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Doppler ultrasound in standing position is superior to demonstrate nutcracker phenomenon in children with varicocele

Ali Tekin [1], Eren İsmailoğlu [2]

[1] Department of Pediatric Surgery, Division of Pediatric Urology, Ege University Faculty of Medicine, Izmir, Turkey
[2] Department of Radiology, Bakircay University, Faculty of Medicine, Cigli Training Hospital, Izmir, Turkey

ORCID ID of the author(s)
AT: 0000-0002-6988-0806
Eİ: 0000-0001-9998-6081

Corresponding Author
Ali Tekin
Ege Universitesi, Tıp Fakültesi, Çocuk Cerrahi AD, İzmir, Turkey
E-mail: dralitekin@gmail.com

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All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: The nutcracker phenomenon refers to the entrapment of the left renal vein between the superior mesenteric artery and the aorta. It is named nutcracker syndrome if accompanied by symptoms such as flank pain, hematuria, proteinuria, and varicocele. This study aimed to determine the rate of nutcracker phenomenon in children with varicocele by left renal vein Doppler US measurements in standing and supine positions.

Methods: The hospital records of patients admitted to our clinic with grades 2 and 3 left varicocele between 2017 and 2019 were reviewed retrospectively. Demographic data, BMI values, blood pressure values, and urinalysis results of the patients were recorded.

The diameter and the peak velocity (PV) of the left renal vein were measured at the level of the hilus and in the aortomesenteric part, both in supine and standing positions by Doppler ultrasonography (US).

Results: Twenty-six cases were included in the study. No additional pathology was found other than varicocele. The diameter of the aortomesenteric part of the renal vein decreased, the hilar part of the renal vein increased, and the rate and the diameter ratio increased at the standing position. The incidence of the nutcracker phenomenon was 42.3-57.7% with different thresholds in the supine position, and 88-96.2% in the standing position.

Conclusion: Doppler ultrasonography in the standing position is superior to that performed in the supine position in detecting the nutcracker phenomenon in patients with varicocele.

Keywords: Varicocele, Nutcracker Phenomenon, Nutcracker Syndrome, Doppler Ultrasonography, Children

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Introduction

The nutcracker phenomenon refers to the entrapment of the left renal vein between the superior mesenteric artery and the aorta [1]. It is named nutcracker syndrome if accompanied by symptoms such as flank pain, hematuria, proteinuria, and varicocele. Many studies have shown that Doppler ultrasonography can be used in the diagnosis by measuring the difference in diameter or peak velocity between the aortomesenteric and the hilar parts of the renal vein [2–4]. However, different threshold values were defined in these studies. The theory that varicocele occurs with the increase in left renal vein (LRV) pressure and the fact that this pressure will increase in the standing position suggests that the measurements should be made in different positions. This study aimed to determine the rate of nutcracker phenomenon in children with varicocele detected by left renal vein Doppler US measurements in standing and supine positions.

Materials and methods

The hospital records of patients admitted to our clinic with grades 2 and 3 left varicocele between 2017 and 2019 were reviewed retrospectively. Cases evaluated with Doppler US were included in the study.

All patients were examined by a single physician. On physical examination, varicose veins that can be palpated but not seen at rest were classified as grade 2, and their presence during rest was classified as grade 3.

Doppler ultrasonography of the left renal vein was evaluated in all patients after 6-8 hours of fasting. All examinations were performed by a single radiologist using a 2-6 Mhz convex transducer (Philips Affiniti 50, Philips Healthcare Netherlands). The diameter of the left renal vein was measured at the level of the hilus (HLRVD) and in the aortomesenteric part (AMLRVD) in the supine position. Then, peak velocity (PV) measurements were made in the same segments (peak velocity at the level of the hilus: HLRVPV, peak velocity at the level of the aortomesenteric part: AMLRVPV) with a Doppler angle of lower than 60º. All measurements were repeated at the standing position. The sampling interval used to obtain the Doppler spectra of the LRV was chosen as 2-4 mm at the hilar level and 4-10 mm at the aortomesenteric level. All measurements were repeated twice.

