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The Impact of Varicocele on Hormonal Function in Hypogonadal and Eugonadal Men: Literature Review

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ABSTRACT

Introduction: Varicocele is a common condition affecting up to 15% of men. It is associated with impaired testicular function due to venous reflux and oxidative stress. While its role in male infertility is well established, the extent to which it impacts hormonal function, particularly testosterone production, is still being debated. The purpose of this review was to evaluate the hormonal outcomes of varicocele surgery, with a particular focus on differences between hypogonadal and eugonadal men. To determine whether both groups benefit from the surgery. **Materials and Methods:** A literature review was conducted using the PubMed and Google Scholar databases to identify published studies from 2014 to 2024. Meta-analyses, systematic reviews, and original studies reporting hormonal parameters before and after varicocele surgery were included in the analysis. Studies were selected based on inclusion and exclusion criteria, and hypogonadism was defined as total testosterone <300 ng/dL, according to AUA guidelines. **Results:** Twelve studies (four meta-analyses and eight original articles) were included. Most meta-analyses and prospective studies showed a significant increase in serum testosterone levels in hypogonadal men after varicocele surgery. In contrast, eugonadal men generally showed no significant hormonal changes. Small decreases in LH and FSH levels were also observed postoperatively, suggesting improved regulation of the hypothalamic-pituitary-testicular axis. **Conclusion:** Varicocele surgery appears to provide endocrine benefits in hypogonadal men with clinically significant varicoceles and can be considered a therapeutic alternative to testosterone replacement therapy. In eugonadal men, routine surgery is not justified. Future research should focus on risk stratification and surveillance strategies to identify patients with varicocele at risk for progressive Leydig cell dysfunction.

Keywords: varicocele, varicocele surgery, testosterone, hypogonadism, Leydig cell function

1. INTRODUCTION

Pathophysiology and Prevalence of Varicocele

Varicocele, defined as dilatation of the pampiniform venous plexus, is one of the most common male reproductive disorders, affecting approximately 15% of the general male population (Damsgaard et al., 2016). The link between varicocele and male infertility is well known. However, the impact of varicocele on endocrine function, particularly testosterone synthesis, remains a topic of ongoing study. The pathogenesis of varicocele is closely related to venous reflux and impaired testicular venous drainage, resulting in increased scrotal temperature, oxidative stress, hypoxia, and hormonal imbalance. The left testis is most commonly affected, probably due to its anatomical drainage into the left renal vein at a perpendicular angle, which generates greater hydrostatic pressure. Despite its high prevalence, only a subset of affected individuals develops fertility-related complications, suggesting that factors such as genetic predisposition, individual oxidative stress tolerance, or compensatory mechanisms in testicular function may modulate clinical outcomes (Clavijo et al., 2017). Interestingly, many men with varicocele are asymptomatic and fertile.

Symptoms and Clinical Implications

Varicoceles are often asymptomatic and commonly discovered during a routine physical examination or infertility evaluation. However, when symptoms are present, patients may report a dull, aching, or throbbing pain in the scrotum, typically on the left side. Some individuals describe a sensation of heaviness or discomfort, particularly after prolonged periods of standing or physical activity. Large varicoceles may present as a soft, compressible mass above the testicle with a characteristic "bag of worms" appearance. In more severe cases, varicoceles can lead to testicular atrophy, impaired sperm production, reduced motility, and abnormal sperm morphology, contributing to infertility.

The association between varicocele and impaired spermatogenesis is well documented. It has been associated with reduced sperm concentration, decreased motility, and abnormal morphology. The exact mechanism involved remains uncertain, but several theories propose that increased scrotal temperature, oxidative stress, and reflux of toxic metabolites are major contributors to testicular dysfunction (Lomboy & Coward, 2016). Surgical correction, particularly microsurgical varicocelectomy, has been shown to improve semen parameters, particularly in men with abnormal baseline values (Schauer et al., 2012).

In addition to infertility, varicocele can cause testicular pain, typically described as a dull, aching discomfort that worsens during physical activity and improves with rest. Higher grade varicocele is more likely to be symptomatic, and surgery can provide pain relief in up to 90% of cases (Park et al., 2011). However, surgery is generally reserved for clinically significant varicoceles, as subclinical forms have not been shown to provide a measurable benefit in either pain relief or fertility improvement (Evers & Collins, 2003).

