Vasectomy reversal vs. sperm retrieval with in vitro fertilization: a contemporary, comparative analysis

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Objective: To explore the primary options available to men who desire fertility after a vasectomy.
Design: Literature review.
Setting: University of Miami Miller School of Medicine.
Patient(s): Men with a previous vasectomy now seeking fertility.
Intervention(s): The two main options to achieve paternity for men following vasectomy include vasectomy reversal (VR) and surgical sperm retrieval with subsequent in vitro fertilization (IVF).
Main Outcome Measure(s): We reviewed and compared the important considerations for men deciding between these 2 options, including: obstructive interval, female partner age, antisperm antibodies, male partner age, female infertility factors, and cost.
Result(s): Both VR and IVF represent reasonable options for the couple seeking fertility after vasectomy. Specific circumstances may favor one modality over another, depending on obstructive interval, possible female fertility factors, female partner age, male partner age, and cost. In the absence of insurance coverage, VR is often more cost-effective than IVF. Alternatively, when a female factor may contribute to infertility in addition to vasectomy, IVF is often the better choice. Antisperm antibodies are unlikely to contribute to infertility following a successful VR.
Conclusion(s): VR or surgical sperm retrieval with IVF are reasonable options for couples seeking children after vasectomy. Pregnancy rates for both options are overall similar, so prior to pursuing either option, a thorough discussion with a reproductive urologist who possesses microsurgical skills in VR and a reproductive endocrinologist with expertise in IVF is imperative. Making a final choice through shared decision-making while considering these points is ideal. (Fertil Steril® 2021;115:1377–83. ©2021 by American Society for Reproductive Medicine.)
Key Words: Infertility, IVF, male infertility, sperm retrieval, vasectomy reversal

A vasectomy is a simple, safe outpatient procedure in which the vasa deferentia are surgically interrupted, preventing transport of sperm beyond the vas deferens. The procedure is common—approximately 500,000 men undergo vasectomies each year in the United States (1). Although this procedure is considered permanent, life events, such as divorce and the desire for pregnancy with a new partner, lead approximately 6% of men to reevaluate their contraception choice (2). In considering their fertility options, couples with male partners who previously underwent vasectomy have two options: vasectomy reversal (VR) or assisted reproductive technology (ART), more specifically, sperm extraction and in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI). In general, comparison of both VR and IVF showed that pregnancy rates were overall similar (3–5).

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VR is performed with two possible approaches, vasovasostomy (VV) or vasoepididymostomy (VE). Of the two, VV overall had higher success, defined as patent vas and return of sperm to the ejaculate, compared with that of VE (89.4% vs. 64.1%, respectively) (6, 7). Indications for performing a VV vs. a VE were based on the intraoperative findings of the vasal fluid. The presence of whole sperm or any sperm parts in the intravasal fluid was associated with positive patency outcomes (8). For this reason, many practitioners performed VVs in the presence of any sperm parts. If there was no sperm in the fluid, VE was indicated (9). Other factors in considering VR pregnancy success include obstructive interval, paternal age, maternal age, and female factor infertility.

ART is the other option for couples desiring fertility after vasectomy. Birth rates vary by age, with increasing age associated with declining success rates. Most notably, birth rates drop significantly in women >37 years of age (30.7% in women aged 35–37 years vs. 19.7% in women aged 38–40 years) (10). Along with maternal age, other factors that influence success rates are female factor infertility, male factor infertility, and paternal age.

In the following review, we address the many considerations that must go into counseling patients on this complex decision. For most couples with male partners who are after vasectomy and now desiring fertility, IVF and VR are both usually viable options; however, through this review, we highlight issues that may favor one intervention over another. Summaries of our review can be found in Figure 1 and Table 1.

