

# Varicocele and the Nutcracker Phenomenon: A Contemporary Review of Anatomical Variants and Hemodynamic Consequences

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## Abstract

About 15–20% of men have varicocele, measured a major cause of male infertility and scrotal discomfort. It is observed by abnormal dilation and tortuosity of the pampiniform plexus veins. Varicocele can occur because of Nutcracker Syndrome (NCS), a medical condition that includes the compression of the left renal vein (LRV), in an important part specifically in patients with abnormal presentation. A thorough understanding of the anatomical and hemodynamic connections between both conditions is necessary due to their complicated connection. In the methods Using information from PubMed, Scopus, and other scientific sources, the present systematic review summarizes varicocele and NCS-related epidemiological data, diagnostic criteria, classification schemes, treatment outcomes, and emerging research trends from studies published between 2020 and 2025. The results Up to 36% of males with NCS have left-sided varicocele as their main symptom, according to current data. specialized Doppler parameters that link with the level of venous reflux become a part of the hemodynamic diagnosis of varicoceles. New advances in diagnostic techniques, such as intravascular ultrasound and three-dimensional reconstruction, have helped with the recognition of LRV compression. With success rates ranging from 61% to 92% depending on the intervention, treatments have evolved to include endovascular stenting, microsurgical methods, and customized approaches using three-dimensional printed extravascular stents. In conclusion the complex connection between variations in anatomy and hemodynamic effects is most clearly demonstrated by the link between varicocele and NCS. For the best care of patients, a multidisciplinary approach with new algorithmic diagnosis and customized therapeutic strategies is essential. Establishing standard, the criteria for diagnosis, validating new classification schemes, and creating evidence-based treatment recommendations should be the main goals of future research.

**Keywords:** varicocele, nutcracker phenomenon, infertility

## 1. Introduction

Varicocele is one of the most important vascular anomalies affecting the male reproductive system, which has been described as the abnormal dilatation and tortuosity of the pampiniform plexus veins inside the spermatic cord [1, 2]. Its clinical important in reproductive medicine is shown by the point that this occurrence rises markedly among males assessed for infertility [1]. While varicocele is commonly thought of as a localized problem, new investigation indicates that it may be a sign of systemic vascular pathology, which might have an impact on cardiovascular health [3].

Nutcracker Syndrome (NCS) is the term used to define the clinical indication of the anatomical compression of the Grant in 1937, when he found that "the left renal vein, as it lies between aorta and superior mesenteric artery, resembles a nut between the jaws of a nutcracker," this

left renal vein (LRV) between the aorta and superior mesenteric artery [4, 5]. Resulting its initial description by medical condition is start to be known as a significant contributor to symptomatic varicoceles, specifically those

that show unusual features [6, 7]. El Sadr and Mina reported LRV compression by the aorta and SMA in 1950. De Schepper first used the term "nutcracker" in 1971, but "nutcracker syndrome" wasn't created until 1972 [4]. The pathophysiological connection between varicocele and NCS is based on the development of venous hypertension inside the LRV, which travels retrogradely down the left gonadal vein to the pampiniform plexus, causing venous dilatation and valvular incompetence [4, 5, 8].

This hemodynamic series finds a visible mechanistic connection between the two that clearly goes beyond their anatomical understanding. A latest comprehensive study of 578 individuals with NCS found that varicocele is one of most typical extrarenal symptoms, especially in male patients [9].

Although increasing knowledge of these illnesses, major diagnosis problems persist, the lack of broadly understood diagnostic criteria for NCS causes variations in diagnosis

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and care, while the hemodynamic categorization of varicoceles continues to change [1, 5].

Additionally, the therapy method must be tailored to the symptom's strength, anatomical factors and preferences of the patient, with choices that range from conservative care to advanced endovascular including surgical techniques [4, 9, 10].

This review aims to cover the latest information on the morphological variations and hemodynamic effects of varicocele and the Nutcracker Phenomenon, with a focus on new developments in designation, diagnostic imaging, and medical therapy. By adding data from new research, we hope to provide doctors with an updated basis for recognizing and controlling these connected disorders.

