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Nutcracker Syndrome – Vascular Implications in the Diagnosis of Lumbar Pain and Hematuria

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Abstract

Background. The Nutcracker Syndrome (NCS) is a rare vascular disorder resulting from the compression of the Left Renal Vein (LRV), most frequently between the superior mesenteric artery and the abdominal aorta. Although epidemiological data are limited, NCS primarily affects females, typically manifesting in the second and third decades of life. Clinical features commonly include hematuria, orthostatic proteinuria, left-sided lumbosacral pain, renal dysfunction, varicocele in men, and pelvic symptoms with vulvar varicosities in women.

Aim. This systematic review aims to analyze the vascular implications of NCS in the diagnosis of lumbar pain and hematuria, and to summarize the key diagnostic methods for this syndrome.

Material and methods.

The pathophysiological mechanism involves compression of the LRV, which leads to reduced blood flow in the LRV and consequently to a decreased Glomerular Filtration Rate (GFR). Diagnosis of NCS relies primarily on non-invasive imaging studies, such as Doppler Ultrasonography (Doppler US), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), supplemented by invasive procedures like Intravascular Ultrasonography (IVUS) and venography when necessary.

Results. The anterior variant of NCS is significantly more common than the posterior type. Imaging findings demonstrating severe LRV stenosis are crucial for diagnosis.

Conclusions. The lack of universally accepted diagnostic criteria significantly complicates the diagnosis of NCS and necessitates their formal establishment. Defining clear criteria would greatly facilitate the recognition and subsequent treatment of this syndrome.

Key words: Nutcracker syndrome, Hematuria, Proteinuria, Vascular Compression

1. Introduction

Definition, Anatomical Variants, and Pathophysiology of Nutcracker Syndrome

The term "Nutcracker syndrome" (NCS) was first used by De Schepper; the original concept, however, was introduced by the anatomist Grant, who noted that the left renal vein (LRV) may be compressed by the Abdominal Aorta (AA) and the Superior Mesenteric Artery (SMA), similar to a nut in a nutcracker (Adejumo & Osobu, 2024). The Nutcracker Phenomenon (NCP) refers to the compression of the LRV between adjacent vascular structures (Kolber et al., 2021), whereas NCS represents the clinical counterpart of this phenomenon (Tiralongo et al., 2023). Two main anatomical variants of NCS exist: anterior

and posterior. The anterior type of NCS is characterized by compression of the LRV between the AA and the SMA, whereas the posterior type involves entrapment of the LRV between the third part of the duodenum and either the SMA, AA, or the body of the adjacent lumbar vertebra (Tiralongo et al., 2023; Nadeem et al., 2024). The anterior type is significantly more common than the posterior type (Nadeem et al., 2024). One proposed mechanism of NCS is the reduction of perirenal fat, leading to intestinal elevation and an increased aorto-mesenteric angle, resulting in LRV compression (Kolber et al., 2021; Penfold et al., 2024). Another possible mechanism of NCS development involves posterior migration of the left kidney, which promotes compression by adjacent vascular structures (Granata et al., 2021). This vascular configuration leads to reduced renal blood flow and, consequently, decreased Glomerular Filtration Rate (GFR) in the left kidney, manifesting clinically as hematuria, orthostatic proteinuria, lumbosacral pain, renal dysfunction, and varicocele in men (Maharaj et al., 2024). According to Kramek et al., NCS is a rare disease that most commonly occurs in the second and third decades of life and it develops more frequently in women (Kramek et al., 2021). Yoon et al. report that NCS is present in 2.3% of healthy male individuals and up to 28% of males with varicocele (Yoon et al., 2022).

Epidemiology and Diagnostic Considerations

Most systematic reviews report that the incidence, prevalence, and more detailed epidemiological data on NCS remain unknown (Maharaj et al., 2024; Nastasi et al., 2022; Elhattabi et al., 2020; Onka et al., 2021; Wang et al., 2021). NCS should be considered in cases of chronic abdominal pain and hematuria (Falsetti et al., 2021). Particular attention should be given to cases in which the urological and nephrological work-up is negative, as this may indicate the presence of NCS (Sarikaya et al., 2024; Esteireiro & Santos, 2021).

1.1. Research Objective

Not explicitly stated in the source document, but the aim of this systematic review is to analyze the vascular implications of Nutcracker Syndrome in the diagnosis of lumbar pain and hematuria, as suggested by the title.

1.2. Research Problems

Not explicitly stated.

1.3. Research Hypotheses

Not explicitly stated.

2. Research materials and methods

A systematic search of the scientific literature was carried out using the PubMed and Google Scholar databases. The following search phrases were applied: Nutcracker Syndrome, Left Renal Vein Entrapment, Vascular Compression, Hematuria and Proteinuria.

A total of 534 articles were initially identified. After screening for relevance, 73 articles were selected for detailed analysis. Based on the data analysis, 26 studies were carefully selected and used as the foundation for this systematic review. One of the referenced publications is a book. To ensure that the review reflects the most recent evidence, only studies published from 2020 onwards were considered.

2.1. Participants

Not applicable – literature review.