Varicocele and hormonal function

Varicocele is implicated in the disruption of testicular endocrine function, particularly testosterone synthesis. However, the literature is mixed. While some studies have shown that varicocele can impair Leydig cell function and lead to reduced testosterone production (Panach-Navarrete et al., 2020; Dabaja & Goldstein, 2016), other studies report no statistically significant effect on serum testosterone levels. Several mechanisms have been proposed to explain this potential association, including increased scrotal temperature, oxidative stress, reflux of adrenal metabolites, and venous stasis, all of which may contribute to Leydig cell apoptosis and impaired androgen biosynthesis (Bellastella et al., 2022). The relationship between varicocele and hypogonadism is inconclusive. While hypogonadal men may benefit hormonally from varicocelectomy, the magnitude of testosterone increase following surgery is often insufficient to justify the procedure for this indication alone (Dabaja & Goldstein, 2016). In addition, studies of men with erectile dysfunction and concurrent varicocele have not found a clear association between varicocele and reduced testosterone levels (Panach-Navarrete et al., 2020). Therefore, current recommendations do not support routine varicocele repair in men with hypogonadism.

2. METHODOLOGY

A literature search was performed using PubMed and Google Scholar to identify relevant peer-reviewed studies published between 2014 and 2024. Search terms included "varicocele and testosterone," "varicocelectomy and hormonal function," "varicocele and hypogonadism," and "varicocele and Leydig cell function." Only English language studies were included.

Selection criteria included:

1. meta-analyses and systematic reviews evaluating the effect of varicocelelectomy on testosterone and other hormonal parameters;
2. individual studies (prospective or retrospective) reporting pre- and postoperative hormonal measurements in men undergoing varicocele repair;
3. studies with clearly defined endocrine outcomes and follow-up protocols.

We excluded:

1. Non-English articles;
2. Case reports, animal studies, and expert opinions;
3. Studies without hormonal endpoints or lacking pre/postoperative comparison;
4. Overlapping datasets or duplicate publications.

A total of 91 (n=91) articles were identified through a database search (PubMed and Google Scholar). After removing duplicates, the number of records was reduced to 47 (n=47). After screening the titles and abstracts, 21 records were excluded, leaving 26 (n=26). After reviewing the full texts of the articles, we included 12 papers (n = 12).

A total of four meta-analyses and eight individual studies that met the inclusion criteria were analyzed. The extracted data included patient demographics, varicocele grade, surgical technique, baseline and postoperative hormone levels (testosterone, LH, and FSH), follow-up time, and indications for surgery (infertility, pain, or hypogonadism). Discrepancies in interpretation were resolved by discussion among the reviewers. Hypogonadism was defined according to the American Urological Association (AUA) guideline as a total testosterone level consistently below 300 ng/dL (Mulhall et al., 2018).

3. RESULTS AND DISCUSSION

Meta-Analyses on the Effects of Varicocelelectomy on Hormonal Profiles

An extensive systematic review and meta-analysis by Cannarella et al., (2024) analyzed data from 48 studies (n=4,191). Varicocelelectomy resulted in a significant overall increase in serum testosterone (mean difference [MD] = +82.45 ng/dL, 95% CI: 64.14-100.76; $p < 0.00001$). This effect was consistent regardless of surgical approach, baseline fertility, or length of follow-up. The increase was most pronounced in men with baseline testosterone levels below 300 ng/dL (MD:+108.47 ng/dL), although men with higher baseline levels also experienced gains (MD:+78.47 ng/dL). Compared to untreated controls, the difference remained significant (MD:+91.64 ng/dL; $p < 0.00001$). FSH and LH levels also decreased after surgery. Postoperative LH was significantly lower than in untreated men (MD: -0.96 IU/L; $p = 0.002$), suggesting improved negative feedback regulation. FSH levels decreased both within the surgical group (MD: -1.43 IU/L; $p < 0.00001$) and relative to controls (MD: -2.35 IU/L; $p = 0.007$), although they remained above the levels observed in healthy men (MD:+2.71 IU/L; $p = 0.0009$).

A meta-analysis by Chen et al., (2017) involving 712 patients from eight studies demonstrated a statistically significant postoperative increase in serum testosterone levels. Pooled data from seven of the studies showed a mean increase of +34.3 ng/dL (95% CI: 22.57–46.04; $p < 0.00001$; $I^2 = 0\%$), indicating an overall hormonal benefit of varicocelelectomy. Subgroup analysis revealed that hypogonadal men experienced a markedly greater increase (+123 ng/dL; 95% CI: 114.61–131.35; $p < 0.00001$; $I^2 = 37\%$) compared to eugonadal patients, for whom the change was not statistically significant ($p = 0.36$). Furthermore, comparisons involving untreated hypogonadal controls showed that the surgical intervention led to an average increase in testosterone of +105.65 ng/dL (95% CI: 77.99–133.32; $p < 0.00001$), which further reinforces the benefit of varicocelelectomy in this subgroup. These findings reinforce the potential effectiveness of varicocelelectomy in restoring or maintaining androgen levels in hypogonadal men with subfertility.

