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MODEL TO PREDICT IF A VASOEPIDIDYMOSTOMY WILL BE REQUIRED FOR VASECTOMY REVERSAL

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ABSTRACT

Purpose: We devised a model to predict, preoperatively, the need for a vasoepididymostomy (VE) when performing a vasectomy reversal. Urologists could use it to identify those patients who need a referral to an experienced VE surgeon.

Materials and Methods: We performed a retrospective review of 483 patients who underwent vasectomy reversal by a single surgeon (AJT) including 393 vasovasostomies and 90 vasoepididymostomies. Selection was based on chart availability. Established criteria were used in deciding the type of reversal (eg gross appearance and microscopic examination of vasal fluid). Type of reversal, patient age and time since vasectomy were recorded. Univariate analysis revealed that patient age (p <0.001) and time since vasectomy (p <0.001) were significant predictors of reversal type. On multivariate logistic regression analysis, time since vasectomy (p <0.001) was the only significant independent predictor. We designed a linear regression algorithm based on time since vasectomy and patient age to predict if a VE would be performed. The model was designed using 433 patients and then tested on a separate randomly selected 50 patient group. The model was designed to be 100% sensitive in detecting patients requiring VE.

Results: In the test group the model was 100% sensitive in predicting VE with a specificity of 58.8%. The area under the ROC curves for the design and test groups was 0.8. Palm (PalmSource Inc., Sunnyvale, California) and Windows (Microsoft Corporation, Redmond, Washington) versions are available as free shareware from www.uroengineering.com.

Conclusions: The model is 100% sensitivity in detecting those patients who may require a VE during vasectomy reversal (specificity of 58.8%). It may allow urologists to preoperatively identify these patients.

KEY WORDS: vasovasostomy, prognosis; models, statistical

About 500,000 vasectomies are performed in the United States every year. Up to 6% of men who undergo a vasectomy will request a reversal. The majority of these reversals are achieved by vasovasostomy (VV). Some of these patients will require a vasoepididymostomy (VE) at the time of vasectomy reversal. VE is a more technically challenging procedure than vasovasostomy and this has driven the development of several improvements in surgical technique.^{2–8}

VE is generally performed by a urologist with experience in advanced microsurgical techniques. Certain urologists who perform vasectomy reversals may not be as experienced in performing a VE. Some urologists use certain general screening guidelines to preoperatively identify patients that may need a referral to an experienced VE surgeon. Previous studies^{9–12} have shown that as the obstructive interval (number of years from vasectomy) increases, the likelihood of needing a VE (1 side or both) increases. Fuchs and Burt¹³ have shown that in men who had a vasectomy more than 15 years ago, approximately 61% of these men required a VE at the time of reversal. Silber and Fuchs and Burt have previously suggested that there may be an absolute duration since vasectomy cutoff (such as 15 years) that could identify patients

Our goal was to develop a highly sensitive model that could predict, preoperatively, the need for a VE (on 1 or both sides), when performing a vasectomy reversal. Urologists could use this program to identify those patients that may require a

that would need a VE. Using such an absolute cutoff may be

quite specific, but not very sensitive in detecting every pa-

this program to identify those patients that may require a referral to an experienced VE surgeon.

Various obstructive intervals were analyzed to assess if a straight forward cutoff would be of benefit to identify those who needed a VE. A model using multiple parameters was then created that offers greater sensitivity in detecting every patient that needs a VE. The model was optimized not only to

identify every patient that needs a VE, but also to be as

specific as possible to minimize redundant referrals to VE

capable microsurgeons. The model was designed to provide a user friendly, portable, reliable and easily accessible plat-

form for any urologist to access.

tient that may need a VE.

The criteria for decision of VE vs VV is made at the time of surgery after microscopic examination of the fluid from the proximal end of the vas. Thick, pasty or creamy fluid with no sperm or only rare sperm parts or no fluid and a long obstructive interval would suggest that there may be a more proximal epididymal obstruction and that a VE is required. Most VE microsurgeons adhere to these general guidelines, however, there is variation in practice patterns between fellowship trained microsurgeons and general urologists. The use of a model to preoperatively identify patients that may need a VE (and thus, consideration for referral to an experienced VE microsurgeon) may help standardize the delivery of care for these patients.

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Nothing to disclose.

Study received Institutional Review Board approval.

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Editor's Note: This article is the fourth of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1834 and 1835.

MATERIALS, PATIENTS AND METHODS

A retrospective study of 483 male patients who underwent vasectomy reversal by a single surgeon (AJT) was performed. The research protocol was approved by our Institutional Review Board. Selection was based on chart availability for cases performed between June 1982 and June 2002. 393 patients had undergone bilateral VVs and 90 had undergone a VE on at least 1 or both sides.

