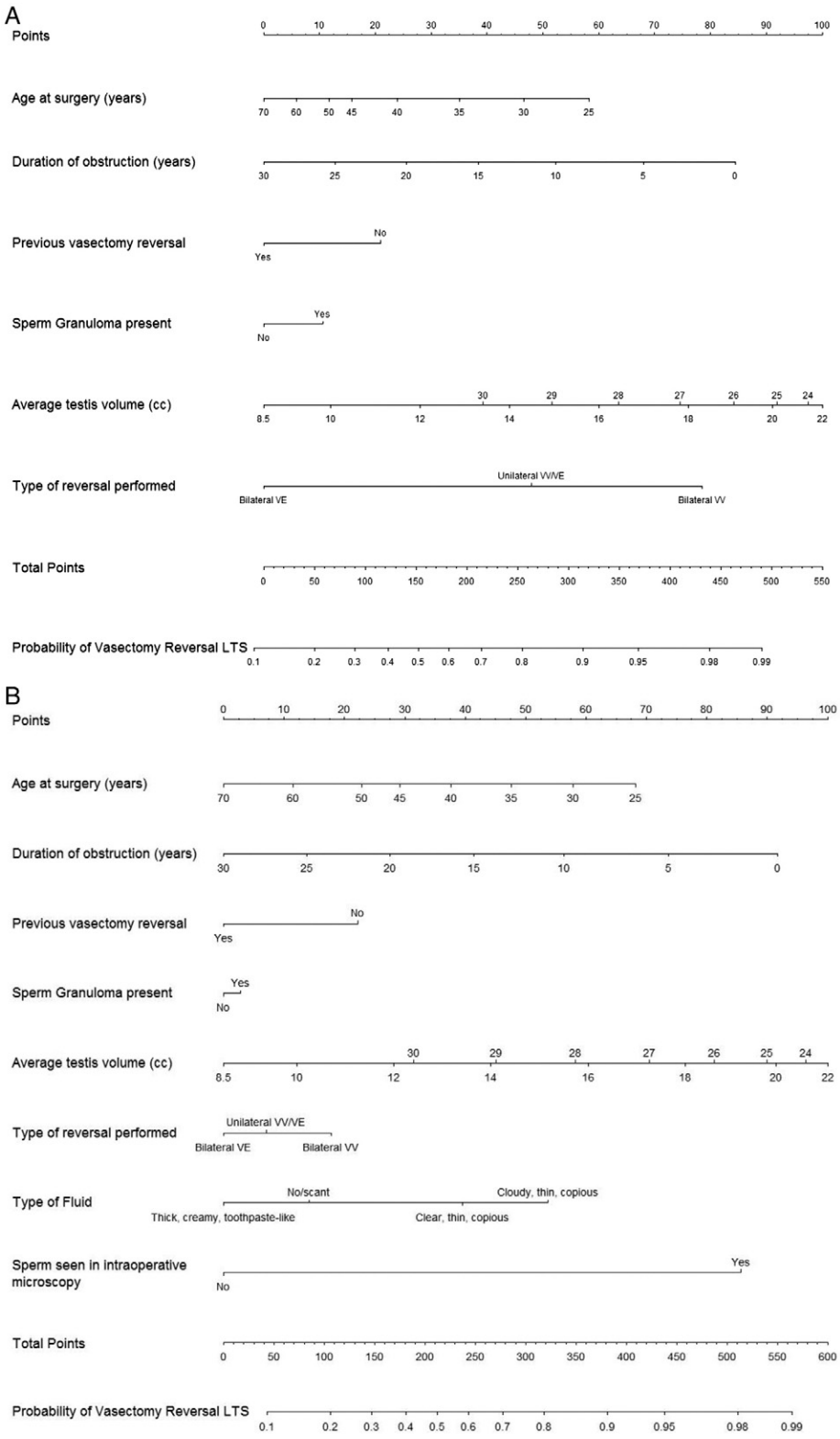

Figure 1. Preoperative (*A*) and postoperative (*B*) nomograms for predicting durable patency after vasectomy reversal. To use nomograms plot patient value of given parameter on appropriate scale and draw vertical line up to points line at top to assign associated point score. Repeat process for each parameter, then sum values to obtain total points score. Plot total points score on total points line and draw vertical line down to bottom line. Value represents probability of durable vasectomy reversal success. *LTS*, long-term success.

