ORIGINAL ARTICLE

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The need for epididymovasostomy at vasectomy reversal plateaus in older vasectomies: a study of 1229 cases

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SUMMARY

Vasectomy reversal involves either vasovasostomy (VV) or epididymovasostomy (EV), and rates of epididymal obstruction and EV increase with time after vasectomy. However, as older vasectomies may not require EV for successful reversal, we hypothesized that sperm production falls after vasectomy and can protect the system from epididymal blowout. Our objective was to define how the need for EV at reversal changes with time after vasectomy through a retrospective review of consecutive reversals performed by three surgeons over a 10-year period. Vasovasotomy was performed with Silber score 1–3 vasal fluid. EVs were performed with Silber score 4 (sperm fragments; creamy fluid) or 5 (sperm absence) fluid. Reversal procedure type was correlated with vasectomy and patient age. Post-operative patency rates, total spermatozoa and motile sperm counts in younger (<15 years) and older (>15 years) vasectomies were assessed. Simple descriptive statistics determined outcome relevance. Among 1229 patients, 406 had either unilateral (n = 252) or bilateral EV's (n = 154) constituting 33% (406/1229) of reversals. Mean patient age was 41.4±7 years (range 22–72). Median vasectomy interval was 10 years (range 1–38). Overall sperm patency rate after reversal was 84%. The rate of unilateral (EV/VV) or bilateral EV increased linearly in vasectomy intervals of 1–22 years at 3% per year, but plateaued at 72% in vasectomy intervals of 24–38 years. Sperm counts were maintained with increasing time after vasectomy, but motile sperm counts decreased significantly ($p < 0.001$). Pregnancy, secondary azoospermia, varicocoele and sperm granuloma were not assessed. In conclusion, and contrary to conventional thinking, the need for EV at reversal increases with time after vasectomy, but this relationship is not linear. EV rates plateau 22 years after vasectomy, suggesting that protective mechanisms ameliorate epididymal 'blowout'. Upon reversal, sperm output is maintained with time after vasectomy, but motile sperm counts decrease linearly, suggesting epididymal dysfunction influences semen quality after reversal.

INTRODUCTION

Patients who desire fertility after vasectomy can choose vasectomy reversal or in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) using retrieved spermatozoa. Our previous decision modelling research showed that the achievable patency rate, or rate of return of motile spermatozoa to the ejaculate after reversal, is a key factor determining whether reversal surgery is more cost effective than assisted reproduction (Meng et al., 2005). We also defined predictors of early patency and time to patency after reversal (Yang et al., 2007). Predictors of early patency after reversal included motile spermatozoa in the intravasal fluid, vasovasovastomy procedure and vasectomy intervals of <8 years at reversal. Thus, as a prerequisite to pregnancy, reversal patency rate is a key predictive tool to assist couples in deciding between assisted reproduction or reversal for vasectomy-associated infertility.

In these analyses, we also observed that the patency rate and time to patency in 'older' vasectomies (i.e. >15 years) at reversal exhibited unexpectedly wide variation. Conventional thought from published algorithms suggests that the need for epididymovasostomy (EV) at reversal rises inexorably with time after vasectomy. A nomogram published by Fenig et al. (2012) predicts the need for EV at reversal using vasectomy obstructive interval and the presence of sperm granuloma as variables. Using this tool, as time after vasectomy increases the chance of needing an EV at reversal approaches 95% with a vasectomy interval of 35 years. Applying another linear regression-based algorithm incorporating patient age and vasectomy obstructive interval, 100% of men with sufficiently aged vasectomies will require an EV (Parekattil et al., 2005, 2006). These data suggest that eventually, as vasectomies age, epididymal 'blowout' will inevitably occur, and an EV will be required for successful reversal.