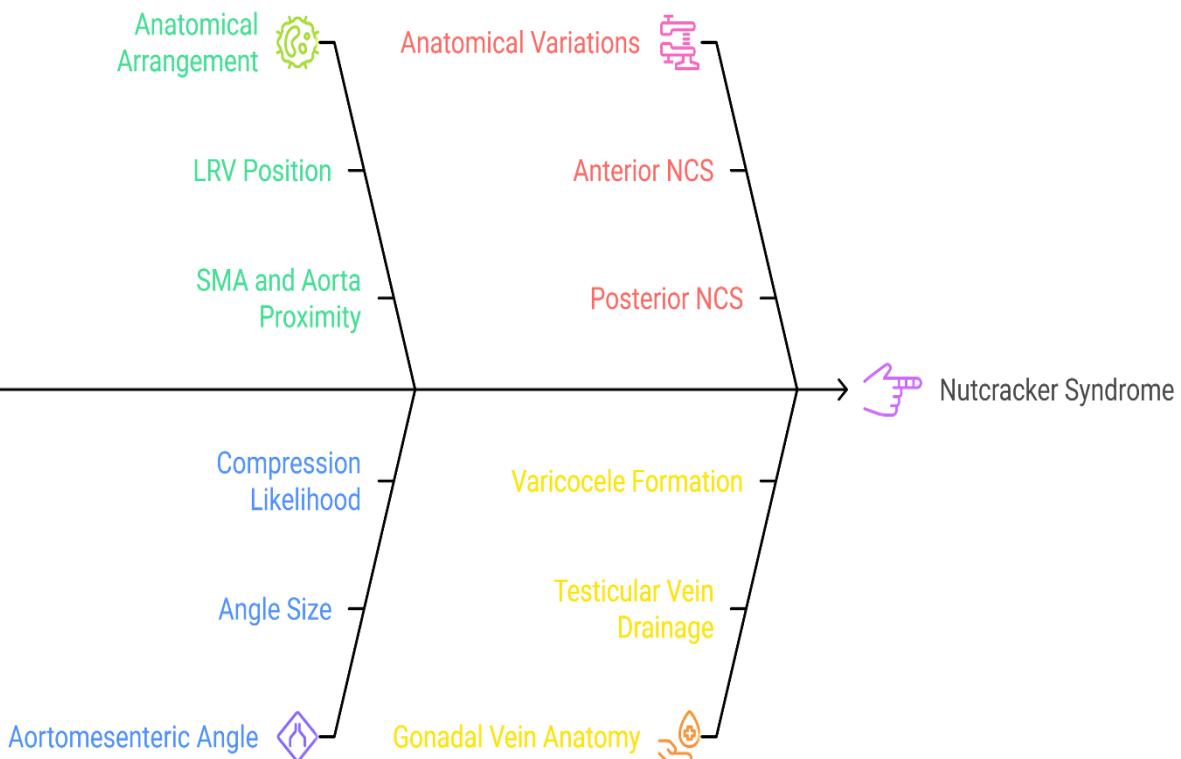
## 2. Anatomy and Pathophysiology

### 2.1. Normal Venous Anatomy and Variants

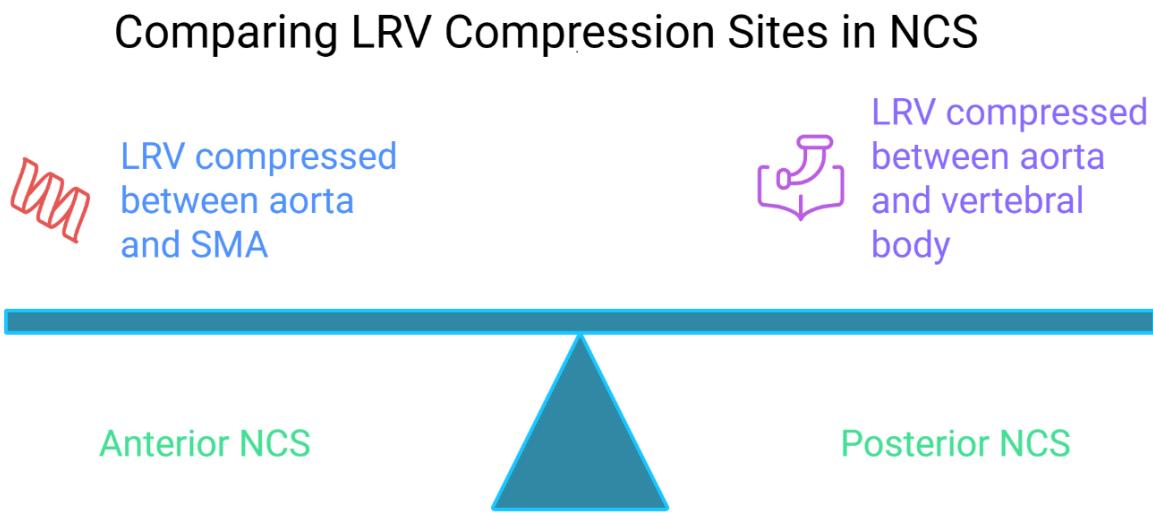
The gonadal arteries and the left kidney's venous drainage system have a specific anatomical arrangement which makes them vulnerable to compression according to certain conditions. The LRV often passes across the anatomical gap between the superior mesenteric artery (SMA) anteriorly and the aorta posteriorly before emptying into the inferior vena cava [11]. A possible area

of compression is produced by this anatomical relationship, especially if anatomical variances are present. An aortic angle of less than 35° is thought to be diagnostic for NCS, and in patients with symptoms, it can be decreased to less than 22° [4, 5]. A typical aortomesenteric angle varies from 38° to 65° [12]. There are mainly two variations in the anatomy of NCS: posterior NCS, where the LRV passes behind the aorta and compresses in between the aorta and vertebral body, and anterior NCS, where the LRV becomes compressed between the aorta and SMA (most common) [8, 13].

Typically, the testicular vein splits into the renal vein on the left and the inferior vena cava on the right. It is uncommon for the left testicular vein to enter the renal vein since venographic investigations show connections between the testicular vein and the inferior vena cava underneath the renal veins. Additionally, the left and right testicular venous systems communicate with one another. Since a quickly growing left-sided varicocele can spread down the renal vein and restrict the testicular vein's exit [4]. The high number of left-sided varicoceles in NCS and the uncommon appearance of isolated right-sided varicoceles, which may cause suspicion for alternative disease, are explained by this anatomical difference [4, 5] (Fig. 1 and Fig. 2).