In contrast, a study by Mahdi et al., (2022) evaluating redo varicocelelectomy found improvements in semen parameters but no significant endocrine changes in testosterone, FSH, LH, prolactin, or estradiol levels. A supporting meta-analysis of seven related studies confirmed this finding.

Finally, Tian et al., (2018) conducted a review of five studies involving 312 participants and found modest but statistically significant reductions in FSH (mean difference: -0.48 ng/dL) and LH (mean difference: -0.58 ng/dL). The range of observed FSH reductions across the studies varied from 0.1 to 4.8 ng/dL, while the range of observed LH reductions varied from 0.2 to 2.1 ng/dL. These findings support the idea that varicocelelectomy improves hypothalamic-pituitary-testicular axis regulation.

Findings from Individual Studies

A prospective controlled study by Abdel-Meguid et al., (2014) evaluated 141 infertile men undergoing varicocelectomy, divided into groups based on indication: infertility with pain (VIT), infertility only (VIC), varicocele with normal semen parameters (VFC), and healthy controls (NC). Baseline testosterone levels were significantly lower in all varicocele groups compared to the control group. Postoperatively, testosterone levels increased substantially in hypogonadal men (+93.7 ng/dL, +40.1%; $p < 0.0001$), while changes in eugonadal men were not significant, suggesting a benefit primarily in those with testosterone deficiency.

In a retrospective cohort of 550 men with grade 3 varicocele, El Bardisi et al., (2025) investigated whether age influences semen and hormonal outcomes after microsurgical subinguinal varicocelectomy (MV). The participants were divided into two groups based on age: younger men (under 40 years old, $n = 441$) and older men (40 years old and over, $n = 109$). Postoperative assessments at three and six months revealed significant improvements in sperm count, total motility ($p < 0.001$) and progressive motility ($p = 0.005$) in the younger group. In contrast, the older group showed significant improvement only in progressive motility ($p = 0.002$). Neither group exhibited significant changes in hormone levels. Importantly, there were no statistically significant differences in the degree of semen improvement or pregnancy rates between age groups post-surgery.

Alfozan (2023) conducted a prospective cohort study involving 186 infertile men undergoing varicocelectomy. While the overall analysis showed no statistically significant postoperative changes in serum testosterone, follicle-stimulating hormone (FSH) or prolactin levels, a subgroup analysis revealed that patients with baseline FSH levels of 10 mIU/mL or less experienced a significant increase in testosterone levels ($p = 0.005$). Additionally, a modest but significant reduction in LH was observed ($p = 0.014$). These results suggest that varicocelectomy may offer hormonal benefits to certain patients with relatively intact spermatogenic capacity, highlighting the importance of preoperative hormonal assessment in identifying those most likely to benefit from surgery.

In a retrospective study by Najari et al., (2016), testosterone levels increased by an average of 115.6 ng/dL in men with hypogonadism, and by 73.0 ng/dL in men with testicular pain. However, the difference between the two groups was not statistically significant ($p = 0.329$), suggesting that the presence of pain does not diminish the potential endocrine benefits of surgery.

Firat and Erdemir (2020) analyzed the hormonal responses of 293 infertile men undergoing microsurgical inguinal varicocelectomy, dividing the patients into three age-related groups. While there were significant improvements in total motile sperm count across all subgroups, no statistically significant changes were observed in serum levels of testosterone, follicle-stimulating hormone (FSH), luteinising hormone (LH), prolactin or oestradiol after surgery ($p > 0.05$). These results imply that varicocelectomy may have a limited impact on endocrine parameters in certain patients, especially when baseline hormone levels are normal or there is no evidence of clinically defined hypogonadism.

In a prospective controlled clinical study, Gomaa et al., (2018) evaluated 135 men who were divided into three groups: those undergoing subinguinal varicocelectomy ($n = 45$); those with untreated varicocele ($n = 45$); and a control group of healthy men without varicocele ($n = 45$). At baseline, the testosterone levels and T: E ratios of all the groups were within the normal range. Six months after surgery, the varicocelectomy group showed significant increases in testosterone (from 4.6 to 5.8 ng/mL) and the T: E ratio (from 17.4 to 23.9; $p < 0.001$). No hormonal changes were observed in the untreated or control groups. These results imply that varicocelectomy can restore an optimal androgen-to-estrogen ratio in men with varicocele, even when baseline testosterone levels are within the normal range.