On the basis of our clinical observations and contrary to algorithmic experience, we hypothesized that adaptive factors exist within the reproductive tract that 'protect' the older vasectomy from epididymal 'blowout' such that an EV would not necessarily be required at reversal. We also predict that one such factor could be impaired sperm production, as originally described by Jarow in a study of testis histology at vasectomy reversal (Jarow *et al.*, 1985). The goal of this study was to further define how the prevalence of epididymal blowout and the need for EV at reversal changes over a broad spectrum of vasectomy time intervals in a large clinical cohort. Furthermore, we quantify ejaculated sperm output after reversal to better understand potential changes in spermatogenesis that occur with vasectomy.

MATERIALS AND METHODS

Patient characteristics

Charts of consecutive patients who underwent vasectomy reversal by three expert micosurgeons (P.J.T., S.F.M and P.J.B.) were reviewed and patient demographics, intra-operative findings and post-operative semen analyses were recorded. Patients were included only if the following intra-operative findings were known: type of reversal, sperm presence or absence and associated fluid findings from each testicular vas deferens. In bilateral cases, findings from both sides were required. In addition, two or more post-operative semen analyses were required to evaluate patency after reversal. As an exception, patients with 1 available semen analysis were included if it showed motile spermatozoa. The analysis of reversal patency rate also included patients without a post-operative semen analysis who had conceived naturally. However, this cohort was excluded from assessment of ejaculated sperm output after reversal. Cases of 'salvage' vasectomy reversals after failed prior procedures were included. Local institution review board approvals for retrospective chart reviews that did not involve patient contact were obtained for the study.

Vasovasostomy technique

The vasovasostomy procedure was performed by either the two-layer or modified one-layer microsurgical techniques, as previously described (Belker *et al.*, 1991). Prior to vasal anastomosis, gross appearance and sperm content of fluid from the testicular vas deferens was assessed in standard fashion (Yang *et al.*, 2007). Vasal fluid appearance was described as watery, opalescent, creamy or absent. Vasal spermatozoa were categorized as normal motile (Grade 1), mature non-motile (Grade 2), sperm heads with some normal spermatozoa (Grade 3), fragments (Grade 4) and absent (Grade 5) (Yang *et al.*, 2007).

Epididymovasostomy technique

A four- or six-point microscopic invagination EV was performed as previously described (Purohit & Turek, 2002). The decision to perform EV was based on the intra-operative finding of no spermatozoa (Grade 5) or occasional fragments (Grade 4) accompanied by thick, creamy vasal fluid.

Outcome measures

Post-operative semen analyses were recommended to all patients at 6 weeks and bimonthly thereafter until conception. Semen analyses were performed in one of two andrology labs and included measurement of semen volume, sperm concentration, motility and forward progression, according to WHO standards (WHO, 2010).

'Patency' after vasectomy reversal was defined simply as presence of motile spermatozoa in the ejaculate (Yang *et al.*, 2007). In vivo conception in the absence of semen analysis data was also deemed patency. In men with two or more semen analyses after reversal, the sample with the highest total motile count (ejaculate volume × sperm concentration × proportion of motile spermatozoa) was selected for analysis. The term vasectomy 'interval' used here is identical to vasectomy 'obstructive interval' in the literature. For this analysis, and based on published experience, vasectomies of various intervals were arbitrarily divided into two cohorts: 'younger' (vasectomy interval 0–15 years) and 'older' (vasectomy interval 16 years and higher) (Magheli *et al.*, 2010a). Pregnancy as a separate outcome was not assessed. Similarly, secondary azoospermia and complications were not evaluated. For these analyses, simple descriptive statistics including Student's *t*-tests (two- tailed) were used to assess relevance with a *p* value of <0.05 considered significant.

RESULTS

Subject characteristics

Overall, 1229 of 1694 possible (73%) patients from two institutions met study inclusion criteria. Mean patient age was 41.4 years (range 22–72 years), mean follow up was 4.4 months (range 1–90 months) and mean vasectomy interval was 9.8 years (range 1–38 years). Among excluded patients, 465 (27%) lacked post-operative semen analyses for review. A total of 105 cases (8.5%) were salvage vasectomy reversals. Among patients who underwent reversal with adequate follow-up, 406 men had either unilateral (*n* = 252) or bilateral EV's (*n* = 154) for an overall rate of 33% (406/1229) of reversals.