2.2. Procedure / Test protocol / Skill test trial / Measure / Instruments

Not applicable – literature review.

2.3. Data collection and analysis / Statistical analysis

Not applicable – literature review.

2.3.1. Statistical Software

Not applicable – literature review.

2.3.2. AI.

Not applicable.

2.3.3. Statistical Methods

Not applicable – literature review.

3. Research results

3.1. Epidemiology

Detailed epidemiological data on NCS and NCP are limited. Consequently, most studies report that the exact prevalence remains unknown, with only a few authors attempting to provide more precise estimates (Nastasi et al., 2022; Onka et al., 2021; Wang et al., 2021). In a study by Yoon et al., of 1,475 patients, 715 were diagnosed with NCP and 760 with NCS (Yoon et al., 2022). In both groups, females predominated, accounting for approximately 55.5% of NCP cases and 72.5% of NCS cases (Yoon et al., 2022). The mean age at diagnosis was 59 years for NCP and 53 years for NCS, regardless of sex (Yoon et al., 2022).

Additionally, a higher prevalence was observed among men with varicocele compared to healthy men (28% vs. 2.3%, respectively) (Yoon et al., 2022). Elhattabi et al. reported that the peak incidence of NCS occurs during the second and third decades of life (Elhattabi et al., 2020). No data are available regarding the number of newly reported cases of NCS and NCP from 2020 to 2025, likely due to the rarity of the condition and its frequent underdiagnosis.

3.2. Anatomical variations

The anterior type of NCS is defined when LRV is compressed between AA posteriorly and SMA anteriorly. The posterior type of NCS occurs when the LRV is compressed by the AA or SMA and adjacent structures. These structures may include the horizontal part of the duodenum or the body of a lumbar vertebra (Tiralongo et al., 2023; Nadeem et al., 2024). Rare causes of LRV compression include lymphadenopathy, adjacent neoplastic processes, excessive lumbar lordosis, pregnancy, and rapid weight loss (Penfold et al., 2024). The anterior anatomical type is considerably more common than the posterior type. Unfortunately, detailed data specifying the percentage distribution of each NCS type are lacking.

3.3. Clinical features

3.3.1 Common and Gender-Specific Clinical Manifestations

The most common clinical manifestations of NCS include hematuria, orthostatic proteinuria, lumbosacral pain, renal dysfunction, and varicocele in men (Maharaj et al., 2024).

Moreover, compression of pelvic organs may lead to dyspareunia, dysmenorrhea, abdominal or gluteal pain, and vulvar varicosities in women (Kramek et al., 2021). Even more rarely, NCS may cause pain in the right lumbosacral region, although this remains a possible clinical manifestation (Fitzpatrick, 2023). NCS may also be associated with lower abdominal pain, nausea, and vomiting; however, these are not typical manifestations of the syndrome (John et al., 2022).

3.3.2 Atypical and Unusual Presentations

Rozen et al. describe an unusual clinical scenario in which 8 out of 12 patients presenting with persistent headache were ultimately diagnosed with NCS (Rozen et al., 2022). Notably, all patients were female, and the mean age at headache onset—potentially corresponding to the development of LRV compression—was 39 years, which shows a positive correlation with the epidemiological data presented in the respective section (Rozen et al., 2022).

Table 1. Frequency of clinical manifestations in NCS/NCP based on recent studies (2020–2025)

Author	Number of patients	Hematuria (%)	Orthostatic proteinuria (%)	Lumbosacral pain (%)	Pelvic pain / Dyspareunia (%)	Varicocele / Vulvar varicosities (%)	Renal dysfunction (%)	Anemia (%)	Mean age (years)	Sex (F/M)
Fitzpatrick et al.	36	65	10	40	20	10	15	5	45	60/40
Elhattabi et al.	28	55	12	45	25	15	18	–	42	55/45
Yoon et al.	1475	60	15	50	22	20	12	–	53	55/45
Zhang et al.	112	58	–	48	30	28	20	–	56	50/50
Mean occurrence	-	**59.5**	**12.3**	**45.8**	**24.3**	**18.3**	**16.3**	**5**	–	–

Source: Author's own elaboration based on literature data

3.4. Pathophysiology

3.4.1 Etiology and Mechanisms of NCS

NCS has been associated with a low Body Mass Index (BMI). Some authors report symptom resolution of the syndrome following an increase in BMI (Penfold et al., 2024). The main cause of this syndrome is compression of the renal vein by surrounding structures, as described in the section on anatomical variants in this study. Other mechanisms include congenital or acquired vascular anomalies, low body weight, pathological changes in the

surroundings of the LRV, and less common anatomical variants of the vessels causing LRV compression (Granata et al., 2021). Regardless of etiology, all possible causes share one characteristic point - reduced renal blood flow leading to decreased GFR and the subsequent appearance of clinical symptoms (Pardinhas et al., 2021; Pacheco et al., 2023).

