Effect of female partner age on pregnancy rates after vasectomy reversal

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Objective: To determine the effect of female partner age on pregnancy rates after vasectomy reversal.
Design: Retrospective review.
Setting: Two academic infertility practices.
Patient(s): Men undergoing vasectomy reversal and their partners.
Intervention(s): Microsurgical vasectomy reversal.
Main Outcome Measure(s): Patency and pregnancy rates.
Result(s): Two hundred ninety-four patients met the inclusion criteria. Groups were similar with regard to types of procedure performed (vasovasostomy or vasoepididymostomy), obstructive interval, female factors, number of repeat procedures, and quality of vasal fluid. Patency rates were 90%, 89%, 90%, 86%, and 83% for patients with female partners aged 20–24, 25–29, 30–34, 35–39, and 40+ years, respectively. Pregnancy rates were 67%, 52%, 57%, 54%, and 14% for patients with female partners aged 20–24, 25–29, 30–34, 35–39, and 40+ years, respectively. The pregnancy rate for couples with female partner aged 40 or older was lower than for those with the female partner aged 39 or younger (14% vs. 56%).
Conclusion(s): Pregnancy rates for vasectomy reversal were good regardless of female age as long as the partner was 39 years old or younger. Pregnancy rates were lower if the female partner was 40 or more years old. (Fertil Steril® 2007;87:1340–4. ©2007 by American Society for Reproductive Medicine.)

Key Words: Vasectomy reversal, vasovasostomy, vasoepididymostomy, male infertility

The pregnancy rate for vasectomy reversal is dependent upon surgeon experience, obstructive interval, the quality of the vasal fluid seen at surgery, whether or not epididymal obstruction is present, and any female factors (1–7). Ovarian reserve, one of the most important determinants of female fertility potential, declines with advancing female age. We evaluated the effect of female partner age on the pregnancy rates after vasectomy reversal.

MATERIALS AND METHODS

We obtained Institutional Review Board approval for this study. We retrospectively analyzed outcomes for microsurgical vasectomy reversals performed by three urologic surgeons between July 1995 and March 2005. Vasovasostomy (VV) was performed under general anesthesia with either a modified one-layer technique or a formal two-layer technique. Vasoepididymostomy (VE) was performed with a two-layer end-to-side technique (7).

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A semen analysis (SA) was obtained between 4 weeks and 3 months after surgery, and generally every 3 months until pregnancy was established or the patient discontinued follow-up. Follow-up data were obtained from review of the medical records, phone contact, and letters from patients. An attempt was made to contact all patients by either phone or letter.

Patency was defined as the presence of motile sperm in at least one postoperative SA. Patients with less than 6 or 12 months follow-up were excluded from the patency rate analysis for VV and VE, respectively, unless they had sperm in the semen. Patients who established a pregnancy but did not have an SA were considered patent cases. Patients with less than 12 months follow-up or those not actively attempting to conceive were excluded from the pregnancy rate analysis unless they had established a pregnancy. Patients followed for 1 year who did not establish a pregnancy were considered to be not pregnant even if they did not have a semen analysis.

Statistical Analysis

Descriptive statistics were used to summarize all continuous and categorical variables. Comparisons between the five age

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groups were performed using analysis of variance, along with the Tukey test as the multiple comparisons test, for continuous variables (male partner age, obstructive interval, and follow-up time), and the Fisher exact test for categorical variables (female factors, repeat procedures, whether or not VE was performed, presence of sperm intraoperatively, patency rate, and pregnancy rate).

When the five different age groups were collapsed into two groups, comparisons for continuous variables were performed using the two-group *t* test, and those for categoric variables were performed using Fisher exact test. Multivariate logistic regression analysis was used to evaluate the patency and pregnancy rates among the age groups while controlling for covariates and potential confounding variables. All statistical tests were two-sided and were performed using a 5% significance level. SAS software (version 9.1; SAS Institute, Cary, NC) was used to perform all statistical analyses.

