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VARICOCELE AND MALE INFERTILITY AN OVERVIEW

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Abstract

Background: ***Aim:*** To evaluate the role of varicocele as a reversible cause of male infertility and to summarize current evidence on its pathogenesis, diagnosis, and management, particularly in subfertile men, those with contralateral subclinical varicocele, and patients with nonobstructive azoospermia (NOA). ***Materials and Methods:*** A comprehensive review of existing literature was conducted, focusing on clinical studies, meta-analyses, and recent advances in molecular biology related to varicocele-associated infertility. Emphasis was placed on mechanisms such as oxidative stress, sperm DNA fragmentation, and the impact of varicocele repair on semen parameters and fertility outcomes. ***Results:*** Varicocele is a common condition associated with impaired spermatogenesis through multiple mechanisms, including increased scrotal temperature, oxidative stress, and hormonal imbalance. Emerging evidence highlights the role of sperm DNA damage in infertility. Varicocele repair has shown improvement in semen parameters in selected patients; however, its benefits remain controversial in subfertile men, those with subclinical varicocele, and individuals with NOA. Outcomes vary depending on patient selection and diagnostic criteria. ***Conclusion:*** Varicocele plays a significant role in male infertility, but the clinical benefit of its treatment remains debated in certain populations. Advances in molecular diagnostics have improved understanding of underlying mechanisms, aiding in better patient selection for intervention. Further high-quality studies are required to establish standardized guidelines for management.

Keywords: Varicocele, Male infertility, Spermatogenesis, Oxidative stress, Sperm DNA fragmentation, Nonobstructive azoospermia, Varicocele repair .

INTRODUCTION

Varicocele is present in approximately 15% of the general male population and is one of the most frequently identified correctable causes of male infertility. Its prevalence increases significantly among infertile men, affecting around 35% of those with primary infertility and up to 80% of those with secondary infertility. Despite this strong association, the causal relationship between varicocele and infertility is not entirely straightforward, as many men with varicocele retain normal fertility. This has contributed to ongoing debate regarding the indications for and benefits of surgical correction. The present review aims to highlight current concepts, controversies and evolving evidence regarding varicocele and its impact on male reproductive health.

EPIDEMIOLOGY

Varicocele is increasingly recognized as a progressive condition, with higher prevalence observed in older individuals and those presenting with secondary infertility. It is detected in approximately 7% of prepubertal boys and 10–25% of postpubertal males. Epidemiological data suggest that varicocele occurs more frequently in lean individuals and may demonstrate familial clustering, supporting a possible genetic predisposition. Additionally, lifestyle factors such as prolonged and intense physical activity appear to exacerbate the detrimental effects of varicocele on semen quality, particularly when sustained over several years.

PATHOPHYSIOLOGY

The pathophysiology of varicocele-related infertility is multifactorial and remains incompletely understood. One of the most widely accepted mechanisms is scrotal hyperthermia, wherein impaired venous drainage leads to increased testicular temperature, adversely affecting spermatogenesis. In addition, venous stasis and hypoxia may result in reduced oxygen delivery and accumulation of metabolic byproducts, further compromising testicular function.

Oxidative stress plays a central role in varicocele-associated damage. An imbalance between reactive oxygen species (ROS) production and antioxidant defenses leads to lipid peroxidation of sperm membranes, impaired motility, and structural abnormalities. Furthermore, oxidative stress contributes to sperm DNA fragmentation, which is increasingly recognized as a key determinant of fertility potential.

Hormonal alterations, particularly impaired Leydig cell function, may result in reduced testosterone production. There is also evidence suggesting disruption of the blood-testis barrier, potentially triggering autoimmune responses against spermatozoa. Histopathological studies have demonstrated vascular changes including endothelial damage, luminal narrowing, and fibrosis, along with ultrastructural abnormalities such as degeneration of the subendothelial layer.

VARICOCELE AND INFERTILITY

The association between varicocele and infertility is supported by several clinical observations. First, varicocele is more prevalent among infertile men compared to the general population. Second, it is frequently associated with abnormalities in semen parameters and reduced testicular volume. Third, surgical correction has been shown to improve semen quality and increase pregnancy rates in selected patients.