Body mass index (BMI) was calculated as the ratio of weight in kilograms (kg) divided by height in meters-squared (m2). BMI percentile values were determined according to the study of Neyzi et al. [5]. Blood pressure measurements of all cases were noted. Care was taken to perform urine dipstick tests in the afternoon not to miss possible orthostatic proteinuria. An informed consent form was obtained from all patients and parents. Ethics approval for this study was obtained from Sağlık Bilimleri University, İzmir Dr. Behçet Uz Children's Hospital, Clinical Research Ethics Committee, 04.07.2019, 2019/11-07.

Selection bias was avoided by recruiting every patient diagnosed with varicocele in the outpatient clinic between the specified dates and including those with Doppler ultrasonography screening.

Statistical analysis

All data were recorded with the Microsoft Excel program. Analyses were performed with the McNemar test, Chi-Square test, Students' T-test, and Kolmogorov-Smirnov test. IBM Statistics SPSS 23.0 for Windows (V 23.0, United States of America, IBM) was used for statistical analyses. A *P*-value of less than 0.05 was considered statistically significant.

Results

Twenty-six cases were included in the study. The mean age was 13.92 (1.72) years. Twelve cases (46.2%) had grade 2 and 14 cases (53.8%) had grade 3 varicocele. Testicular dimensions were compatible with the ages. No additional pathology was found other than varicocele. The overall mean BMI, and those of patients with grades 2 and 3 varicocele were 18.24 (3.91) kg/m^2, 20.13 (5.03) kg/m^2, and 16.62 (1.38) kg/m^2, respectively (P=0.02, Student T-Test). When the BMI data were compared with the BMI values of Turkish children, it was observed that 8 cases were below the 5th percentile, 7 of which (87.5%) had grade 3, and one of which (12.5%) had grade 2 varicocele (P=0.036, Chi-Square).

Doppler US results of all cases are given in Table 1. The diameter of the aortomesenteric part of the renal vein decreased, the hilar part of the renal vein increased, and the rate and the diameter ratio increased at the standing position compared to the supine position. The incidence of the nutcracker phenomenon in our cases according to different threshold values defined in different studies is given in Table 2. When the diameter ratio (DR) and peak velocity ratio (PVR) thresholds were taken as 4.7 or 5 based on the studies of Kim et al. [6] and Cheon et al. [7], the rate of nutcracker phenomenon was significantly higher at the standing position than in the supine position (P=0.01, McNemar Test).

Table 1: Doppler Measurements of left renal vein

Position		Mean
Supine position	AMLRVPV (cm/sec)	100.27 (45.01)
	HLRVPV (cm/sec)	25.23 (6.76)
	AMLRVD (mm)	2.05 (0.63)
	HLRVD (mm)	8.76 (1.32)
	PVR	4.26 (2.14)
	DR	4.61 (1.51)
Standing position	AMLRVPV (cm/sec)	147.19 (42.31)
	HLRVPV (cm/sec)	18.35 (4.27)
	AMLRVD (mm)	1.51 (0.34)
	HLRVD (mm)	10.36 (1.48)
	PVR	8.54 (3.39)
	DR	7.21 (1.89)

AMLRVPV: Aortomesenteric peak velocity of left renal vein, HLRVPV: Hilar peak velocity of left renal vein, AMLRVD: Aortomesenteric diameter of left renal vein, HLRVD: Hilar diameter of left renal vein, PVR: Peak velocity ratio= AMLRVPV/HLRVPV, DR: Diameter ratio=HLRVD/AMLRVD