Öztekin et al., (2020) followed 57 men (mean age: 26.8 years) after varicocelectomy. Testosterone increased significantly (from 507.6 ± 174.3 to 547.0 ± 184.6 ng/dL; $p = 0.003$), while other hormones remained stable. The T:E ratio was unchanged, suggesting estrogenic compensation or limited metabolic shift despite improved androgen levels.

In a retrospective study of 46 adolescents, Porto et al., (2023) found no significant hormonal changes after varicocelectomy. Preoperative testosterone levels were in the normal range. Although sperm concentration improved, the change was not statistically significant ($p = 0.272$). No cases of postoperative hypogonadism or need for testosterone therapy were observed during long-term follow-up (median: 36.5 months), confirming endocrine stability in young patients.

Current evidence suggests that varicocele may negatively affect not only spermatogenesis but also testicular endocrine function, particularly testosterone production. Several meta-analyses, and individual studies have demonstrated that varicocelectomy can lead to a significant increase in serum testosterone levels, particularly in men with hypogonadism (Cannarella et al., 2024; Chen et al., 2017; Abdel-Meguid et al., 2014). Cannarella et al., (2024) provided a more comprehensive analysis with a larger cohort of patients and confirmed that hypogonadal men experience the most significant benefit in terms of hormonal recovery after surgery. The 2023 EAU guidelines refer to the findings of Chen et al., (2017) and acknowledge the potential of varicocelectomy to improve testosterone levels in

selected patients. However, they urge caution and analysis when considering surgery as an alternative to pharmacological treatment, such as testosterone supplementation (TRT). The guidelines highlight the lack of high-quality, prospective, randomised clinical trials. Guidelines recommend that varicocelectomy should only be considered for hypogonadal men after extensive counselling of the patient.

Based on recent evidence, varicocelectomy appears to be a promising therapeutic option for hypogonadal men with clinically significant varicoceles. The hormonal improvements observed in this subgroup support the idea that surgery may partially restore Leydig cell function and delay or even prevent the need for lifelong TRT. A summary of reported hormonal outcomes in hypogonadal and eugonadal patients undergoing varicocelectomy is presented in Table 1. Therefore, surgery should be more strongly considered in men with hypogonadism and varicocele, especially if fertility preservation or symptom relief is also a concern. Conversely, the benefits of varicocelectomy in eugonadal men remain uncertain. Most studies report no statistically significant increase in testosterone levels in men with normal baseline hormonal profiles (Chen et al., 2017; Mulhall et al., 2018; Alfozan, 2023; Porto et al., 2023).

Therefore, varicocelectomy should not be routinely recommended for eugonadal men based solely on the presumed endocrine benefit. However, this group should not be overlooked. It is plausible that some eugonadal men are at increased risk of progressive Leydig cell dysfunction and subsequent hypogonadism over time. This raises a significant clinical challenge: how to identify individuals with varicocele who are at risk for future hormonal decline. However, the ideal timing and precise criteria for initiating treatment have yet to be clearly established. In eugonadal men, careful surveillance rather than immediate surgery appears to be the most appropriate course of action. Future research should focus on risk stratification, biomarkers of Leydig cell decline, and timing of surgery to optimize outcomes in this heterogeneous patient population.

Table 1. Comparative outcomes of varicocelectomy in hypogonadal and eugonadal men

Outcome Domain	Hypogonadal Men	Eugonadal Men
Serum testosterone	Significant increase (ΔT often >100 ng/dL)	Small or no significant change
LH	Typically decreases postoperatively	Usually, unchanged
FSH	May decrease, especially if elevated pre-op	Generally stable
Clinical recommendation	Surgery often justified due to symptomatic hypogonadism	Surgery not routinely indicated for hormonal reasons

4. CONCLUSIONS

Varicocelectomy appears to improve testosterone levels primarily in hypogonadal men, supporting its consideration as a treatment option in this subgroup. In contrast, the endocrine benefits in eugonadal patients are less clear and do not justify routine surgery. Future research should focus on identifying markers of progressive Leydig cell dysfunction to guide early intervention and establish surveillance protocols for men with varicocele at risk of developing hypogonadism.

Author’s Contributions

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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