Relationship between vasectomy obstructive interval and type of reversal procedure

When vasectomy interval was stratified into three-year periods and plotted against the reversal procedure type (Fig. 1), two interesting patterns emerged. For vasectomies from 0 to 22 years of age, there was a relatively linear relationship between increasing vasectomy interval and the need for EV on one or both sides at reversal. We observed that the chance of needing an EV at reversal increased by 3% per year of time since vasectomy. However, this relationship changed after a vasectomy interval of 22 years as the effect plateaued (see best fit line in Fig. 1), implying that the need for EV does not increase further with vasectomy intervals of 22–38 years. This plateau suggests that a maximum of 72% of vasectomies will require either unilateral or bilateral EVs at reversal, regardless of the time interval since vasectomy.

Relationship between reversal patency rate and vasectomy obstructive interval

The overall patency rate among 1229 vasectomy reversal cases was 84% (range among vasectomy intervals 64–95%). In the 'younger' (age ≤15 years) vasectomy cohort, the mean patency rate was 93% compared to 75% among 'older' (>15 years) vasectomies, a difference that was significant (*p* = 0.01, *t*-test). As

observed in Fig. 2 (grey bars), in general, the patency rates in all stratified age groups of younger vasectomies was above 90% (range 92–95%), whereas the patency rates in cohorts of older vasectomies was <90% (range 64–87%). However, there was no specific point in the spectrum of vasectomy intervals that predicted a lower patency rate at reversal.

Relationship between sperm output and time after vasectomy

Sperm output after vasectomy reversal was assessed by semen analysis findings and evaluated in two ways: (i) total sperm

Figure 1 Relationship between vasectomy obstructive interval and type of reversal procedure. The need for epididymovasostomy (EV) at reversal increases linearly with vasectomy intervals up to 22 years, after which the need for a unilateral or bilateral EV flattens or plateaus. Absolute number of cases indicated at top of each vasectomy interval. White bars (□), grey bars (▨) and black bars (■) represent proportion of cases in each vasectomy age cohort that are bilateral VVs, unilateral VV-EV and bilateral EVs, respectively. VV/VV, bilateral vasovasostomy; VV-EV, unilateral vasovasostomy and epididymovasostomy; EV/EV, bilateral epididymovasostomy.
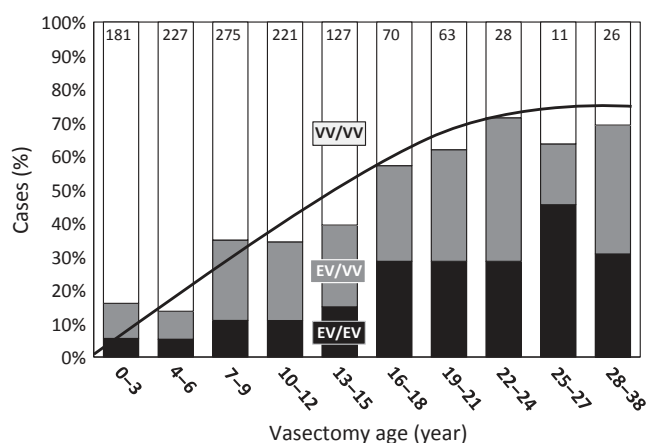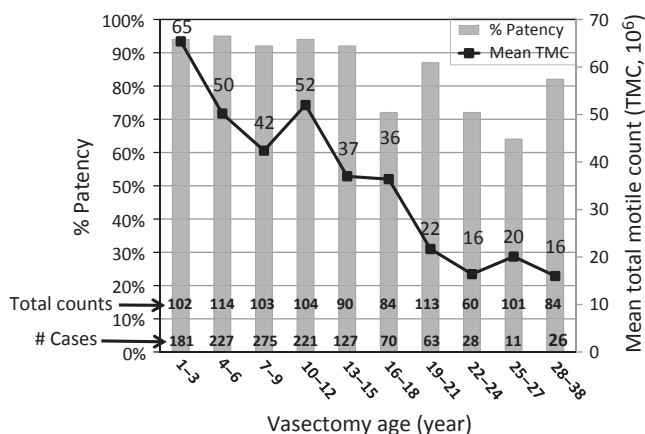

