Is a Varicocelectomy Beneficial in the Era of Assisted Reproductive Technologies

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Abstract
Clinical varicoceles are the most frequent physical finding associated with infertile men and impaired semen parameters. There is evidence that suggests varicocelectomy repair improves semen parameter and increases the chance of natural pregnancy. Today, varicocelectomy repair is often combined with assisted reproductive techniques (ART) such as intrauterine insemination (IUI), in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI). In this literature review, data examining whether varicocelectomy before ART leads to improved pregnancy outcomes is reviewed. Current data suggest that there is a significant clinical benefit when correcting a varicocele in oligospermic men before IVF/ICSI. Similarly, men with non-obstructive azoospermia also benefit from varicocelectomy before IVF/ICSI, but not significantly. Furthermore, in couples seeking to use ART to conceive, varicocelectomy may offer improvement in semen parameters and therefore, decrease the level of ART needed to achieve pregnancy.

Keywords: Varicocele, varicocelectomy, in vitro fertilization, intracytoplasmic sperm injection, efficacy, cost effectiveness

Introduction
A varicocele is an enlargement (or dilation) of the veins within the scrotum that provide testicular venous drainage. Clinically, it is graded by a size grade: grade I (palpable only during Valsalva maneuver), grade II (palpable in the standing position) and grade III (visible without palpation).

Although present in 15% of the male population, varicoceles are prevalent in 30–50% of men with primary infertility

Several studies have reported a link between varicoceles and increased testicular hypoxia, elevated testicular temperature, increased testicular venous pressure, DNA fragmentation and ROS (associated with abnormal sperm morphology, and reduced motility)

With the rise of assisted reproductive technologies (ARTs) such as in vitro fertilization (IVF) and intracytoplasmic sperm injections, questions have been raised about the need for a varicocelectomy

This paper aims to explore and summarize current varicocele treatment options and their efficacy, varicocelectomy repair in combination with ART and finally, cost effectiveness for treatment of infertility using varicocelectomy versus ART as a combination of both.

Statement of the Problem
The role of clinical varicocele in male infertility and reduced semen parameters has been well established, dating back to studies conducted as early as 1965. Subsequently, studies have shown that varicocelectomy repair can improve live birth rates for men with clinical varicocele. However, in the advent of ARTs and their proven effectiveness in achieving live birth for couples with infertility issues, the question remains whether varicocelectomy repair should be considered before ART in order to increase success with ARTs.

Research Question
• In men with clinically diagnosed varicocele, does the method of varicocelectomy chosen (ligation vs embolization) improve fertility outcomes?
• In men with oligospermia vs azoospermia with a varicocele, does varicocelectomy before ART improve fertility outcomes?
• In men with clinically diagnosed varicocele, is it cost effective to undergo a varicocelectomy before ART?

Literature Review

Efficacy or Outcome of Varicocele Treatment
• Per the American Urological Association and American Society of Reproductive Medicine, varicoceles should be considered for men with a palpable varicocele, abnormal semen parameters, documented infertility, and a female partner with normal fertility or potentially correctable female infertility.

• Current treatment approaches to varicocele repair include surgical ligation (retroperitoneal/open, subinguinal ligation, ligation, inguinal ligation, microsurgical subinguinal ligation and laparoscopic) or percutaneous embolization.

• In a meta-analysis by Schauer et al. (2012) comparing subinguinal, subinguinal and inguinal ligation for treatment of varicocele, all three treatments led to significantly improved semen parameters with a mean increase in sperm count of 10.85 x 10^6/mL (95% CI 3.16-18.54; P = 0.006), 7.17 x 10^6/mL (95% CI 3.73-10.61; P = 0.001) and 9.75 x 10^6/mL (95% CI 3.38-16.02; P = 0.002), respectively, and a mean increase in sperm motility of 6.80% (95% CI 3.95-9.66; P = 0.0001), 9.44% (95% CI 3.72-15.16; P = 0.001) and 12.25% (95% CI 4.76-19.75; P = 0.001), respectively.

Efficacy of Varicocelectomy in Men with Oligospermia Before Assisted Reproduction

<table>
<thead>
<tr>
<th>Study</th>
<th>Varicocele Before IVF/ICSI</th>
<th>Cost of Treatment</th>
<th>Cost per Live Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inci et al. (2009)</td>
<td>$33,486</td>
<td>$22,114</td>
<td></td>
</tr>
<tr>
<td>Pasqualotto et al. (2012)</td>
<td>$22,122</td>
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</tbody>
</table>

Cost effectiveness of varicocelectomy before assisted reproduction
• In couples with a clinical varicocele associated with oligospermia, varicocelectomy and IUI provide the least expensive intervention when compared to IVF/ICSI (Penson et al., 2002).

Discussion

• Varicocelectomy has a greater benefit for men with clinical varicocele and oligospermia compared to men with non-obstructive azoospermia.

• Men with NOA may benefit more from direct testicular extraction than IVF/ICSI.

• Nevertheless, evidence has shown that in some men with NOA, varicocele repair can lead to slight improvement in seminal concentration in the ejaculate, thus eliminating the need for testicular extraction before IVF/ICSI.

In regard to cost, current literature supports the recommendation of repair before ART for oligospermic or severely oligospermic patients and as a cost effective measure, but shows that in men with NOA, immediate testicular extraction is a better option.

Applicability to Clinical Practice
• Per the Society for Reproductive Medicine, recommendations for varicocelectomy are to be offered to men attempting to conceive only when there is (1) a palpable varicocele, documented infertility, one or more abnormal semen parameter and the female partner has normal fertility or potentially correctable female infertility.

• Research suggests that varicocelectomy has a greater benefit for men with clinical varicocele and oligospermia compared to men with non obstructive azoospermia.

• As such, the latter may benefit more from direct testicular extraction before IVF/ICSI.

• Other considerations include maternal age; advancement in age reduces the success of IVF/ICSI. Therefore, delaying IVF/ICSI in place of a varicocelectomy may be inadvisable.

• Number of children desired is another; if only one child is desired, ART may be better especially in men with NOA, whereas if multiple children are desired, varicocelectomy may be of benefit in increasing the chances of spontaneous pregnancy

• The main point here is that each patient should be treated on a case by case basis guided by these recommendations

References


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