**Figure 1: Anatomy and Pathophysiology: understanding Nutcracker Syndrome**



**Figure 2: Venous Anatomy and Variants: Comparing LRV sites in NCS.**

## 2.2. Pathophysiological Mechanisms

Multiple interconnected steps occur in the hemodynamic cascade that starts with LRV compression. Venous hypertension, which occurs by compression of the LRV, moves retrogradely down the left gonadal vein to the pampiniform plexus [4, 5, 8]. The venous valve system is stressed by prolonged venous hypertension, which leads to venous dilatation, valvular incompetence, and possibly varicocele development [1, 4]. These hemodynamic concepts have influenced the way venous reflux in varicoceles is categorized. There are four grades of varicoceles according to a recommended hemodynamic classification system [1, 14].

A buildup of harmful substances raised scrotal temperature, elevated oxidative stress, and finally testicular parenchymal damage are all consequences of long-term venous hypertension. The relationship between varicoceles and reduced spermatogenesis, testosterone production, and testicular atrophy is explained by these processes.

## 3. Varicocele Classification

Varicocele is generally classified in several different ways, the most famous and common of which is the clinical classification based on physical examination.

### 3.1. Clinical Grading

This classification is based on the size and palpability of the varicocele during physical examination (in the supine and standing positions and during the Valsalva maneuver). This system is the most common way to describe the severity of varicocele [10]. (Table 1)

Grade 1 (mild) The veins are palpable only during the Valsalva maneuver (straining) and cannot be felt or seen in normal conditions. This grade is more difficult to diagnose and is usually only diagnosed by an experienced physician during the Valsalva maneuver.