YOUNG FEMALE PARTNER WITH OBSTRUCTIVE INTERVAL < 10 YEARS

The female partner's age and the obstructive interval (OI), or time from the male partner's vasectomy to reversal, have both been shown to be important considerations for treatment options. Fertility success must evaluate both the male and female partners' health and medical histories. A woman's fertility is known to decline rapidly after the age of 35. In the scenario in which the woman is young (<35 years old) and the man has recently (within 10 years) undergone vasectomy, what is the best fertility option for the couple? One recent study directly compared live birth rates between VR and IVF in this population. The mean age of the female partner was 34.1 years and the mean OI was 9.53 years (1). The investigators found no differences in live birth rates between the treatment modalities (11). They did find, however, a significantly shorter time from initiation of treatment to pregnancy in the IVF arm than that in the VR arm (8.2 months vs. 16.3 months, respectively). An important consideration here as well was that over half the patients in the VR arm subsequently received ART.

Patients tend to want to know specific numbers that describe their chances of success with a particular treatment modality. Knowing the chance of success of a certain treatment is critical, particularly considering the extreme costs, both economic and otherwise, associated with fertility treatments. Urologists may choose to report their own data for patency and pregnancy rates, as this would be the most clinically relevant number to the couple, but they should always inform their patients of the general success rates based on the literature. A 2015 meta-analysis of VV found that the pooled patency and pregnancy rates were 89.4% and 73.0%, respectively (6). This meta-analysis included older women and those with longer OI and found that the pregnancy rates were higher if the OI was <10 years (6). As a comparison, data published by the Society for Assisted Reproductive Technology quotes singleton birth success rates per IVF cycle at 42.6% in women younger than 35, and 30.7% success rates in women between the ages of 35 and 37 (10).

Based on the current evidence, both VR and ART would be very reasonable treatment options in women aged <35 with an OI <10 years,. The benefits of each must be carefully considered and weighed against the potential drawbacks or concerns prior to initiating treatment, and shared decision-making is essential.

ADVANCED MATERNAL AGE (>35 YEARS)

The desire for fertility in women aged >35 has been on the rise, and as a result, more couples have been seeking infertility consultations, with a subsequent and consistent increase in children born via ART (4). Reproductive specialists commonly encounter a clinical scenario of couples with advanced maternal age and a male partner with a history of vasectomy. Just as in other women's fertility scenarios, the chances for pregnancy with IVF decrease precipitously in women after the age of 35 (12–14). Such patients may experience considerable anxiety and distress because of these factors, and it is important for the clinician to be familiar with available data so as to best counsel them.

Unfortunately, there is a paucity of high-quality evidence to guide patients toward IVF or VR, particularly in the advanced maternal age group. In a 2008 retrospective review of 212 patients undergoing VR, Hinz et al. (14) found that age >40 years was an independent predictor of reduced pregnancy rates. In this review, VR compared favorably with published IVF/ICSI rates, and they concluded that VR should be the treatment of choice for patients, with careful counseling, particularly in those with advanced maternal age. In a 2018 retrospective review, subgroup analysis of older female age groups >35 years demonstrated comparable pregnancy rates when compared with the IVF pregnancy rates published by the Centers for Disease Control and Prevention in 2015 (4). The authors concluded that VR should be considered in couples with female partner age ≤40 years. Niederberger and Makhlouf (15) found that IVF offered only a marginal benefit for women aged ≥38 years.

A definitive age at which one treatment modality is preferable has not been identified, and, as such, recommendations made in guidelines are based on expert opinion. The American Urological Association's best practice statement recommends couples consider IVF if the female partner is >37 years old (16). There have been considerable advances in the surgical technique for VR, and it appears to achieve results at least similar to those of IVF in terms of both pregnancy and live birth rates in women with advanced maternal age (17). VR requires time. The average interval from successful surgical repair to pregnancy is 12 months, and especially in those with advanced maternal age, time is limited and of the essence (18). This becomes especially true if the couple desires multiple children. The likelihood of pregnancy drops dramatically after the maternal age of 40, regardless of the treatment modality.

An important consideration as well is that patients may believe that because IVF is a more involved process, that they are taking a more active role, which can alleviate stress in the process as there is a set time line with sequential plans along the way. Patients who express anxiety or distress over a narrow fecundity window and those desiring multiple children may be better served with IVF, although clinicians may also offer VR as a reasonable treatment option.

