Varicocelectomy before assisted reproductive technology: are outcomes improved?

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Clinical varicoceles have been associated with impaired semen parameters and male-factor infertility. Varicocele repair can improve live birth rates for men with clinical varicocele. Varicocelectomy is often combined with assisted reproductive techniques (ART) such as intrauterine insemination (IUI), in vitro fertilization (IVF), or intracytoplasmic sperm injection (ICSI). Here we review the literature examining varicocelectomy before ART to evaluate whether improved pregnancy outcomes are realized. Although insufficient evidence exists to determine if correcting a varicocele improves IUI outcomes, a clinical benefit is observed when correcting a clinical varicocele in oligospermic and nonobstructed azoospermic men before IVF/ICSI. In couples seeking fertility with the use of ART, varicocele repair may offer improvement in semen parameters and may decrease the level of ART needed to achieve successful pregnancy. (Fertil Steril® 2017;108:385–91. ©2017 by American Society for Reproductive Medicine.)

Key Words: Varicocele, varicocelectomy, intrauterine insemination, in vitro fertilization, intracytoplasmic sperm injection

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Infertility is defined as the inability to conceive after 1 year of unprotected intercourse (1). It is estimated that one in six couples experience infertility in their lifetime (2). Of these infertile couples, a male factor plays a role in 50% of cases (3). The most common and correctable cause of male-factor infertility is a varicocele. Although varicoceles are present in 15%–20% of postpubertal men, those presenting to infertility clinics have varicoceles at 2–3 times the frequency found in the general population and in those with proven fertility (4, 5). In a World Health Organization study of 9,034 infertile men, a varicocele was identified in 25.4% of men with abnormal semen parameters compared with only 11.7% of men with normal semen parameters (6). Although the mechanism of impaired sperm production resulting from varicocele has not been clearly established, poor testicular drainage may result in varicocele-associated testicular dysfunction (7).

A varicocele is a pathologic dilation of the pampiniform venous plexus of the spermatic cord, one of three venous drainage pathways of the testicle. Clinically, the dilated venous plexus is graded by size: subclinical (detected by ultrasound only), grade I, grade II, or grade III. Several etiologies for varicocele have been proposed. The veins of the pampiniform plexus may have dysfunctional valves, permitting retrograde blood flow and pooling close to the testicle. The left gonadal vein joins with the left renal vein at a perpendicular angle, leading to increased venous pressure compared with the right. Varicoceles can also result from left renal vein compression between the superior mesenteric artery and the abdominal aorta (the "nutcracker effect") (8–10).

Numerous theories have been proposed for how poor testicular drainage impairs fertility. An early study by Goldstein et al. in 1989 demonstrated that intratesticular and scrotal temperatures were higher in men with a varicocele compared with control subjects without a varicocele, suggesting that testicular hyperthermia induced by varicocele may impair sperm production (11). Other studies have found that men with varicocele have more reflux of adrenal metabolites in penile blood, testicular hypoxia, antisperm antibodies, and reactive oxygen species in sperm compared with men without varicoceles (12–14). These biochemical changes have been implicated in testicular atrophy, higher levels of