Grade 2 (moderate) The veins are palpable in the standing position without the need for the Valsalva

maneuver, but are not visible. This grade is easily diagnosed on examination.

Grade 3 (severe) The dilated veins are easily visible and even before palpation, their protrusion in the scrotum is visible. They feel like a "sack full of worms". This advanced grade is usually easily recognizable by the person themselves [14].

**Table 1: Hemodynamic Classification of Varicoceles Based on Doppler Ultrasonography [14]**

Grade	Characteristics	Clinical Significance
<b>Grade 1</b>	Venous reflux lasting >1 second only during Valsalva maneuver	Early-stage valve failure
<b>Grade 2</b>	Spontaneous, discontinuous venous reflux not increased by Valsalva	Intermediate stage
<b>Grade 3</b>	Spontaneous, discontinuous venous reflux increased by Valsalva	Advanced valve failure
<b>Grade 4</b>	Spontaneous, continuous reflux not increased by Valsalva	Complete valvular incompetence

### 3.2. Subclinical Grade

When a varicocele cannot be detected on physical examination, but is detected on ultrasound using certain criteria (such as increased diameter of the veins and the presence of reflux or backflow of blood during the Valsalva maneuver), it is called a subclinical or non-clinical varicocele. This type of varicocele usually does not require treatment [10].

#### 4. Classification by Location

Primary (idiopathic) is the most common type. It is caused by insufficiency or absence of valves in the spermatic veins, which causes blood to back up and dilate the veins. It has no other obvious cause [10]. Secondary is a rare type that is caused by another disease or obstruction (for example, a tumor in the back of the abdomen that puts pressure on the veins). This type usually develops suddenly in older age and does not go away even when lying down [10].

Left-sided is the most common type of cases. It occurs due to the specific anatomy of the veins of the left testicle (the more perpendicular angle of the left spermatic vein to the left renal vein) [14].

Right-sided is very rare. It is rare to occur alone and if it does occur, secondary causes (such as tumors) should be looked for.

Bilateral is about 10-20% of cases when both testicles are involved.

#### 5. Systemic Consequences

According to new investigation, varicocele may have pathophysiological effects that go beyond the reproductive system and affect the systemic circulatory system [3]. Major variations in echocardiographic parameters were found in recent prospective research that compared 103 varicocele patients with 133 healthy controls. These differences included greater diastolic blood pressure, altered aortic distensibility, and elevated pulmonary arterial pressure in varicocele patients. These results provide support to the idea that varicocele could be a symptom of systemic vascular dysfunction rather than an additional scrotal disease [3]. Endothelial dysfunction, an imbalance between vasoconstrictor and vasodilator mediators, and elevated oxidative stress which may impact vascular tone outside of the gonadal vessels are the suggested causes for these systemic consequences [3]. With implications for general cardiovascular health, this knowledge reframes our view of varicocele as perhaps suggestive of more extensive vascular dysfunction.

#### 6. Diagnostic Approaches

##### 6.1. Clinical Presentation and Physical Examination

Clinical indicators of varicocele include scrotal pain, a palpable mass, testicular atrophy, and infertility, as well as asymptomatic findings and serious symptoms that affect quality of life [1, 4, 5]. The Dubin and Amelar approach is used to organize varicoceles clinically into three categories (low, moderate and high-grade) [1, 15, 16]. To measure reflux and identify between idiopathic and secondary varicoceles, the first evaluation entails an examination of the body in both supine and upright postures [1, 4, 17]. Hematuria, proteinuria, bilateral involvement, or quick start are examples of atypical signs that may point to secondary causes and call for more diagnostic testing [4, 5, 18].

##### 6.2. Ultrasound and Doppler Assessment

Due to its availability, non-invasiveness, and absence of ionizing radiation, Doppler ultrasonography (DUS) is the recommended image technique for the first examination for vascular problems [1, 4, 17]. It measures hemodynamic factors like peak flow velocities and

morphological characteristics like the diameters of the LRV at the compressed and hilar segments [5, 17, 19]. A peak velocity ratio of  $\geq 4.2-5.0$  between the aortomesenteric and hilar segments of the LRV is the diagnosis indicator for DUS, with a sensitivity and specificity [5, 19]. Patient placement has a considerable impact on diagnostic accuracy; standing increases detection rates compared to supine sitting, which can be explained by the gravitational influence on vascular systems [17, 19, 20].