RESULTS

There were 294 patients (21 with partner aged 20–24 years, 80 with partner aged 25–29 years, 117 with partner aged 30–34 years, 62 with partner aged 35–39 years, and 14 with partner aged 40 years and older) who met the inclusion criteria for the study. The results for these five age groups and for the overall group of 294 patients are summarized in Table 1.

Male partner age was significantly different among the female partner age groups ($P<.001$); the specific pair-wise differences in the age groups are listed in Table 1. Obstructive interval displayed a weak trend toward significance among the age groups ($P=.099$). The age groups were similar with regard to types of procedure (VV or VE) performed ($P=.67$), female factors ($P=.87$), number of repeat procedures ($P=.48$), and quality of vasal fluid ($P=.46$).

Patency rates were 90%, 89%, 90%, 86%, and 83% for the respective female partner age groups, and these rates were not significantly different ($P=.83$). Pregnancy rates were 67%, 52%, 57%, 54%, and 14% for the respective female partner age groups, and these rates were not significantly different ($P=.22$). There were also no significant differences among the available mean follow-up times for the age groups for patency ($P=.45$) or for pregnancy ($P=.67$). Patency rates were similar for the three surgeons that participated in this study (91%, 89%, and 83%; $P=.33$).

Statistical analyses were also performed on the data after couples were separated into those with female partners less than 40 years old and greater than or equal to 40 years old (280 patients with partner aged 20–39 years and 14 patients with partner aged 40 years and older). The results for these analyses are summarized in Table 2.

Male partner age was significantly greater in the 40 years and older female partner age group compared with the 20–39 year female partner age group (46.3 years vs. 39.3 years; $P<.001$). The pregnancy rate for couples with female partner 40 or more years old was significantly less than that for couples with female partner aged 20–39 years (14% vs. 56%; $P=.049$). These two age groups were similar with regard to types of procedure (VV or VE) performed ($P=.61$), female factors ($P=1.0$), number of repeat procedures ($P=1.0$), quality of vasal fluid ($P=.16$), patency rates ($P=.63$), and mean follow-up times for patency ($P=.18$) and for pregnancy ($P=.63$).

Multivariate analyses were performed for the primary outcome measures (patency and pregnancy). All variables in Table 1 were included in these analyses. However, follow-up time was included in only some of these analyses, because it had not been recorded for some couples (which led to data from fewer couples being included in the analyses). Analyses that included follow-up time are discussed separately from those that did not include follow-up time. For the analyses involving the five female partner age groups, obstructive interval and presence of sperm or sperm parts intraoperatively were the only significant predictors of patency ($P=.019$ and $P=.001$, respectively). When follow-up time was included in this analysis, obstructive interval was the only significant predictor of patency ($P=.044$).

For pregnancy, obstructive interval and presence of sperm or sperm parts intraoperatively were again the only significant predictors ($P=.025$ and $P=.033$, respectively); however, female factors displayed a weak trend toward significance ($P=.092$). When follow-up time was included in the pregnancy analysis, presence of sperm or sperm parts intraoperatively and follow-up time were significant predictors of pregnancy ($P=.048$ and $P=.049$, respectively); obstructive interval displayed a trend toward significance ($P=.083$).

After couples were separated into those with female partners <40 years old and ≥ 40 years old and multivariate analyses were performed, the results were similar to those already described for patency: $P=.020$ for obstructive interval, and $P=.001$ for presence of sperm or sperm parts intraoperatively. When follow-up time was included in this analysis, obstructive interval was the only significant predictor of patency ($P=.037$).

For pregnancy, predictors were $P=.024$ for obstructive interval and $P=.031$ for presence of sperm or sperm parts intraoperatively. When follow-up time was included in the pregnancy analysis, obstructive interval, presence of sperm intraoperatively, and follow-up time displayed trends toward significance ($P=.074$, $P=.075$, and $P=.056$, respectively).