OBSTRUCTIVE INTERVAL

The OI is thought by some to be the most important prognostic factor in VR success (19). A common hypothesis is that obstruction causes time-dependent morphologic changes on the seminiferous tubules and epididymis. Jarow et al. (20) found a significant reduction in the mean number of Sertoli cells as well as increased seminiferous tubule wall thickness in the after vasectomy group. The exact effect that time has on patency is unclear. Earlier research by the Vasovasostomy Study Group found that there was a consistent drop in patency rates (18), whereas Silber (21) found a substantial drop in patency 10 years after vasectomy. However, more contemporary studies demonstrated that excellent patency and at least comparable pregnancy rates can be achieved despite an OI of >10–20 years (22–24).

In a 2015 meta-analysis and systematic review evaluating VV specifically, Herrel et al. (6) found that patients with an OI <10 years demonstrated only modestly higher patency and pregnancy rates compared with that of those with an OI ≥10 years. Unfortunately, there was significant heterogeneity between studies under review as even definitions of patency and pregnancy differed. The study also excluded two large databases, as a considerable number of patients in these studies received at least 1 VE, and the meta-analysis was evaluating only VV. Of note, these 2 large series excluded from the meta-analysis both found patency was not influenced by OI, although only one measured pregnancy outcomes.

Although recent data suggest that the OI is less important in terms of patency and pregnancy rates than early studies suggested, OI does appear to strongly influence the type of vas reconstruction performed (i.e., VV vs. VE). Several studies highlighted a linear correlation between OI and the likelihood that the patient will require a VE on one or both sides (13, 24). One large series of 1,229 patients found that the rate of unilateral/bilateral VE plateaued at 22 years after vasectomy (25). Technical advances and experience have no doubt influenced the improved surgical outcomes in VR patients. Several studies demonstrated that patency rates close to 90% can be achieved even with extended OIs, as long as at least 1 VV is performed as part of the repair (22, 23, 25). In cases in which bilateral VE was performed, the patency rates were lower, ranging between 54% and 72% (23, 26, 27).

Although outside of the scope of this review, nomograms may be helpful preoperatively in determining which patients will require VEs (26, 28). Although the integrity of the primary surgery should not be compromised, cryopreservation may be offered to patients with an increased likelihood of requiring VEs. Typically, cryopreservation must be arranged preoperatively, whereas the decision to perform VEs is made intraoperatively. Preoperative discussions regarding sperm cryopreservation at the time of repair may be warranted, particularly in patients with longer OIs. If couples present with a history of remote vasectomy, the surgeon should be comfortable with both surgical techniques, in case a VE is required. If the surgeon is not comfortable performing a VE, referral to a different surgeon may be warranted. Sperm extraction with IVF/ICSI remains an excellent option for patients with extended OIs. Overall, OI >10 years should not be a deterrent to performing VR in couples desiring fertility.