#### 6.3. Cross-Sectional and Invasive Imaging

The anatomical connection between the LRV, aorta, and superior mesenteric artery (SMA) may be apparent by computed tomography angiography (CTA) and magnetic resonance imaging (MRI) [4, 21]. With a sensitivity of 92% and specificity of 89%, the CTA may recognize significant data like the "beak sign," which indicate LRV narrowing at the aortomesenteric junction [22]. The aortomesenteric angle varies between 38 to  $65^\circ$  in healthy people, however it is frequently less than  $35^\circ$  in patients with non-compressive syndrome [22, 23]. Although milder instances could be neglected, the hilar-to-compressed LRV diameter ratio, with ratios  $\geq 4.9$ , can detect severe compression with 100% specificity [24]. Invasive techniques including venography and intravascular ultrasonography (IVUS) may be employed if non-invasive imaging is unsatisfactory; a renocaval gradient greater than 3 mm Hg indicates substantial LRV compression [8, 22, 23] (Fig. 3).

#### 7. Therapeutic Management

##### 7.1. Conservative Management

For children and adolescents with mild to moderate NCS-associated varicoceles, conservative care is the first line of treatment. Growth-related modifications that reduce LRV compression and the formation of collateral routes help around 75% of younger patients achieve spontaneous resolution within 24 months [10, 25, 26]. Elastic compression stockings, painkillers, and lifestyle modifications to reduce aggravating variables are all part of the treatment [26]. For orthostatic proteinuria, angiotensin-converting enzyme inhibitors such as alacepril are used to lower protein excretion and control hypertension [25]. To evaluate progress and identify the need for additional intervention, regular monitoring is crucial [10] (Table 2).