count (ejaculate volume × sperm concentration) as a measure of overall sperm output, and (ii) total motile sperm counts as a measure of functional sperm output. The rationale for assessing both parameters is that in an open or patent reproductive tract, total sperm output largely reflects testicular function, whereas total motile sperm output also incorporates the influence of epididymal function and motility maturation on sperm output (Turek, 2010).

As illustrated in Fig. 2, among patent cases after reversal, total sperm counts were excellent across all vasectomy time intervals, ranging from 60 million to 114 million spermatozoa/ejaculate. The mean total sperm counts after reversal of younger vasectomies was 103 million spermatozoa/ejaculate, not significantly different from that obtained from older vasectomies (84 million spermatozoa/ejaculate, $p = 0.34$). This suggests that despite differences in complexity in procedures performed for younger and older vasectomies, the total sperm output among patent cases after reversal is high and remarkably consistent.
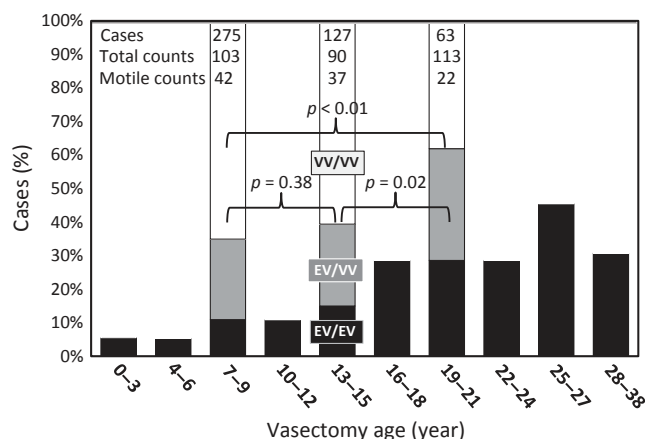
The total motile sperm output after reversal, however, was different in younger compared with older vasectomies. As illustrated in Fig. 2 (black line), the total motile sperm counts declined almost linearly as vasectomy intervals increased, decreasing 1.3 million motile spermatozoa/year after vasectomy. When the mean total motile counts from younger (49 million spermatozoa/ejaculate) and older (22 million spermatozoa/ejaculate) vasectomy intervals were compared, the difference was significant ($p < 0.001$). Notably, the mean age of subjects in the younger vasectomy group (39.8 years; SD 6.28) was significantly different ($p < 0.0001$) than those in the older vasectomy group (49.5 years; SD 7.14). The observed difference in motile sperm counts between younger and older vasectomies at reversal may therefore reflect paternal age differences in the cohorts, variations in the integrity of surgical anastomoses, relative impairment in epididymal function, presence of antisperm antibodies, oxidants from prolonged blockage or other alterations to spermatozoa after prolonged vasal obstruction.

Relationship between sperm output and type of vasectomy reversal procedure

To better understand the reason for lower motile sperm counts associated with reversal of older vasectomies, we performed a subset analysis. Our goal was to dissect out the influence of the increased need for more complex reversal procedures (i.e. EVs) in older vasectomies from other causes of low sperm motility after reversal. To control for the effect of procedural complexity on sperm findings, we compared the outcomes from younger and older vasectomy age cohorts that exhibited a similar composition of bilateral VV, VV-EV and bilateral EV cases. Unfortunately, it was not possible to find ideally case-matched groups, one young and one old, from among the various vasectomy time intervals (Fig. 1). However, we chose the most closely matched cohorts and statistically compared sperm outputs among them (Fig. 3).