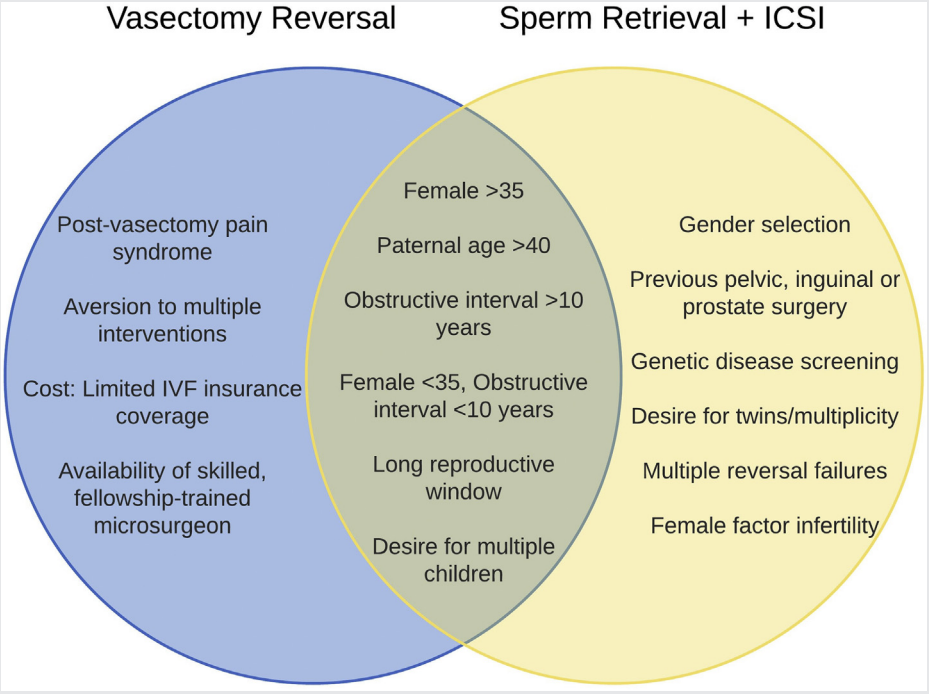
ADVANCED PATERNAL AGE

As we mentioned, age must be considered in determining the best fertility intervention for couples. Often the focus is on maternal age; however, does paternal age matter when deciding between VR and IVF? Data suggests that over the last 40 years, the mean paternal age in the United States has increased, and the rates of children being born to men >40 and 50 years old, respectively, has approximately doubled (29). This overall trend in older men seeking paternity may be an issue for patients, as increasing paternal age is associated with several fertility concerns, including worsening semen parameters, prolonged time to pregnancy, and declining conception rates (30, 31). In assessing outcomes of VR, however, a recent study by Nusbaum et al. (32) demonstrated similar pregnancy rates for men >50 years old who underwent VR compared with that of men <50 years old. Younger female partners were associated with higher pregnancy rates (32). In addition, embryo aneuploidy rates are not affected by advanced paternal age, providing further evidence that older men are still good candidates for VR (33). Paternal age therefore should only be considered when maternal age and other health factors may influence fertility concerns associated with prolonged time to achieve pregnancy. Otherwise, paternal age alone should not be a major factor in couple fertility planning and decision-making.

FEMALE FACTOR INFERTILITY

Another important consideration in whether to recommend IVF or VR is whether the female partner has risk factors that have either caused issues with her fertility previously or put her at risk for future fertility concerns. A thorough history of the female partner should include any previous pregnancies, whether she has had surgeries, and her medical conditions. Other than age, female factor infertility risk factors include: history of tubal ligation, congenital abnormalities, endometriosis, solitary ovary, low antimüllerian hormone levels, and polycystic ovary syndrome. The prevalence of these diseases is relatively high—polycystic ovary syndrome affects 5%–10% of women and endometriosis affects approximately 6% (34, 35). Women who are already at risk for or who have previously demonstrated subfertility are likely to have more difficulty conceiving naturally. In many cases, women with a previous history of tubal ligation or known obstructed fallopian tubes may be unable to conceive naturally. In the setting of known obstruction that would prevent the couple from conceiving naturally, VR is not the best option, and IVF should be pursued. In less clear situations, in which the female partner has known female factor infertility that can decrease fertility, but natural conception is still possible, VR should be discussed with the couple and shared decision-making that aligns with the couple's overall goals is recommended.

FIGURE 1



Venn diagram of indications for vasectomy reversal vs. IVF. IVF = in vitro fertilization.

Dubin. Vasectomy reversal vs IVF. Fertil Steril 2021.

One final comment is in order regarding female factor infertility and IVF/ICSI. Over the last few years, technology has focused on assessing embryos to identify those with the highest chances for success after transfer. One of the more common tests identifies only euploid embryos, known as preimplantation genetic testing for aneuploidy (PGT-A). Use of this test prior to IVF/ICSI has increased, and female factors including age >38 years old, recurrent pregnancy loss, disease discovery, and family balancing have been considered indications for its use. However, because of concerns of cost, false-positive rates, and overall lack of sufficient evidence from current research, the American Society for Reproductive Medicine (formerly The American Fertility Society) does not recommend the routine use of PGT-A in all infertile patients (36).