DISCUSSION

Fertility is a couple phenomenon, and impairment of either the male or female partner's fertility can impede a pregnancy. In the present study, we examined the impact of female age, one critical variable related to female fertility potential, on pregnancy rates after vasectomy reversal. We

TABLE 1

Summary of results for vasectomy reversal related to female partner age (n = number of couples).

Variable	Overall (n = 294)	Female partner age group 20–24 (n = 21)	25–29 (n = 80)	30–34 (n = 117)	35–39 (n = 62)	≥40 (n = 14)	*P* value
Female partner age (yrs) (mean ± SD)	31.3 ± 4.6	22.8 ± 1.5	27.4 ± 1.3	31.6 ± 1.4	36.5 ± 1.4	40.6 ± 0.8	.001†
Male partner age (yrs) (mean ± SD)	39.7 ± 6.6	35.5 ± 6.7	37.9 ± 6.5	40.3 ± 6.4	40.7 ± 5.6	46.3 ± 5.3	.001‡
Obstructive interval (yrs) (mean ± SD)	9.4 ± 5.3	7.2 ± 4.4	8.7 ± 5.1	9.5 ± 5.3	10.2 ± 5.5	11.2 ± 6.6	.099
Couples with female factors	19 (6.5%)	2 (9.5%)	6 (7.5%)	7 (6.0%)	3 (4.8%)	1 (7.1%)	.87
Couples with repeat procedures	29 (9.9%)	3 (14.3%)	11 (13.8%)	8 (6.8%)	6 (9.7%)	1 (7.2%)	.48
VE performed§	19 (6.5%)	1 (4.8%)	4 (5.0%)	11 (9.5%)	3 (4.8%)	0 (0%)	.67
Sperm intraoperatively (%)	89.8 (254/283)	95.0 (19/20)	89.6 (69/77)	88.3 (98/111)	93.4 (57/61)	78.6 (11/14)	.46
Patency Rate (%)*	88.7 (236/266)	90.0 (18/20)	89.3 (67/75)	90.3 (93/103)	85.7 (48/56)	83.3 (10/12)	.83
Follow-up time, patency (mos) (mean ± SD)**	28.0 ± 26.3	34.7 ± 35.3	29.3 ± 28.3	28.8 ± 25.1	24.6 ± 23.8	12.5 ± 11.9	.45
Pregnancy rate (%)*	54.3 (113/208)	66.7 (10/15)	51.8 (29/56)	57.1 (52/91)	53.9 (21/39)	14.3 (1/7)	.22
Follow-up time, pregnancy (mos) (mean ± SD)**	32.5 ± 27.0	40.6 ± 36.5	34.1 ± 30.1	32.9 ± 26.1	27.4 ± 21.5	23.3 ± 12.3	.67

* Assuming a sufficient follow-up time (explained in text).

† Statistically significant differences ($P<.05$) exist between each pair of means for the five age groups.

‡ Statistically significant differences ($P<.05$) exist between the following pairs of means: 20–24 and 30–34, 20–24 and 35–39, 20–24 and ≥40, 25–29 and ≥40, 30–34 and ≥40, and 35–39 and ≥40.

§ VE performed = patients where bilateral vasoepididymostomy performed or unilateral vasoepididymostomy performed with solitary testis.

** The number of actual known follow-up times for patency are 207 (overall), 15 (20–24 age group), 56 (25–29 age group), 84 (30–34 age group), 47 (35–39 age group), and 5 (≥40 age group); the number of actual known follow-up times for pregnancy are 152 (overall), 10 (20–24 age group), 42 (25–29 age group), 68 (30–34 age group), 30 (35–39 age group), and 2 (≥40 age group). All patients entered into patency and pregnancy rate calculations had at least 6 and 12 months follow-up, respectively.

Gerrard. Female age and vasectomy reversal. Fertil Steril 2007.

TABLE 2

Summary of results for vasectomy reversal related to female partner age (n = number of couples)–female partner age 20–39 vs. ≥40.