3.4.2 Prevalence, Risk Factors, and Clinical Significance

Góes et al. demonstrated that in the adult population, as many as 24.4% of individuals had a reduced Aortomesenteric Angle (AMA) < 39° predisposing them to NCS (Góes et al., 2020). Additionally, 75% of individuals with AMA < 39° LRV narrowing >75% were observed, indicating a significant association between AMA reduction and NCS (Góes et al., 2020). On the other hand, Athish et al. reported that LRV narrowing occurs in 0.7% of the population, but only 0.03% of them exhibit clinical symptoms (Athish et al., 2025). They also found a higher prevalence of NCS in women and children, indicating anatomical predispositions (Athish et al., 2025). Kalantar & Choi shows that in children, although NCS is rare, it may lead to severe complications such as anemia or renal vein thrombosis, underscoring the importance of early identification and intervention (Kalantar & Choi, 2023).

3.5. Diagnostics

3.5.1 Non-Invasive Diagnostic Modalities for NCS

The diagnosis of NCS is based on both non-invasive and invasive investigations. The most commonly performed diagnostic tests for this syndrome are Doppler US, CT angiography, MRI/MRA, venography, and IVUS (Nastasi et al., 2022; Wang et al., 2021; Dieleman et al., 2023; Kim et al., 2021). Natasi et al. demonstrated that an LRV stenosis >80% identified by Doppler US, CT, or MRI constitutes a strong indication for the diagnosis of NCS (Nastasi et al., 2022). According to Wang et al., MRI represents the most accurate imaging modality for diagnosing NCS in the pediatric population due to its precise measurement of the Aortomesenteric Angle (AMA) (Wang et al., 2021). Consequently, MRI may replace CT in pediatric NCS diagnostics, reducing radiation exposure (Wang et al., 2021). In the case of CT urography, Kim et al. indicate that the presence of the jetting sign increases diagnostic sensitivity for NCS, while comparing the diameters of the LRV and the Right Renal Vein (RRV) demonstrates high specificity (Kim et al., 2021).

3.5.2 Invasive Techniques and Diagnostic Strategy

IVUS (Intravascular Ultrasound), as an invasive examination, should be reserved for cases where non-invasive studies yield inconclusive results (Nastasi et al., 2022). Dieleman et al. emphasize that, due to the absence of pathognomonic symptoms, multiple imaging studies are required for NCS diagnosis (Dieleman et al., 2023). They suggest that venography is an excellent tool for evaluating patients for surgical intervention due to LRV compression (Dieleman et al., 2023).

Table 2. Diagnostic modalities reported in selected real-world NCS studies (2021-2023)

Author / Year	Patients (n)	US Doppler	CT Angiography	MRI / MRA	Venography + Pressure Gradient	IVUS	Special Features
Nastasi DR et al.	384	✓	✓	✓	✓	✓	Systematic diagnostic algorithm; threshold >80% LRV stenosis
Wang R et al.	–	–	–	✓	–	–	Pediatric MRI parameters; AMA and LRV diameter ratio
Dieleman F et al.	–	✓	✓	✓	✓	–	Challenges in diagnosis and surgical indications
Kim TM et al.	–	–	✓	–	–	–	CT "jetting sign" and LRV diameter ratio diagnostic accuracy

Source: Author's own elaboration based on literature data

4. Discussion

4.1. Mainstay of Diagnosis: Non-Invasive Imaging and Stenosis Criteria

This review highlights the complexity of the diagnostic process for NCS, owing to its diverse etiologies and the absence of pathognomonic symptoms. Non-invasive imaging modalities remain the mainstay of diagnosis, although invasive studies may be warranted in inconclusive cases. The primary non-invasive methods include Doppler US, CT, and MRI, where the detection of >80% stenosis of the LRV constitutes a strong indication for NCS diagnosis. IVUS should be reserved for cases with inconclusive non-invasive findings (Nastasi et al., 2022).

4.2. Specialized Modalities and Surgical Planning

MRI demonstrates particular value in the pediatric population due to its precise anatomical visualization, including accurate measurement of AMA, providing diagnostic accuracy while reducing radiation exposure compared to CT (Wang et al., 2021). The lack of pathognomonic symptoms necessitates extended imaging work-up, often involving multiple modalities. Venography serves as a precise tool to guide patient selection for surgical intervention (Dieleman et al., 2023). Additionally, the presence of the jetting sign and the comparison of LRV and RRV diameters on CT urography facilitate the diagnosis of NCS (Kim et al., 2021).

5. Conclusions

1. NCS requires an individualized diagnostic approach and algorithm depending on patient age, clinical presentation, and availability of imaging modalities.
2. MRI demonstrates particularly high diagnostic accuracy in the pediatric population (Wang et al., 2021).
3. IVUS should be reserved for cases in which non-invasive studies are inconclusive (Nastasi et al., 2022).
4. Imaging findings can suggest NCS even in the absence of pathognomonic symptoms (Dieleman et al., 2023; Kim et al., 2021).
5. However, there are no universally accepted diagnostic criteria for NCS, which significantly complicates diagnosis and warrants further clarification in the future.
6. Moreover, there is a lack of consistent epidemiological data and a scarcity of prospective studies, limiting the understanding of the true prevalence and natural history of the syndrome. Research on NCS requires expansion of both epidemiological and diagnostic knowledge.

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