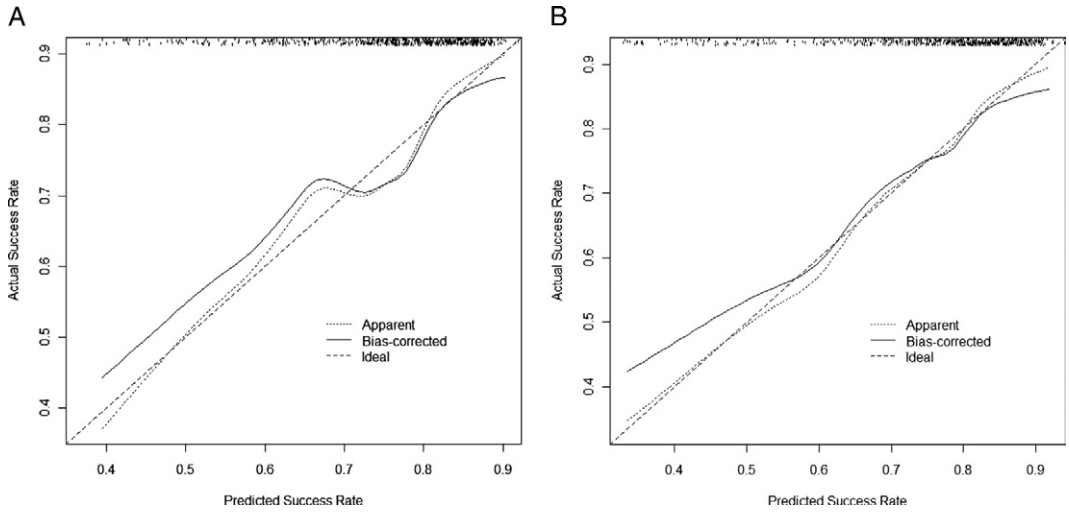

Figure 2. Nomogram calibration by bootstrapping for preoperative (*A*) and postoperative (*B*) model. Line at 45-degree angle indicates ideal nomogram reference line. Apparent line is calculated directly from data set. Bias corrected line is bootstrap corrected line which uses bootstrap sampling to validate model.

model to predict the need for VE rather than VV at the time of vasectomy reversal.[13,14] While a later study by Kavoussi and Bird questioned the validity of the VE predicting model,[15] the model of Parekattil et al represented the first use of nomograms in male infertility. However, our study represents the first attempt at quantification of individual patency outcomes after vasectomy reversal using nomograms.

Better prognostication of patency after vasectomy reversal has several advantages in clinical decision making. The preoperative nomogram may better inform men about their chance of patency when deciding between vasectomy reversal and sperm retrieval coupled with IVF. With simple information easily obtained on history and physical examination, our nomogram can determine a range of patency rates by using the nomogram twice, once assuming a VV will be performed and once assuming a VE will be performed. In the postoperative setting our nomogram may better guide the decision to cryopreserve sperm after the return of sperm to the ejaculate. For those with a high likelihood of long-term patency, a longer attempt at natural pregnancy may be feasible if female factors do not preclude the earlier use of ART. Conversely men with a lower chance of durable success may be advised to bank sperm sooner or proceed to ART earlier. Of course, the final decision to proceed to ART is a complex one involving the presence of female factors, cost, couple age and number of children desired. Yet by providing the patient with a more specific outcome, we believe our nomograms may help the patient and the physician make rational, realistic treatment decisions.

The data in this nomogram regarding duration of obstruction, presence of sperm on intraoperative microscopy, type of fluid seen, and type of reversal performed are consistent with previously published data.[4,8,16,17] Surprisingly while sperm granuloma had traditionally been thought to greatly affect patency rates,[8] in our model it had little effect on long-term patency. It is also notable that testicular volume had a significant effect on long-term patency, with those men with an average testis size of 20 to 25 cm^3 having the highest patency rates. For men with significantly smaller testes, lower volume was probably a marker of lower sperm production which may decrease fluid flow across the anastomosis. Why testes with volumes larger than 20 to 25 cm^3 have lower patency remains unknown, although it is possible that these larger testes are more likely to have larger volumes of hydrocele fluid, leading to suboptimal sperm production. In fact, we have previously shown using thermodynamic modeling that even hydroceles as small as 4.2 ml can substantially alter testicular cooling.[18]

Determining a definition of success in vasectomy reversal is also a challenge. Even if 2 studies are similar in other respects, the task of comparing outcomes becomes difficult (if not impossible) when different end points are used. Definitions in the literature have ranged from any presence of sperm in the ejaculate, to the presence of any motile sperm in the ejaculate and finally to cutoff sperm concentrations (as high as 15 million).[4,19–21] For this study we used a rather strict definition of patency, including only those patients who achieved a sperm concentration of 100,000 or more sperm per ml with motile sperm present and without evidence of late failure (secondary azoospermia) or the need for any further surgical procedure. We believed that these criteria were sufficient to prove patency and give some chance of spontaneous preg-

nancy (our lowest sperm concentration that resulted in a natural pregnancy was 200,000 spermatozoa per ml). It is clear that standardizing reporting measures would greatly advance this field.

A possible criticism of this study is that the reported patency rates were lower than we previously reported.[5–7] However, it should be noted that the data used to generate this nomogram represent almost 30 years of experience at a tertiary referral center. Techniques have changed and improved over time.[5,7] In addition, men who reported pregnancy but never had a postoperative semen analysis were excluded from this study, further lowering our patency rate. Finally, our patency rate was lower because we took into account so-called late failures. What causes late obstruction is still poorly understood, but is most likely multifactorial and related to the quality of the anastomosis, wound healing, sperm granuloma or suture granuloma. Rates of late failure varied from 3% to 21%, with most studies having a limited followup of less than 1 year.[17,19,22,23] Our late failure rate in this cohort was 9.7% with a mean followup of 1.8 years. If we were to consider patients with transient patency as successful, the patency rates would be bilateral VV 89.6%, unilateral VV with unilateral VE 77.9% and bilateral VE 66.2%. Nevertheless, we believe our study uses the best definition of successful surgery, which is patency with motile sperm without evidence of late failure.

CONCLUSIONS

We generated nomograms to predict the chance of patency after microsurgical vasectomy reversal. These nomograms allow for the integration of multiple variables and are helpful in guiding treatment decisions. The preoperative nomogram may give a better estimate of the likelihood of patency after vasectomy reversal and, thus, help in the initial decision between vasectomy reversal and surgical sperm retrieval followed by assisted reproduction. By giving more accurate estimates of patency after vasectomy reversal, the postoperative nomogram may help guide the decision to bank ejaculated sperm sooner or to proceed to assisted reproductive technologies sooner. To our knowledge this is the first attempt at such nomograms.

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