Variable	Female partner age group		
	20–39 (n = 280)	≥40 (n = 14)	*P* value
Female partner age (yrs) (mean ± SD)	30.8 ± 4.2	40.6 ± 0.8	.001
Male partner age (yrs) (mean ± SD)	39.3 ± 6.5	46.3 ± 5.3	.001
Obstructive interval (yrs) (mean ± SD)	9.3 ± 5.3	11.2 ± 6.6	.18
Couples with female factors	18 (6.4%)	1 (7.1%)	1.0
Couples with repeat procedures	28 (10.0%)	1 (7.2%)	1.0
VE performed§	19 (6.8%)	0 (0%)	.61
Sperm intraoperatively (%)	90.3 (243/269)	78.6 (11/14)	.16
Patency rate (%)*	89.0 (226/254)	83.3 (10/12)	.63
Follow-up time, patency (mos) (mean ± SD)**	28.4 ± 26.4	12.5 ± 11.9	.18
Pregnancy rate (%)*	55.7 (112/201)	14.3 (1/7)	.049
Follow-up time, pregnancy, (mos) (mean ± SD)**	32.6 ± 27.2	23.3 ± 12.3	.63

* Assuming a sufficient follow-up time (explained in text).

§ VE performed = patients where bilateral vasoepididymostomy performed or unilateral vasoepididymostomy performed with solitary testis.

** The actual follow-up times for patency were known for 202 patients in the 20–39 age group and 5 patients in the ≥40 age group. The actual follow-up times for pregnancy were known for 150 patients in the 20–39 age group and 2 patients in the ≥40 age group. All patients entered into patency and pregnancy rate calculations had at least 6 and 12 months follow-up respectively.

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observed no difference in pregnancy rates unless the female partner was over 40 years old. This observation is consistent with a known decline in female fertility potential with advancing age (8).

The data presented in the present study allow couples pursuing vasectomy reversal to be counseled more specifically about their chance for pregnancy. Couples can currently receive this type of specific information about the obstructive interval and pregnancy rates (1). Similarly, pregnancy rates for IVF are reported based on the female partner's age (9).

Information about female age and pregnancy rates after reversal is more limited. In a study by Deck and Berger (4), pregnancy and live delivery rates for partners older than 37 years were 22% and 17%, respectively. Fuchs and Burt (5) stratified pregnancy and live delivery rates by female age for obstructive intervals of 15 years or more. They demonstrated a decline in pregnancy and delivery rates with advancing female age, particularly after age 35. For female partners 36–40 years old and 40 or more years old, respectively, the pregnancy rates were 32% and 29% and live delivery rates were 28% and 14%. Kolettis et al. (6) reported pregnancy outcomes after vasectomy reversals for couples with female partners 35 years or older. The overall pregnancy rate was 35%, and it was 46% for female partners aged 35 to 39 years.

The only other study to date, to the authors' knowledge, to examine the effect of female age on pregnancy after vasectomy reversal across all obstructive intervals is a recent review by Silber and Grotjan (10). In a review of Silber's large series of vasectomy reversals, the pregnancy rate decreased with increasing female partner age. For partners 35–40 years old, the pregnancy rate was 81.7%, whereas for partners over 40 it was 59.1%.

The other option for couples with vasectomy-related infertility to have their own biologic children is with sperm retrieval and intracytoplasmic sperm injection (ICSI). Although previous studies have shown that vasectomy reversal is less costly, comparing success rates between reversal and sperm retrieval and ICSI is difficult, because different centers have different selection criteria and success rates (11, 12). It is clear, however, that pregnancy rates decrease with increasing female age, beginning in the middle thirties. For example, in the most recent Society for Assisted Reproductive Technology report (9) the delivery rate decreased from 36.8% at age 30 to 24.9% at age 38. This decline in success rate is related to the relationship of IVF pregnancy rates to gonadotropin response and number of oocytes retrieved, both of which decrease with advancing age. We did not observe such a decrease in pregnancy rate until the female partner was over 40. These data support the recommendation that couples with female partners in their middle thirties with vasectomy-related infertility proceed with vasectomy reversal, and they argue against advising such couples to proceed with IVF.