The surgeon used specific criteria in deciding the type of reversal based on the gross and microscopic appearance of the vasal fluid from the proximal vas (testicular side). A vasoepididymostomy was performed if the proximal vasal fluid had characteristics such as no fluid (after irrigation and milking of the vas), no sperm with thick pasty fluid or few sperm heads with thick pasty or creamy fluid.

The age of the patients in the study group ranged from 27 to 66 years (mean 41 years old). Racial background was not recorded. All patients had previously undergone a vasectomy and had decided to proceed with vasectomy reversal. Patient age, time since vasectomy and type of reversal were recorded during chart review. Type of reversal was categorized into the distinct types of bilateral VV, or VE on 1 side or both.

The 483 patients in the study were randomized into a 433 patient training group used for data analysis and prediction model design¹ and a 50 patient testing group that the model would be tested on to assess its prediction accuracy.² The 433 patient training group was further subdivided into patients who required bilateral VV (359) and those that required a VE on 1 side or both (74). Patient age and time since vasectomy parameters were analyzed for patients who required bilateral VV vs those that required a VE (on 1 side or both). Univariate analysis was performed to identify significant predictors of type of reversal required. A sufficient number of patients were present in the training group to identify statistically significant predictors. Multivariate logistic regression analysis of these predictors was then performed to identify the most significant predictor. The results of these analyses were used to generate a linear regression algorithm to predict the type of reversal required. 16,17

The model was designed with the criteria that it had to be 100% sensitive in detecting every patient that required a VE (no false negatives) and false positives would be tolerated to achieve the high sensitivity. Thus a urologist using this program could be assured that if the model predicted a bilateral VV preoperatively, then the likelihood of needing a VE (1 side or both) intraoperatively was zero.

This model was then tested on the 50 patient test group to assess its accuracy in detecting every patient that would require a VE. Testing was performed on this separate group to avoid any training bias in the model.

The 433 patient training group or design group was also analyzed for the likelihood of needing a VE based on the obstructive interval. A number of cutoffs were assessed to see if the model would perform any better than a straight forward obstructive interval cutoff.

RESULTS

Univariate analysis in the 433 patient group (table 1) identified that both time since vasectomy (p <0.001) and age of the patient (p <0.001) were significant predictors of the type of reversal that was performed. Logistic regression analysis was used for the univariate analysis.

Multiple logistic regression analysis was performed on the 2 patient characteristics (table 1) and time since vasectomy was found to be the independent significant predictor of the type of reversal. This analysis was used to identify the appropriate weighting for the 2 characteristics in the design of a linear regression prediction algorithm. Patient age and time since vasectomy were used to optimize the accuracy of the model.

Table 1. Univariate and multiple logistic regression analysis for type of reversal

	Time Since Vasectomy	Pt Age
Univariate:		
OR	1.28	1.11
95% CI	1.21-1.36	1.07 - 1.16
p Value*	< 0.001	< 0.001
Multivariate:		
OR	1.25	1.03
95% CI	1.17-1.34	0.98 - 1.98
p Value*	< 0.001	0.216

* Comparison of patients who had VE (1 side or both) vs those who had bilateral VV $\,$

The equation for the model is VE prediction score = (Age x 0.31) + (Obstructive interval x 0.94). If the prediction score is greater than 20, then a VE (1 or both sides) is predicted. If the score is less than 20, a bilateral VV is predicted. The model creates a linear obstructive interval cutoff based on the age of the patient. For example, a 29-year-old patient would be predicted to need a VE if his obstructive interval was greater than 11 years. A 39-year-old patient would be predicted to need a VE if his obstructive interval was greater than 8 years. The older the patient, the less the obstructive period needed to predict a VE. The model is only valid for men between the ages of 27 to 66 (the age range of our design group) and for obstructive intervals from 1 year to 27 years (the range of obstructive intervals in our design group).

The accuracy (sensitivity and specificity profile) of the model in the 433 patient training group and the 50 patient test group is presented in table 2. The model was 100% sensitive and 58.8% specific in detecting patients that required a VE in the 50 patient test group. The specificity was decent, but not 100% since it had to be compromised to obtain 100% sensitivity. The area under the ROC curve for the training group and the test group was 0.8.

Analysis of the 433 patient training group revealed a trend in the likelihood of needing a VE based on obstructive interval of less than 3 years—0%, 3 to 8 years—2.6%, 9 to 14 years—26.3% and greater than 14 years—43.2%. No VEs were performed in any patient with 4 or less years of obstruction. If we used a 5-year obstructive interval as a cutoff above which to recommend referral to a microsurgeon, the sensitivity of this test would be 100% in detecting every VE, but the specificity would only be 28.2%. Thus, twice as many men who only need bilateral VVs would be referred to a microsurgeon when compared with our model. Using any obstructive interval cutoff greater than 5 years would improve the specificity, but would then decrease the sensitivity to less than 100%, and thus miss patients that need a VE.