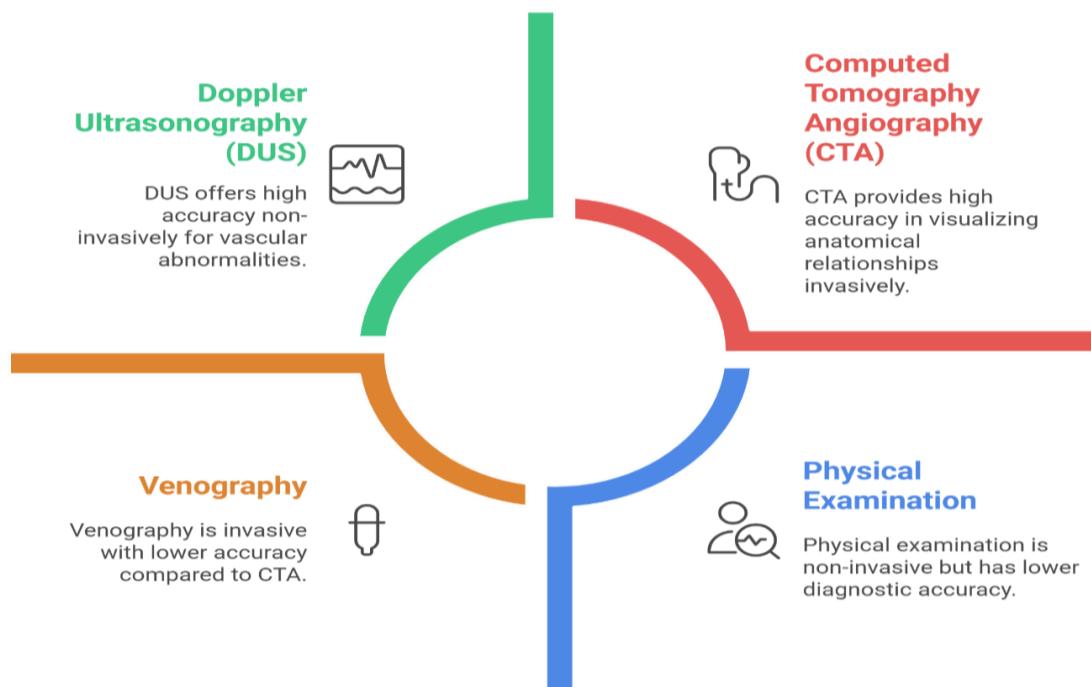
##### 7.2. Surgical Interventions

Both conventional and minimally invasive surgical methods are now available for NCS-associated varicocele [10]. The patient's anatomy, the intensity of their symptoms, the surgeon's experience, and their preferences all play a role in the surgery choice [26]. The usual method, LRV transposition, has a 28.5% reintervention rate but most of symptom relief and instant decompression [9]. For refractory instances, renal autotransplantation is a more comprehensive strategy that avoids aortomesenteric compression; nonetheless, it has hazards

associated with major renal surgery [1, 4, 10]. Varicocelectomy alternatives such as the Ivanissevich, Palomo, and microscopic subinguinal techniques are available for the treatment of solitary varicocele; the latter has a low recurrence rate and improved structural

preservation [6, 27, 28]. In individuals with mild NCS symptoms, recent reports show full remission of scrotal

discomfort and hematuria following varicocelectomy [28, 29] (Table 2).



**Figure 3. Diagnostic algorithm for varicocele: integration of physical examination, criteria to guide treatment decision-making**

### 7.3. Endovascular and Emerging Therapies

By inserting a self-expanding stent into the constricted LRV, endovascular stenting provides a less invasive option to surgery for restoring venous outflow [4, 10]. Research indicates that 76% of patients get symptom relief and 85.2% of patients have primary patency [30, 31]. Its implementation is disadvantaged, particularly in younger patients, by issues such as stent migration (6.7% occurrence), in-stent restenosis or thrombosis (about 5%), and the need for extended anticoagulation [31]. Accurate stent size and placement are made possible by new technologies like IVUS, which may reduce problems [9]. Additionally, three-dimensional printed extravascular stents offer tailored treatments for unique anatomical variances [9, 10]. Although long-term evidence is currently missing, teenagers employing polyether ether ketone (PEEK) stents

have shown early favorable outcomes [31] (Table 2).

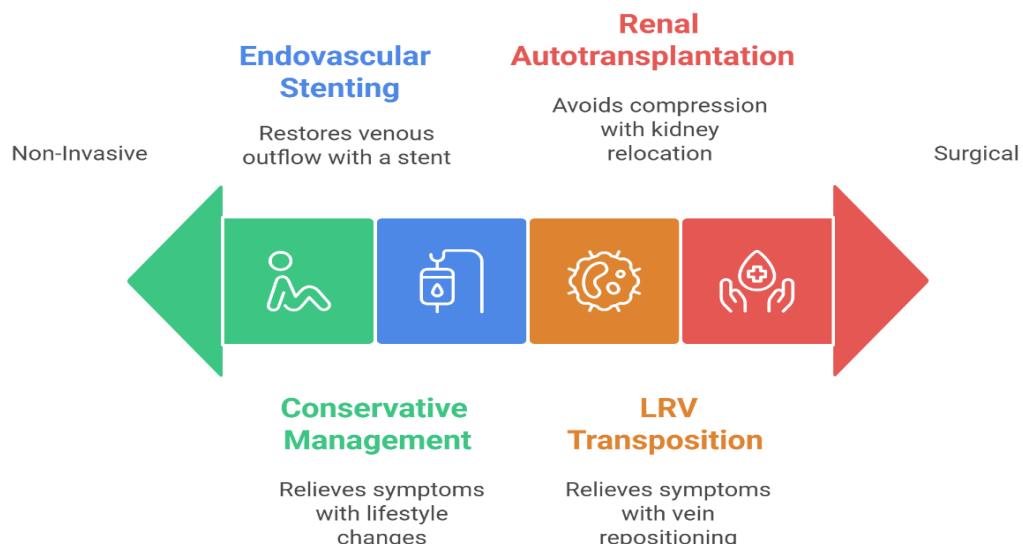
### 7.4. Comparative Effectiveness and Selection Strategy

LRV transposition achieved the greatest symptom resolution rate at 92%, followed by extravascular stenting at 80% and endovascular stenting at 76%, according to a comprehensive evaluation of 578 individuals from 24 trials [9]. Also, extravascular stenting, LGV transposition, and hybrid procedures had no reinterventions, but LRV transposition had the greatest reintervention rate at 28.5% [9]. The results support a multidisciplinary strategy involving urologists, vascular surgeons, and interventional radiologists and highlight the necessity of tailored therapy selection that takes patient specific appearances into account [25, 32] (Table 2) (Fig. 4).

