2019

Is a Varicocelectomy Beneficial in the Era of Assisted Reproductive Technologies?

Chukwuka Oscar Nnoli
University of North Dakota

Is a Varicocelectomy Beneficial in the Era of Assisted Reproductive Technologies?

Chukwuka Oscar Nnoli
Department of Physician Assistant Studies, University of North Dakota School of Medicine & Health Sciences
Grand Forks, ND 58202-9037

UND School of Medicine & Health Sciences
University of North Dakota

Abstract

Clinical varicoceles are the most frequent physical finding associated with infertile men and impaired semen parameters. There is evidence that suggests varicocele repair improves semen parameter and increases the chances of natural pregnancy. Today, varicocele 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 scale: grade I (palpable only during Valsalva maneuver), grade II (palpable in the standing position) and grade III (visible without palpation)
- Although only 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 hypertension, 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, varicocele repair in combination with ART and finally, cost effectiveness for treatment of infertility using varicocelectomy versus ART or 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 varicocele 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 varicocele 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 embolectomy) 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, varicocelectomy 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, suprainguinal ligation, ligation, inguinal ligation, microsurgical subinguinal ligation and laparoscopic) or percutaneous embolization.
- In a meta-analysis by Schauer et al. (2012) comparing suprapubic, 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 3.48-16.02; P 0.002), respectively; and a mean increase in sperm motility of 6.80% (95% CI 3.95-9.66; P < 0.00001), 9.44% (95% CI 3.72-15.16; P = 0.001) and 12.25% (95% CI 4.76-19.75; P = 0.001), respectively.

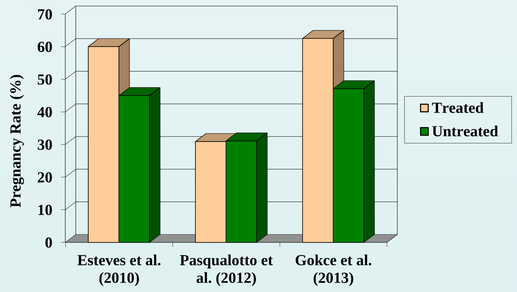
Efficacy of Varicocelectomy in Men with Oligospermia Before Assisted Reproduction

TABLE 1

Pregnancy outcomes following IVF/ICSI for Oligospermic men with treated and untreated varicoceles

	Treated Varicocele			Untreated Varicocele			Statistical Sig.?
Study	**Preg.**	**Couples**	**Preg. rate**	**Preg.**	**Couples**	**Preg. rate**	***P<0.05***
Esteves et al. (2010)	48	80	60.0%	73	162	45.0%	Yes
Pasqualotto et al. (2012)	52	169	30.9%	25	79	31.1%	No
Gokce et al. (2013)	105	168	62.5%	65	139	47.1%	Yes

Impact of varicocele repair on pregnancy rates following IVF/ICSI



Efficacy of Varicocelectomy in Men with Non-obstructive Azoospermia (NOA) Before Assisted Reproduction

- With advances in ART, such as testicular sperm extraction (TESE) and ICSI combined with varicocelectomy, urologist are now able to offer fertility treatment to couples whose male partner has NOA
- Inci et al. (2009), Haydardedeoglu et al. (2012) and Esteves et al. (2016), each showed that men who underwent a varicocele repair had significantly greater sperm retrieval rate via TESE than men who did not (P = 0.036, 0.01 and 0.001, respectively)

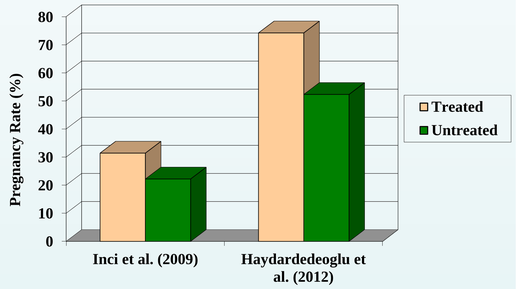
Literature Review Cont'd

TABLE 2

Pregnancy outcomes following IVF/ICSI for non-obstructed azoospermic men with treated and untreated varicoceles