DISCUSSION

The model performed as designed to preoperatively identify every patient that required a VE. There would be false positives given the specificity of 58.8%. However, this could be tolerated since patient care would not be compromised in this situation. The general urologist would have referred a patient that only needed a VV to a VE experienced microsurgeon. On the other hand, the program would minimize the

Table 2. Accuracy of the VE/VV predictor model in training and test patient groups

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	Training Group	Testing Group	
% Sensitivity	100	100	
% Specificity	55	58.8	
% Pos predictive value	33.7	53.3	
% Neg predictive value	100	100	
Area under ROC curve	0.8	0.8	

possibility of a patient that required a VE from being operated on by a nonVE experienced surgeon. This study presents a model that identifies patients that would need a VE by our previously described criteria. Unfortunately we do not have patency and pregnancy outcomes on all of the patients in the design group. Thus this surrogate end point was used for the model design.

Our results illustrate that a model to preoperatively identify patient that may need a VE at the time of vasectomy reversal can be designed. This model can be used as an adjunct to our current standard of care, but it is not a replacement for clinical judgment. The model provides the urologist and the patient with a fairly accurate prediction of the type of reversal that may be required. This allows the patient and urologist to make an informed decision as to the optimal plan of action —whether or not a referral to a VE experienced microsurgeon is necessary. This will enable more efficient use of our medical resources and optimize the delivery of care to patients.

The model performs significantly better than using a straight forward obstructive interval cutoff. The use of the age of the patient in addition to obstructive interval improved the prediction accuracy of the model. Men who are older at the time of vasectomy appear to be more likely to form epididymal obstructions in shorter obstructive intervals than younger men. There is some evidence that there may be changes in the epididymis with aging. 18 However, it is unclear if such changes may predispose the epididymis to earlier obstruction. The model may be hinting that age would be an independent significant predictor on multivariate analysis if we had more patients. Unfortunately older men are likely to have had a longer obstructive interval, thus even though age was significant on Univariate analysis, we would need more men in the study group to demonstrate an independent relationship by Multivariate analysis.

The model provides a stable and fairly accurate prediction that may minimize variation in preoperative clinical predictions between some urologists and experienced microsurgeons. It is also possible that this analysis of the most important predictors and their weighting in such a model can function as a training aid for residents to help improve their clinical assessment of a patient presenting for a vasectomy reversal

Objective criteria are used in the calculation of the prediction, namely, age of the patient and time since vasectomy. Since the model is not based on any interpretation of physical examination findings by the physician, the prediction is less likely to be affected by any physician bias.

Similar computer algorithms have been used for other systems. Dayhoff et al have illustrated the beneficial use of neural networks in coronary heart disease risk prediction. Schwarzer et al have argued that feed forward neural networks (programs that learn and pick up associations on their own) can lead to serious errors in model design compared with traditional statistical counterparts such as logistic regression. Thus, our design was based on strict statistical methods of univariate analysis and logistic regression as described by Jekel et al and Matthews and Farewell All statistical analysis was performed using SigmaStat (SPSS Inc., Chicago, Illinois).

The ultimate decision as to what type of reversal to be performed was made by 1 microsurgeon (AJT) at our institution. Therefore, the model may be biased to that person's clinical judgment. However, well established, standardized (used by most other microsurgeons) clinical criteria were used at the time of the reversal to decide whether a VV or a VE would be performed as previously described. This helped minimize any bias effect.

The model would likely be further enhanced by testing and validation at several different institutions. The 100% sensitivity achieved in our 50 patient test group is likely to de-

crease when we test on more patients and on patients at other medical centers. However, the results are promising so far. Handheld and Windows based computer versions of the model where created. A web based distribution platform was designed and the programs can be downloaded as free shareware from <code>www.uroengineering.com</code>. This allows physicians to use the model in their practice and to validate the effectiveness of the model at their institution.

In the 50 patient test group, 30 patients would have been predicted as needing a VE using this model. 16 of these patients had a VE on at least 1 side at the time of surgery and 6 underwent bilateral VE. One may argue that a urologist may simply perform a bilateral VV on a pt that may require a VE on 1 side by our criteria since pregnancy and patency outcomes are superior after a VV compared with VE. Our assumption is that the most successful reconstructive procedure was being offered to the patient for each side, despite what was done on the other side. This model is simply designed to try to ensure that a patient that needs a VE by our criteria is offered that option preoperatively.