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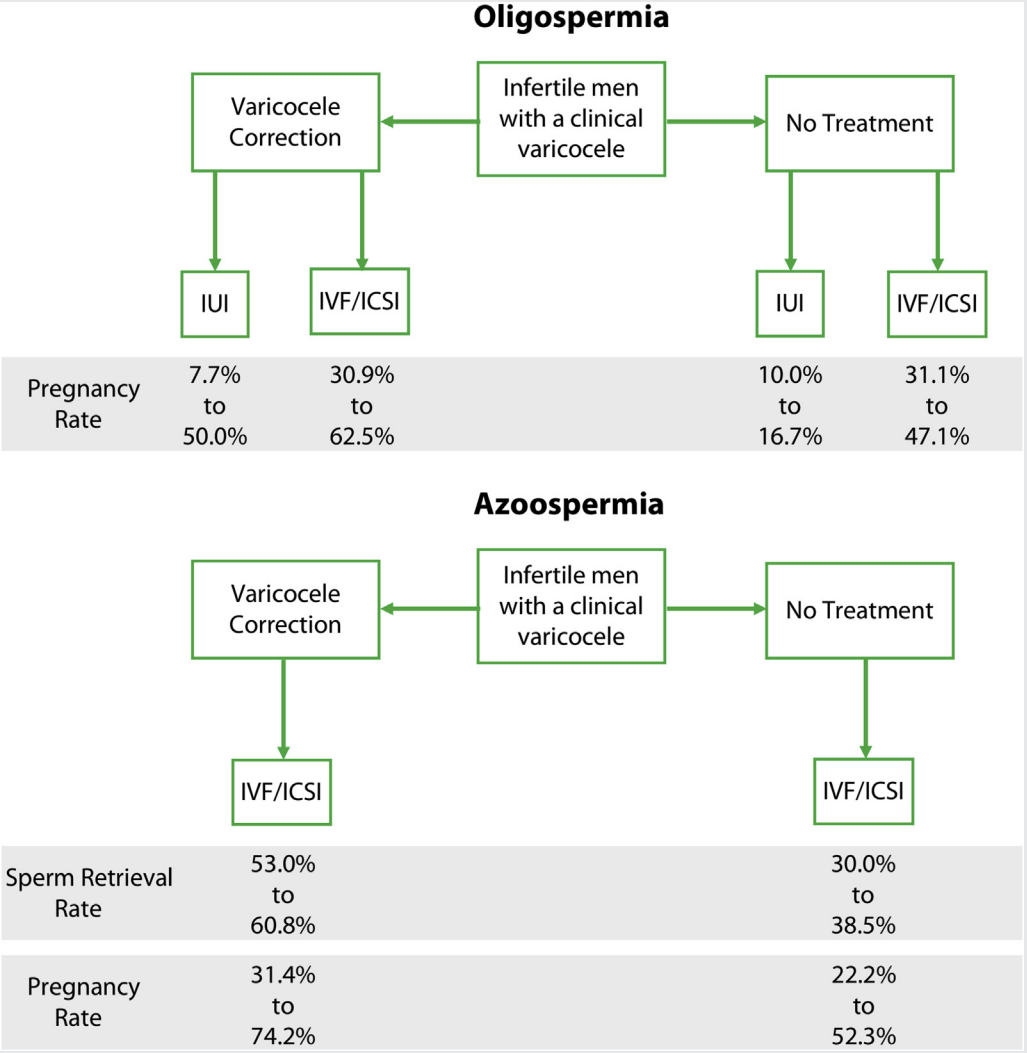
reactive oxygen species, and decreased testosterone production by Leydig cells (13,15–17). A recent study from Mostafa et al. found that men with varicoceles have elevated levels of apoptosis-associated microRNA in seminal fluid (18). Ultimately, it may be a combination of these factors that result in impaired fertility.

The correction of a varicocele can be performed in numerous ways, microsurgical ligation being the most effective; venous embolization is another common option. Several randomized controlled trials and meta-analyses have found that in men with both a varicocele and abnormal semen parameters, varicocelectomy improves the chances of achieving a pregnancy (17,19–21). Although the studies demonstrated a benefit in pregnancy outcomes, whether improvement in pregnancy outcomes after surgical correction of a clinical varicocele is due to improvement in typical semen parameters is unclear, because several studies and meta-analyses have demonstrated improvement in only one semen parameter or no improvement at all after varicocelectomy, despite increases in pregnancy and live birth rates (22, 23). However, several studies have demonstrated improvements in sperm DNA fragmentation and in the presence of reactive oxygen species after surgical correction of varicocele (24–28). These molecular-level improvements may explain why varicocelectomy results in improved pregnancy rates although traditional semen parameters remain relatively unchanged.

Assisted reproductive techniques (ART), such as intrauterine insemination (IUI), in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI), can be used to help infertile couples achieve a pregnancy. In the United States and Europe, more than 348,000 cycles of IVF and 400,000

FIGURE 1



Summary of possible assisted reproductive techniques and range of pregnancy rates and sperm recovery rates for men with a clinical varicocele and oligospermia or azoospermia. ICSI = intracytoplasmic sperm injection; IUI = intrauterine insemination; IVF = in vitro fertilization.

Kohn. Impact of varicocelectomy on IUI or IVF/ICSI. Fertil Steril 2017.

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