**Table 2: Therapeutic Management Comparison**

Characteristic	Suitability	Resolution Rate	Reintervention Rate	Key Considerations	Monitoring
<b>Conservative Management</b>	Mild to moderate L	spontaneous resolution	Not applicable	Lifestyle modifications	Regular monitoring crucial
<b>Surgical Interventions</b>	Varies by patient anatomy	symptom relief	28.5% LRV transposition)	Surgeon's experience	Post-operative care
<b>Endovascular Therapies</b>	Less invasive option	76% symptom relief	Varies, up to 5%	Stent migration risk	Extended anticoagulation

## Varicocele treatment options range from non-invasive to surgical.



**Figure 4.** Varicocele treatment spectrum: non-invasive (observation, scrotal cooling), percutaneous embolization, and microsurgical ligation, progressing from conservative to definitive care.

## 8. Conclusion

The complicated interaction between variations in anatomy and associated hemodynamic effects is most clearly demonstrated by the complicated link between varicocele and Nutcracker Syndrome [33]. Many significant aspects of this connection are highlighted in this thorough analysis [34]. First, a complicated structure for grasping the different types of venous reflux is provided by the hemodynamic categorization of varicoceles, which has consequences for both diagnostic and therapy choice [1, 34]. Second, we can now detect LRV compression and identify patients with NCS-associated varicocele much more easily because to sophisticated imaging modalities such Doppler ultrasonography, CTA, and MRI [6, 35]. Third, the therapeutic landscape has been expanded by including a range of choices from advanced endovascular and surgical techniques to moderate care, enabling an individual approach depending on patient variables [34].

Although these developments, there are still numerous challenges to overcome [4, 9]. Differences in both diagnosis and therapy occur due to the lack of widely accepted diagnostic standards for NCS [34]. Newer treatments, especially endovascular stenting and three-dimensional printed extravascular stents, need careful adoption and careful follow-up due to a lack of long-term outcome information [10, 26]. Further study is necessary to clarify the underlying processes and clinical importance of varicocele's possible systemic effects, particularly correlations with cardiovascular parameters [32]. Multicenter studies should be the main focus of future research in order to compare treatment outcomes across various patient groups and validate diagnostic criteria [1]. The consistency of varicocele categorization and therapy monitoring will be enhanced by standardizing hemodynamic evaluation procedures [6]. The therapeutic

functions of novel therapies, such as enhanced endovascular procedures and extravascular stenting, will become clearer with long-term data [6, 32]. Additionally, researching the biological ways connecting testicular dysfunction and venous hypertension may support novel treatment targets [27, 36].

In conclusion, a thorough understanding of anatomy, hemodynamics, and presented treatments is required for the management of varicocele in the setting of Nutcracker Syndrome. The best chance for the best patient outcomes is given by a multidisciplinary strategy that considers new investigation and technology developments [4]. Further development of diagnostic and therapeutic paradigms will improve our capacity to handle this intricate clinical entity as research advances.

## Abbreviation

NCS: Nutcracker Syndrome, LRV: left renal vein, SMA: superior mesenteric artery, CTA: computed tomography angiography, MRI: magnetic resonance imaging, IVUS: intravascular ultrasonography, PEEK: polyether ether ketone

## Author Contribution

M.S and J.H conceived and designed the review; M.S and H.D performed the literature search and screening and created figure and tables; all author revised and approved the final manuscript.

## Conflict of Interest

Authors have no conflict of interest related to the presented review article.

## Ethical Consideration

Not applicable.

## Artificial Intelligence

In this work, artificial intelligent was applied exclusively for the creation of the design figures. And played no role in the experimental design, data analysis, or the writing of the manuscript.

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