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Varicocelectomy to "upgrade" semen quality to allow couples to use less invasive forms of assisted reproductive technology

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Objective: To determine the magnitude of improvement in semen parameters after a varicocelectomy and the fraction that have improvements such that couples needing IVF or IUI are "upgraded" to needing less invasive assisted reproductive technology (ART).
Design: Retrospective review of prospectively collected data.
Setting: Academic medical centers.
Patient(s): Men presenting for a fertility evaluation with a clinical varicocele.
Intervention(s): Varicocele repair (surgical or embolization).
Main Outcome Measure(s): Total motile sperm count (TMSC) before and after repair, and the proportion of men considered candidates for: natural pregnancy (NP) >9 million, IUI 5–9 million, or IVF < 5 million.
Result(s): A total of 373 men underwent varicocele repair. The TMSC increased from 18.22 ± 38.32 to 46.72 ± 210.92 (P=.007). The most pronounced increase was with baseline TMSC <5 million, from 2.32 ± 1.50 to 15.97 ± 32.92 (P=.0000002); 58.8% of men were upgraded from IVF candidacy to IUI or NP. For baseline TMSC 5–9 million, the mean TMSC increased from 6.96 ± 1.16 to 24.29 ± 37.17 (P=.0004), allowing 64.9% of men to become candidates for NP. For baseline TMSC of >9 million, TMSC increased from 36.26 ± 52.08 to 81.80 ± 310.83 (P=.05).
Conclusion(s): Varicocele repair has an important role in the treatment of infertility. Even for low TMSCs, a varicocelectomy may reduce the need for IVF. Varicocele repair (by embolization or microsurgery) potentially reduces the need for IVF and IUI. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: Varicocele, semen, assisted reproductive technology, intrauterine insemination, in vitro fertilization

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Varicoceles are the most commonly seen and correctable male infertility factor (1). Varicoceles have an incidence of 4.4%–22.6% in the general population, 21%–41% in men with primary infertility, and 75%–81% in men with secondary infertility (2, 3). Although many men with varicoceles are able to father children, in some men varicoceles will negatively impact their fertility. This may manifest with impaired semen parameters (4), reduced natural pregnancy (NP) rates (5), lower IUI pregnancy rates (PRs) (6), lower IVF PRs (7), and/or higher rates of sperm DNA damage (8).

In some men, repair of varicoceles will result in an improvement in semen parameters or sperm DNA health. As such, it is the practice guideline of the American Urological Association and American Society of Reproductive Medicine that varicocele repair be offered to subfertile men with a palpable varicocele and one or more abnormal semen parameters (9, 10). Varicocele repair may result in improvements in semen parameters (4), sperm DNA fragmentation (8), NP rates (5), IUI PRs (6), and IVF PRs (7).

Although varicocele repair results in improved semen quality in most infertile men, the degree of improvement in

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semen parameters is less well studied. One study of 530 infertile men with a clinical varicocele found that varicocele repair may also allow for less invasive modalities of assisted reproductive technology (ART) to be used by couples (11). We sought to determine the magnitude of improvement in semen parameters after a varicocelectomy and what fraction of the men might have improvements such that couples needing IVF or IUI might be "upgraded" to needing less invasive ART.

MATERIALS AND METHODS

Men presenting for evaluation at a Male Infertility specialty clinic from 2008 to 2012 who underwent repair (microsurgical subinguinal or embolization) of a clinical varicocele were identified by a prospectively collected database. The data were reviewed in a retrospective manner. A varicocele was palpable in all cases, as performed by a fellowship-trained specialist in male infertility (A.Z., E.G., K.L., or K.J.). Physical examination for varicocele was performed according to the Dubin grading system with the patient upright in a heated examination room (12). The collection and the analysis of this data were approved by the Research Ethics Board of the Mount Sinai Hospital.

In brief, the microscopic subinguinal approach involved the following surgical technique. A 3- to 5-cm incision was made over the inguinal canal. The spermatic cord was elevated and the spermatic cord fascia opened. The testicle was not routinely delivered. Under the operative microscope, each component of the spermatic cord was identified. A microscopic Doppler was used to identify these as either arteries or veins. The veins were ligated using either sutures or surgical clips. The vas deferens, testicular arteries, and any lymphatic channels were preserved. For the percutaneous varicocele embolization, under venogram guidance, 0.018 coils were placed in the dilated main channel of the gonadal vein and back-filled, followed by 1-mL aliquots of sotradecol foam.

Semen analysis was performed using a standard protocol with a computer-assisted semen analysis technique (World Health Organization [WHO] 2010) (13). Semen parameters were analyzed for volume, sperm count, sperm motility, sperm morphology, and total motile sperm count (TMSC) before and after varicocele repair. Semen samples were collected at least 48 hours, but not >7 days, after the time of last ejaculation. After varicocele repair, semen analyses were performed at 3 months and for some men again at 6 months. The principal parameter used was the TMSC as this is often used as a means of deciding whether couples will require IVF or IUI. The TMSC was calculated before and after varicocele repair by the formula, TMSC = ejaculate volume × concentration × motile fraction, in all semen analyses.

For the purposes of this study, men were divided into three groups, as stratified by their baseline TMSC. These groups were representative of the type of ART that may have been recommended if varicocele repair was not performed to minimize the male factor infertility. Men with TMSC <5 million were considered candidates for IVF, 5–9 million for IUI, and >9 million for NP. Men were then regrouped after varicocele repair into the same three groups to determine changes in ART candidacy after varicocele repair. Student's *t*-test was used to compare changes in the semen parameters, with $P < .05$ considered indicative of significant differences.

There is known variability in semen parameters. To determine whether the improvements in semen parameters after varicocelectomy were due to the natural variability in the semen parameters or due to the varicocelectomy itself, we compared the changes in the first and second semen parameters before varicocelectomy to the changes in the semen parameters before and after varicocelectomy. We performed a χ^2 test on these groups comparing the fraction of men within each group who were "upgraded."

RESULTS

We identified 373 men who underwent varicocele repair. The mean age was 35 years (range, 23–62 years). Varicocelectomy was bilateral in 174 (46.6%), left side only in 198 (53.1%), and right side only in 1 (0.2%). Sixty-eight (18.2%) of the repairs were performed by radiographic embolization and 305 (81.8%) were performed by microsurgical subinguinal varicocelectomy. A total of 186 (49.9%) men had unilateral varicoceles and 187 (50.1%) had bilateral varicoceles. With respect to maximum varicocele grade, 38 of 166 men had a grade 1 varicocele, 66 of 166 had a grade 2 varicocele, and 62 of 166 had a grade 3 varicocele; 205 men did not have the grade of their varicocele noted. A total of 84 of the men had 2 semen analyses before repair and 97 men had 2 semen analyses after repair. The mean of these values was calculated and used for analysis.

The results are presented in Tables 1 and 2. Before varicocele repair, 168 of 373 men (45%) had TMSC >9 × 10^6 and were considered to have high enough TMSCs to be

TABLE 1

Total motile sperm count before and after varicocele repair.

Characteristic	Before varicocele repair TMSC (million sperm/mL)	After varicocele repair TMSC (million sperm/mL)	*P* value
IVF (<5 million)	2.32 ± 1.50	15.97 ± 32.92	.0000002
IUI (5–9 million)	6.96 ± 1.16	24.29 ± 37.17	.0004
Natural pregnancy (>9 million)	36.26 ± 52.08	81.80 ± 310.83	.05
All men	18.22 ± 38.32	46.72 ± 210.92	.007

Note: Data presented as mean ± standard deviation, unless noted otherwise. TMSC = total motile sperm count.

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