CONCLUSIONS

Our model provides 100% sensitivity in preoperatively detecting patients that may require a VE (1 side or both) during vasectomy reversal (specificity 58.8%). This model may allow urologists to preoperatively identify these patients for possible referral to VE experienced microsurgeons. Palm OS and Windows PC versions of this model may be downloaded as free shareware from <code>www.uroengineering.com</code>.

REFERENCES

- Potts, J. M., Pasqualotto, F. F., Nelson, D., Thomas, A. J., Jr. and Agarwal, A.: Patient characteristics associated with vasectomy reversal. J Urol, 161: 1835, 1999
- Berger, R. E.: Triangulation end-to-side vasoepididymostomy. J Urol, 159: 1951, 1998
- Boeckx, W. and Van Helden, S.: Microsurgical vasoepididymostomy in the treatment of occlusive azoospermia. Br J Urol, 77: 577, 1996
- Chan, P. T. K., Li, P. S. and Goldstein, M.: Microsurgical vasoepididymostomy: a prospective randomized study of 3 intussusception techniques in rats. J Urol, 169: 1924, 2003
- Marmar, J. L.: Modified vasoepididymostomy with simultaneous double needle placement, tubulotomy and tubular invagination. J Urol, 163: 483, 2000
- McCallum, S., Li, P. S., Sheynkin, Y., Su, L.-M., Chan, P. and Goldstein, M.: Comparison of intussusception pull-through end-to-side and conventional end-to-side microsurgical vasoepididymostomy: prospective randomized controlled study in male wistar rats. J Urol, 167: 2284, 2002
- Shekarriz, B. M., Thomas, A. J., Jr., Sabanegh, E., Kononov, A. and Levin, H. S.: Fibrin-glue assisted vasoepididymostomy: a comparison to standard end-to-side microsurgical vasoepididymostomy in the rat model. J Urol, 158: 1602, 1997
- Shekarriz, B. and Pomer, S.: Re: Comparison of intussusception pull-through end-to-side and conventional end-to-side microsurgical vasoepididymostomy: prospective randomized controlled study in male Wistar rats (letter to the editor). J Urol, 169: 294, 2003
- Belker, A. M., Thomas, A. J., Jr., Fuchs, E. F., Konnak, J. W. and Sharlip, I. D.: Results of 1,469 microsurgical vasectomy reversals by the Vasovasostomy Study Group. J Urol, 145: 505, 1991
- Belker, A. M.: Vasectomy and its reversal. Prim Care, 12: 703, 1985
- Kolettis, P. N., Sabanegh, E. S., D'Amico, A. M., Box, L., Sebesta, M. and Burns, J. R.: Outcomes for vasectomy reversal performed after obstructive intervals of at least 10 years. Urology, 60: 885, 2002
- Kolettis, P. N., D'Amico, A. M., Box, L. and Burns, J. R.: Outcomes for vasovasostomy with bilateral intravasal azoospermia. J Androl, 24: 22, 2003
- Fuchs, E. F. and Burt, R. A.: Vasectomy reversal performed 15 years or more after vasectomy: correlation of pregnancy out-

- come with partner age and with pregnancy results of in vitro fertilization with intracytoplasmic sperm injection. Fertil Steril, **77:** 516, 2002
- Silber, S. J.: Reversal of vasectomy and the treatment of male infertility. Role of microsurgery, vasoepididymostomy, and pressure-induced changes of vasectomy. Urol Clin North Am, 8: 53, 1981
- Crain, D. S., Roberts, J. L. and Amling, C. L.: Practice patterns in vasectomy reversal surgery: results of a questionnaire study among practicing urologists. J Urol, 171: 311, 2004
- Jekel, J. F., Elmore, J. G. and Katz, D. L.: Epidemiology, Biostatistics, and Preventive Medicine. Philadelphia: W. B. Saun-

- ders, Co., chapt. 13, p. 172, 1996
- Matthews, D. E. and Farewell, V. T.: Using and Understanding Medical Statistics, 3rd ed. Basel: Karger, chapt. 11, p. 136, 1996
- La Perle, K. M., Blomme, E. A., Sagartz, J. E. and Capen, C. C.: Epididymal cribriform hyperplasia with nuclear atypia in p53 homozygous knockout mice on a mixed 129/Sv-FVB/N background. Comp Med, 52: 568, 2002
- Dayhoff, J. E. and DeLeo, J. M.: Artificial neural networks: opening the black box. Cancer, 91: 1615, 2001
- Schwarzer, G., Vach, W. and Schumacher, M.: On the misuses of artificial neural networks for prognostic and diagnostic classification in oncology. Stat Med, 19: 541, 2000