Clinical studies indicate that approximately 60–70% of men experience improvement in semen parameters following varicocelectomy, with spontaneous pregnancy occurring in a subset of cases. Improvements typically include increased sperm concentration, motility, and morphology, as well as enhanced chromatin integrity. However, the variability in response highlights that not all patients benefit equally and a significant proportion of men with varicocele remain fertile without intervention.

DIAGNOSIS

The diagnosis of varicocele is primarily clinical, with physical examination performed in the standing position remaining the cornerstone. The widely used Dubin and Amelar grading system classifies varicocele into three grades based on palpability and visibility, while subclinical varicoceles are not detectable on examination and require imaging.

Color Doppler ultrasound is the most reliable imaging modality and is particularly useful when physical findings are equivocal. It provides objective assessment of venous diameter and reflux. Although adjunctive techniques such as Doppler probes may detect subclinical disease, the clinical relevance of these findings, especially in infertile men, remains uncertain.

TREATMENT

The primary objective of varicocele treatment is to improve or preserve testicular function and enhance fertility potential. While medical therapy has been explored, including the use of antioxidants, pentoxifylline, and hormonal agents, evidence supporting their impact on pregnancy outcomes remains limited. These therapies may provide some improvement in semen parameters, particularly in cases associated with oxidative stress, but are generally considered adjunctive rather than definitive treatment.

Surgical repair remains the mainstay of management. Microsurgical varicocelectomy, particularly via the subinguinal approach, is widely regarded as the gold standard due to its high success rates and low complication profile. This technique allows for precise identification and preservation of arteries and lymphatics, thereby minimizing the risk of recurrence and hydrocele formation.

Laparoscopic varicocelectomy offers the advantage of magnification but is associated with slightly higher complication rates. Percutaneous embolization represents a minimally invasive alternative, with favorable success rates and rapid recovery, although it may not be universally available.

Following surgical intervention, improvement in semen parameters is typically observed within 3 to 6 months, with spontaneous pregnancies occurring within 6 to 12 months. Patients achieving a higher total motile sperm count postoperatively have a greater likelihood of successful conception.

SUBCLINICAL VARICOCELE

Subclinical varicocele, detectable only through imaging, remains a subject of controversy. Current evidence does not support routine treatment in infertile men, as studies have not consistently demonstrated significant benefit in terms of pregnancy outcomes. However, in select cases where a subclinical varicocele coexists with a contralateral clinical lesion, treatment may be considered. Overall, most clinical guidelines recommend against intervention in isolated subclinical varicocele.

VARICOCELE AND AZOOSPERMIA

Varicocele is identified in a subset of men with nonobstructiveazoospermia, although its exact role in the pathogenesis of azoospermia remains unclear. In some cases, varicocelectomy has been associated with the reappearance of sperm in the ejaculate, thereby enabling natural conception or less invasive assisted reproductive techniques.

However, the majority of patients remain azoospermic even after surgery. In such cases, microdissection testicular sperm extraction (micro-TESE) offers a reasonable chance of sperm retrieval, with success rates of approximately 50–60%. Importantly, prior varicocele repair may enhance the outcomes of sperm retrieval and assisted reproduction.

TREATMENT RECOMMENDATIONS

Current guidelines recommend varicocele repair in men with a clinically palpable varicocele, abnormal semen parameters, and infertility. Increasing evidence suggests that even men with borderline or low-normal semen parameters may benefit from early intervention, given the progressive nature of testicular damage associated with varicocele.

The goal of treatment is not only to improve existing semen abnormalities but also to prevent further deterioration of spermatogenic function. This approach underscores the importance of individualized patient selection and careful clinical judgment.

CONCLUSION

Varicocele is a prevalent and clinically significant contributor to male infertility, characterized by complex and multifactorial pathophysiology. The condition is associated with progressive testicular dysfunction mediated by hyperthermia, oxidative stress, and vascular abnormalities, ultimately affecting sperm quality and DNA integrity.

Although controversies persist regarding the optimal management strategy, current evidence supports the role of varicocelectomy in appropriately selected patients, particularly those with clinical varicocele and abnormal semen parameters. Microsurgical techniques provide the best outcomes with minimal complications.

Future research focusing on molecular markers and advanced sperm function tests may help refine patient selection and improve treatment outcomes. Additionally, evolving definitions of normal semen parameters necessitate cautious interpretation to ensure timely intervention and prevention of irreversible testicular damage.

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