When comparing the sperm output in 7- to 9-year-old vasectomies to 13- to 15-year-old vasectomies, there was no difference in total sperm output or total motile sperm output after reversal (Fig. 3). However, when comparing either of these cohorts to an older cohort (vasectomy age 19–21 years) that was most similar in procedural complexity, the older cohort (19–21 years) exhibited a significant decrease in total motile sperm output relative

Figure 2 Relationship between vasectomy obstructive interval and reversal patency and sperm output rates. Total sperm output after reversal is high across all vasectomy ages. However, total motile sperm count decreases significantly across same. Grey bars (▨) denote patency rates for each vasectomy age cohort. The black line denotes the total motile sperm output across all cohorts, with exact numerical values provided for each cohort. Within the graph, the numbers at the bottom are the number of reversal cases within each age cohort. The numbers immediately above the case numbers indicate the total sperm count in millions of spermatozoa/ejaculate for each vasectomy age cohort. TMC, total motile count of spermatozoa (in millions).

Figure 3 Relationship between sperm output and type of vasectomy reversal procedure. Derived from Fig. 1, this figure analyses the sperm output findings after reversal from three individual vasectomy intervals: 7–9, 13–15 and 19–21 years. These cohorts were chosen based on similarity of case composition and the need for a sufficient difference in vasectomy obstructive intervals to detect any differences in sperm output. Notably, although total sperm counts did not differ among the three vasectomy intervals, total motile sperm counts differed significantly between 7–9 and 19–21 years groups and 13–15 and 19–21 years groups, but not between 7–9 and 13–15 years groups. Total counts, mean total sperm counts/ejaculate; motile counts, mean total motile sperm counts/ejaculate. Listed *p* values refer only to differences in total motile counts.

to both younger cohorts (Fig. 3). This finding of maintained total sperm output along with dramatically lower sperm motility after reversal of complexity-matched, older vasectomies suggests, but in no way proves, that other factors besides the surgical procedure influences semen quality after reversal of older vasectomies.

DISCUSSION

The goal of this study was to define how the prevalence of epididymal blowout and the need for EV at reversal changes with time after vasectomy over a broad spectrum of vasectomy intervals in a large clinical cohort. We also sought to quantify ejaculated sperm output after reversal to better understand potential changes that occur in the reproductive tract with prolonged blockage. Viewed in the context of other, generally smaller, contemporary series of vasectomy reversal studies, our overall sperm patency rates compare very favourably across all vasectomy intervals (Lee, 1986; Matthews *et al.*, 1995; Kolettis *et al.*, 2002; Purohit & Turek, 2002; Schiff *et al.*, 2005; Yang *et al.*, 2007; Hsiao *et al.*, 2012; Schwarzer, 2012; Schwarzer & Steinfatt, 2013). In addition, the case complexity in this series mirrors those in other large series of reversals, such that 30-40% of cases involve at least unilateral EV (Yang *et al.*, 2007; Fuchs & Burt, 2002; Hsiao *et al.*, 2012; Schwarzer & Steinfatt, 2013). Uniquely, this large cohort analysis of reversals focuses on procedural performance among dedicated microsurgeons, and more specifically compares outcomes after reversal of 'younger' and 'older' vasectomies.

One clear finding is the demonstration of a 'plateau' effect in the need for EV relative to vasectomy obstructive interval at the time of reversal. Contrary to predictions based upon 'calculated' wisdom from algorithmic experience (Parekattil *et al.*, 2005, 2006; Fenig *et al.*, 2012), not all men require epididymal bypass

surgery with prolonged time after vasectomy. In fact, it appears that fully one-fourth of men will avoid EV regardless of vasectomy obstructive interval.