COST AND ACCESS TO CARE

Achieving fertility for a couple requires attention to multiple couple health factors, but another important consideration must always be cost. Infertility treatment is expensive, and although some states and companies are now providing some coverage for IVF, most patients are not covered. When counseling patients on infertility options, practitioners should consider discussing their budget for fertility treatment. Setting realistic financial goals that align with fertility goals is essential in achieving both fertility and overall patient satisfaction. Multiple studies have compared cost-effectiveness for IVF vs. VR in couples with female partners aged ≤39 years, and they have concluded that VR is the more cost-effective treatment option. In 1997, Pavlovich and Schlegel (37) calculated the cost of VR at $25,475 per live delivery compared with $72,521 per live delivery for IVF; similar cost-effectiveness was calculated in the same year by Kolettis and Thomas (38) at $31,099 per live delivery for VR compared with $51,024 per live delivery for IVF. Both of these studies considered direct and indirect costs.

The sperm retrieval approach for couples undergoing IVF can also affect cost. Men with obstructive azoopermia can undergo either percutaneous epididymal sperm aspiration (PESA), which is performed in the office under local anesthesia, or microsurgical epididymal sperm aspiration (MESA), which is performed with a microscope under general anesthesia in the operating room. Both PESA and MESA have been shown to be effective means for obtaining sperm for IVF, and data suggests that surgically extracted epididymal sperm from men with obstructive azoospermia results in similar pregnancy and live birth rates when compared with those of couples undergoing IVF with normal ejaculated sperm (39, 40). However, cost is one major difference. MESA surgical costs have been calculated to be approximately 3-times more expensive than PESA costs ($3,000 vs. $1,000, respectively), so when counseling couples who will be pursing IVF, it is important to consider the cost differential in these 2 procedures (37). In addition, it must be noted that intrauterine insemination (IUI) is not an option for fertility when retrieval of testicular or epididymal sperm is performed.

TABLE 1

Summary of indications for vasectomy reversal vs. IVF

Clinical Scenario	Vasectomy Reversal	IVF/ICSI
Healthy woman, obstructive interval <10 years	✓	✓
Female partner with history of fertility	✓	✓
Obstructive interval >10 years	✓	✓
Female partner aged >35 years	✓	✓
Paternal age >40 years	✓	✓
Family balancing		✓
Genetic disease screening		✓
Fallopian tube obstruction		✓
Female factor infertility: natural conception possible	✓	✓
Female factor infertility: natural conception not possible		✓
Cost: Limited insurance coverage for IVF	✓	
Positive antisperm antibodies[a]	✓	✓
Aversion to multiple interventions	✓	
Postvasectomy pain syndrome	✓	
Previous prostate/pelvic/inguinal surgery		✓
Multiple reversal failures		✓
Desire for twins/multiplicity		✓
Long reproductive window	✓	✓
Desire for multiple children	✓	✓
No access to microsurgical reversal		✓

Note: IVF = in vitro fertilization; IVF/ICSI = in vitro fertilization/intracytoplasmic sperm injection

[a] Should be performed in men with significant difference between total and progressive motility, or significant agglutination on semen analysis.

Dubin. Vasectomy reversal vs IVF. Fertil Steril 2021.

For couples with budget considerations and advanced maternal age, can VR be offered as a reasonable fertility option? A study by Deck and Berger (41) compared cases of VR and IVF in ovulating women >37 years old and demonstrated a live delivery rate of 17% with VR compared with a 19.7% live delivery rate for IVF in women aged 38–40 years old. The cost per live delivery in this population for VR was $28,530 compared with $103,940 for IVF (41). Thus, VR is a cost-effective, reasonable option for couples with more advanced maternal ages and less financial flexibility.

It must be noted that all considerations for cost-effectiveness in the preceding studies assumed that the female partners were ovulating and overall had no significant health consideration that would compromise fertility—the sole cause of the couple's infertility was secondary to the after vasectomy male partner. Although VR is a more cost-effective option, other factors such as female factor infertility, advanced maternal age, and lack of access to microsurgical-trained urologists to perform a VR may prevent VR from being a realistic option for fertility, and IVF may then be the only option (42). In situations in which couples opt for VR to be performed by a surgeon outside of their local region, at-home semen analysis kits are a cost-effective, rapid option for follow up assessment of VR success (43).