It is important to recognize the limitations of the present study. One limitation is the small number of couples with female partners older than 40 years. It is not surprising that the number of couples in this category is small, because it is less common for women in their forties to pursue fertility. Despite the small number of couples in this category, the results support a widely supported concept of declining fertility with advancing female age. Therefore, this information is extremely important when counseling patients about their options.

Couples should be advised that the chance for pregnancy and live delivery are less when the female partner is older. Also, if a couple with an "older" female partner is contemplating vasectomy reversal they should be encouraged to do so quickly because of their declining fertility potential. The present data also showed that the male partners were older in the groups with older female partners. Although advancing male age is associated with declining fertility, the magnitude of this change is far smaller than the effect of female age (13, 14). Therefore, the male age is not likely a factor in the lower pregnancy rate and probably reflects the tendency for older women to have older male partners.

In conclusion, pregnancy rates for vasectomy reversal were good regardless of female age as long as the partner was 39 years old or younger. Pregnancy rates were lower if the female partner was 40 of more years old. The latter couples should have careful preoperative counseling about their chance for pregnancy so they can make an informed decision. The older male age seen in the group with female partner over 40 probably reflects the fact that older men tend to have older partners and is not likely the cause of the lower pregnancy rate.

REFERENCES

1. Belker AM, Thomas AJ, Fuchs EF, Konnak JW, Sharlip ID. Results of 1,469 microsurgical vasectomy reversals by the Vasovasostomy Study Group. J Urol 1991;145:505–11.
2. Nagler HM, Rotman M. Predictive parameters for microsurgical reconstruction. Urol Clin N Amer 2002;29:913–9.
3. Silber SJ. Epididymal extravasation following vasectomy as a cause for failure of vasectomy reversal. Fertil Steril 1979;31:309–15.
4. Deck AJ, Berger RE. Should vasectomy reversal be performed in men with older female partners? J Urol 2000;163:105–6.
5. Fuchs EF, Burt RA. Vasectomy reversal performed 15 years or more after vasectomy: correlation of pregnancy outcome with partner age and with pregnancy results of in vitro fertilization with intracytoplasmic sperm injection. Fertil Steril 2002;77:516–9.
6. Kolettis PN, Sabanegh ES, Nalesnik JG, D'Amico AM, Box LC, Burns JR. Pregnancy outcomes after vasectomy reversal for female partners 35 years old or older. J Urol 2003;169:2250–2.
7. Thomas AJ, Howards SS. Microsurgical treatment of male infertility. In: Lipshultz LI, Howards SS, Infertility in the male. 3rd ed. St. Louis: Mosby, 1997:371–84.
8. Tietze C. Reproductive span and rate of reproduction among Hutterite women. Fertil Steril 1957;8:89–97.
9. Centers for Disease Control and Prevention, United States Department of Health and Human Services. 2002 Assisted Reproductive Technology Success Rates. Available at: http//www.cdc.gov/reproductivehealth/index/htm. Accessed November 26, 2005.
10. Silber SJ, Grotjan HE. Microscopic vasectomy reversal 30 years later: a summary of 4010 cases by the same surgeon. J Androl 2004;25:845–9.
11. Pavlovich CP, Schlegel PN. Fertility options after vasectomy: a cost-effectiveness analysis. Fertil Steril 67;133:1997.
12. Kolettis PN, Thomas AJ Jr. Vasoepididymostomy for vasectomy reversal: a critical assessment in the era of intracytoplasmic sperm injection. J Urol 1997;158:467.
13. De La Rochebrochard E, McElreavey K, Thonneau P. Paternal age over 40 years: the "amber light" in the reproductive life of men? J Androl 2003;24:459–65.
14. Kuhnert B, Nieschlag E. Reproductive functions of the ageing male. Hum Reprod Update 2004;10:327–39.