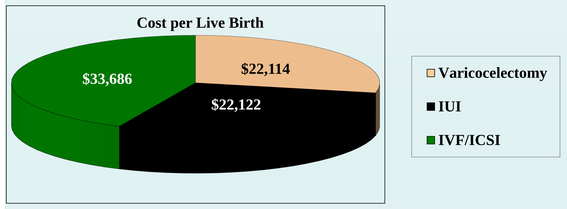
	Treated Varicocele			Untreated Varicocele			Statistical Sig.?
Study	**Preg.**	**Couples**	**Preg. Rate**	**Preg.**	**Couples**	**Preg. rate**	***P<0.05***
Inci et al. (2009)	21	66	31.4%	7	30	22.2%	No
Haydardedeoglu et al. (2012)	23	31	74.2%	34	65	52.3%	Yes

Impact of varicocele repair on pregnancy rates following IVF/ICSI



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).



- In couples with a clinical varicocele associated with NOA, directly proceeding to TESE then IVF/ICSI was more cost effective than undergoing a varicocelectomy before IVF/ICSI when direct and indirect costs were considered, $69, 731 vs $75, 576 respectively (Lee et al., 2009)

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 infertility.
- Research presented shows 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

- Esteves, S. C., Oliveira, F. V., & Bertolla, R. P. (2010). Clinical outcome of intracytoplasmic sperm injection in infertile men with treated and untreated clinical varicocele. *The Journal of Urology*, 184(4), 1442–1446. https://doi.org/10.1016/j.juro.2010.06.004
- Esteves, S., Miyaoka, R., Roque, M., & Agarwal, A. (2016). Outcome of varicocele repair in men with nonobstructive azoospermia: Systematic review and meta-analysis. *Asian Journal of Andrology*, 18(2), 246. https://doi.org/10.4103/1008-682x.169562
- Gokce, M. I., Gülpınar, Ö., Süer, E., Mermerkaya, M., Aydos, K., & Yaman, Ö. (2013). Effect of performing varicocelectomy before intracytoplasmic sperm injection on clinical outcomes in non-azoospermic males. *International Urology and Nephrology*, 45(2), 367–372. https://doi.org/10.1007/s11255-013-0394-2
- Haydardedeoglu, B., Turunc, T., Kilicdag, E. B., Gul, U., & Bagis, T. (2010). The effect of prior varicocelectomy in patients with nonobstructive azoospermia on intracytoplasmic sperm injection outcomes: A retrospective pilot study. *Urology*, 75(1), 83–86. https://doi.org/10.1016/j.urology.2009.09.023
- Inci, K., Hascicek, M., Kara, O., Dikmen, A. V., Gürgan, T., & Ergen, A. (2009). Sperm retrieval and intracytoplasmic sperm injection in men with nonobstructive azoospermia and treated and untreated varicocele. *The Journal of Urology*, 182(4), 1500–1505. https://doi.org/10.1016/j.juro.2009.06.028
- Lee, R., Li, P. S., Goldstein, M., Schattman, G., & Schlegel, P. N. (2009). A decision analysis of treatments for nonobstructive azoospermia associated with varicocele. *Fertility and Sterility*, 92(1), 188–196. https://doi.org/10.1016/j.fertnstert.2008.05.053
- Pasqualotto, F. F., Braga, D. P., Figueira, R. C., Setti, A. S., Iaconelli, A., & Borges, E. (2012). Varicocelectomy does not impact pregnancy outcomes following intracytoplasmic sperm injection procedures. *Journal of Andrology*, 33(2), 239–243. https://doi.org/10.2164/jandrol.110.011932
- Penson, D. F., Paltiel, A. D., Krumholz, H. M., Palter, S. (2002). The cost-effectiveness of treatment for varicocele related infertility. *The journal of Urology*, 68(6), 2490–2494. https://doi.org/10.1016/s0022-5347(05)64175-4
- Report on varicocele and infertility: a committee opinion. (2014). *Fertility and Sterility*, 102(6), 1556–1560. https://doi.org/10.1016/j.fertnstert.2014.10.007

Acknowledgements

- To my wife, Briona and family, thank you for all your support and encouragement
- I wish to express my most sincere appreciation to the faculty and staff over the course of this program and a special thank you to Daryl Sieg, PA-C for his patience and willingness to answer countless questions.
- I would also like to thank Dawn Hackman and Dr. Marilyn G. Klug for their assistance and expertise