Even though IVF is the more expensive out-of-pocket option, practitioners must consider the locoregional laws where they practice and their patient's insurance coverage options. Currently, there are 16 states that require insurers to either cover or offer coverage for infertility diagnoses and treatment. In addition, companies are now starting to provide coverage for IVF for their employees. For patients who are provided insurance coverage for IVF, it may be the more cost-effective and time-effective option compared with VR. A recent study by Dupree et al. (44) showed that employer-sponsored IVF coverage more than doubled IVF treatment rates overall, with an almost 10-fold increase in usage of IVF among the couples in the low salary group. When covered by insurance, IVF may be considered the more cost-effective option.

Access to a skilled microsurgeon is an important consideration for VR. Although approximately 77% of urology residency programs had fellowship-trained physicians practicing microsurgery, there still remains a group of practices and areas in the country that lack access to appropriately trained microsurgeons (42). In this scenario, VR may not be an option. More concerning, data show that most men were not referred to a male infertility specialist by reproductive endocrinologists. Because reproductive endocrinologists are usually the first physicians to assess couples for fertility, data suggest that many couples with male factor infertility are treated with ART prior to any male infertility assessment (45). Without any opportunity to assess this infertile male population, VR may never be presented as an option. In order to overcome this barrier of access to care, it is important that practicing urologists have a strong, open communication with practicing reproductive endocrinologists within the community.

ANTISPERM ANTIBODIES

The presence of semen antisperm antibodies (ASA) after vasectomy and subsequent reversal is occasionally considered a reason to seek IVF (46–49). Although vasectomy and subsequent VR invariably do lead to ASA, studies have shown no correlation of ASA to postreversal fertility (50–55). Understanding this lack of association is difficult, as in nonvasectomized men, ASA were shown to interfere with natural conception in a subfertile population (56, 57).

It is possible that the semen characteristics of postreversal men are substantially different than those of infertile men, which may explain the lack of effect of ASA in this subgroup. The rationale behind this is that these men are, in most cases, already proven fertile, and thus routine infertility parameters and guidelines may not be accurate. For instance, the World Health Organization (WHO) sperm reference ranges do not appropriately predict pregnancy rates in men after VR. Majzoub et al. (58) found that after surgery semen parameters of VR patients with spontaneous pregnancy were substantially lower than the WHO values. Pregnancy rates in this population were at their highest at a total motile sperm count (TMSC) of $>5 \times 10^6$ (pregnancy rate 71.4%). Under 5×10^6, the pregnancy rates dropped drastically to 27.9%. The effect of ASA may be different in this group as well.

The potential issue of ASA after VR arose because of the difference between anastomotic success (89%) and pregnancy rates (73%) following VR (6). This difference is likely because

of a multitude of contributing factors, including female partner age, presence of partial obstruction, and other clinical factors (5, 26, 53, 55). In a study that looked at competing risks for persistent infertility following VR, partial obstruction, not ASA, was found to be the main contributor (53). It is very unlikely that the formation of ASA in previously fertile men undergoing VR will lead to any deleterious effects.

Overall, we believe that ASA testing has a limited role in men after VR. In men with a significant difference between total and progressive motility, or in men with significant sperm agglutination on semen analysis, ASA testing should be performed. If ASA are thought to be contributing in these cases, steroids are rarely useful, whereas IUI with sperm washing is effective in couples who otherwise have normal TMSC. IVF is a reliable solution if IUI fails in these cases, or if the TMSC is low (59).

CONCLUSION

In conclusion, there are many factors to be considered during fertility planning for couples, including paternal age, maternal age, female factor infertility, OI, and cost of care. For couples in which the men have undergone vasectomies, there are very few situations in which VR or IVF cannot be considered. Fertility planning can take a mental, physical, and financial toll on couples. Each couple is unique, and what may work for one couple will not necessarily work for another. As physicians, we must consider the multifactorial complexities of fertility planning and provide our patients with a thorough explanation of their options, including the risks and benefits of both VR and IVF. Shared decision-making between the couple and the physician will ensure that the treatment chosen is the one most likely to result in both fertility success and overall patient satisfaction.

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