This finding begs the question of what biological alterations occur to prevent an epididymal 'blowout' with time after vasectomy. Our hypothesis was that sperm production is impaired by prolonged obstruction and that this 'protects' the system from epididymal 'blowout'. This is based on published evidence of adverse changes in testis histology that occur after vasectomy, and the observation of significantly different patency rates after similar procedures (EVs) were performed in older compared with younger vasectomies (Jarow *et al.*, 1985; Schoor *et al.*, 2002) Instead, we observed that total sperm output remains constant amongst patent cases after reversal, regardless of obstructive interval (Fig. 2). In fact, this finding supports previous observations that sperm counts among patent reversal cases are preserved across all vasectomy obstructive intervals (Magheli *et al.*, 2010a,b). We acknowledge that this does not exclude the possibility that some men can have dramatic impairments to sperm production after vasectomy (as these men may in fact may not have shown patency in this series), but it suggests that the majority of men who have vasectomies do not have impaired sperm output after prolonged obstruction.

The finding of maintained total sperm output along with dramatically lower sperm motility (Fig. 3) after reversal among complexity-matched vasectomies of various intervals suggests, but in no way proves, that other factors exist besides technical or microsurgical issues influence semen quality after reversal of older vasectomies. What else could account for our observation of a decline in motile sperm counts with prolonged time after vasectomy? We noted a significant difference (10 years) in the mean ages of men with younger compared with older vasectomies. Based upon this age difference, and the published observation that sperm motility decreases 0.7%/year after age 30 years, one would expect a paternal age-related motility decline of 7% in older compared with younger vasectomies in our series (Smith & Walsh, 2013). However, more impressive declines in motility were in fact observed that are not entirely explained by paternal age. Persistent immunological reactions within the epididymis and to spermatozoa (Hinz *et al.*, 2010), increased oxidants (Nandipati *et al.*, 2005), the presence of 'partial' anastomotic blockages or other irreversible epididymal dysfunction impairing sperm maturation after prolonged obstruction are other possible explanations. In fact, recently described molecular changes in epididymal gene profiles after vasectomy, some of which are irreversible, also support the concept that epididymal dysfunction contributes to loss of motile spermatozoa after reversal of older vasectomies (Thimon *et al.*, 2008; Sullivan *et al.*, 2011) Thus, the balance of clinical and molecular evidence supports the idea that spermatogenesis is well maintained as vasectomies age but epididymal function is altered.

This study does have limitations. Regarding patient selection bias, 23% of potential study subjects were excluded from analysis because of insufficient post-operative semen analyses. Arguably, many of these men established natural pregnancies which suggests patency, but it remains unclear how their exclusion affects sperm output findings. Given that our intent was to explore factors influencing patency and quantitative sperm output after reversal, the absence of complete pregnancy data

does not significantly limit our conclusions. What may be more limiting is our inability to dissect out the effects of the following on patency rate and sperm output after reversal: vasectomy location within the vas deferens, the presence or absence of a sperm granuloma or varicocoele, the effect of partial anastomotic strictures, the relatively short post-operative follow-up and underlying sperm production abnormalities pre-vasectomy. In addition, the use of ejaculated sperm output in this study is certainly a convenient way to assess spermatogenesis, but may not accurately reflect ongoing testicular function. Finally, complications and secondary azoospermia rates were also not assessed but can have a significant impact on fertility outcomes.

CONCLUSIONS

This study defined how the prevalence of epididymal blowout and the need for epididymovastomy (EV) at vasectomy reversal change with time after vasectomy. In a large clinical cohort, it showed that there is a linear increase in the need for EV (unilateral or bilateral) until a vasectomy interval of 22 years, after which the need for EV during reversal plateaued at 72% of cases. In addition, among patent reversal cases, ejaculated sperm output was maintained across all vasectomy intervals, but motile sperm counts declined linearly with time after vasectomy, decreasing by about 1.3 million motile spermatozoa/ejaculate/year. Molecular and clinical evidence implicates epididymal dysfunction as a significant factor affecting motile sperm output after reversal. How these changes influence fertility rates after reversal needs further study.

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