Table 2: Nutcracker prevalence of patients with different threshold values

Study	Specified threshold value	Measurement position	Nutcracker Phenomenon Positive n (%)	Nutcracker Phenomenon Negative n (%)
Hangge et al. [9]	DR>2.25	Supine	26 (100)	0
		Standing	26 (100)	0
Kim et al. [6]	DR>5	Supine	11 (42.3)	15 (57.7)
		Standing	24 (92.5)	2 (7.7)
	PVR>5	Supine	11 (42.3)	15 (57.7)
		Standing	23 (88.5)	3 (11.5)
Cheon et al. [7]	PVR>4.7	Supine	11 (42.3)	15 (57.7)
		Standing	23 (88.5)	3 (11.5)
	DR> 4.7	Supine	11 (42.3)	15 (57.7)
		Standing	24 (92.3)	2 (7.7)
Romera-Villegas [13]	PVR>2.99	Supine	15 (57.7)	11 (42.3)
	PVR>3.73	Standing	25 (96.2)	1 (3.8)
	DR>3.85	Supine	16 (61.5)	10 (38.5)
	DR>4.12	Standing	25 (96.2)	1 (3.8)

PVR: Peak velocity ratio (AMLRVPV/HLRVPV), DR: Diameter ratio (HLRVD/AMLRVD)

Protein positivity was found in 6 cases in dipstick urinalysis. Among them, the supine peak velocity ratio was 5.27 (1.36), the supine diameter ratio was 5.12 (1.64), the standing PVR was 9.47 (3.20), and the standing DR was 7.42 (2.07). These values were insignificantly higher than the mean values in cases without protein in the urinalysis (P=0.20, P=0.35, P=0.45 and P=0.76, respectively Students' T test). There was no significant difference in peak velocity or diameter ratios when BMI values below the 5th percentile were compared with those without (P=0.55, P=0.92 respectively Chi-Square). In addition, no hematuria or flank pain was found in the cases, which are other clinical manifestations of nutcracker syndrome.

With this sample size, the effect size was 0.97%, and the power was 94%, with a margin of error of 5%, in the standing position and supine AMLRVPV. Furthermore, the standard effect size was 1.07%, and the power was 97% with a 5% margin of error in the standing position and supine nutcracker phenomenon rates.

A total of 3 cases were operated. Two had testicular pain, and one had a disorder in sperm analysis. One of these patients, who was operated in a different clinic, was admitted with recurrence. In this patient, the PVR and DR were 2.20 and 3.9, respectively, in the supine position, and 7.56 and 8.16, respectively, in the standing position.

Discussion

Increased pressure in the left renal vein is considered among the causes of varicocele. The Nutcracker phenomenon is the most important known cause of this pressure increase. The gold standard in diagnosis is to measure the pressure difference between the left renal vein and the vena cava by selective angiography [6]. Computerized tomography (CT) and Doppler US were also used for diagnosis instead of this highly invasive method [2, 7]. It is possible to reveal the difference caused by stenosis by measuring the renal vein flow velocity and diameter after and before the stenotic segment with Doppler US. Many researchers have shown that the left renal vein narrows in the aortomesenteric section, and the peak flow velocity in this section increases significantly in patients with varicocele [4, 8, 9]. In this study, we observed that the peak velocity in AMLRV increased more than four times compared to HLRV and the diameter decreased more than 4.5 times in children with varicocele in the supine position. This result is compatible with other studies in the literature.

Hangge et al. [9] showed that the mean value of DR was higher in the patient group with CT. They stated that with a cutoff value of 2.25, nutcracker can be diagnosed with high sensitivity and specificity. Kim et al. [6] defined the threshold of PVR and DR as 5 in their study according to Doppler US measurements. In the study of Cheon et al. [7] it was shown that the nutcracker phenomenon could be detected with high sensitivity and specificity with a PVR threshold of 4.7. In this study, the rate of nutcracker phenomenon was 42.3% when PVR and DR threshold values were 5 or 4.7. This data was consistent with the rate of 30.1-56.2%, reported in the literature [8, 9]. When this ratio was taken as 2.25, as in the study of Hangge et al. [9], all of our cases had nutcracker phenomenon.

The standing position increases the renal vein pressure by narrowing the aortomesenteric angle and visceral ptosis [3, 12]. Therefore, the researchers thought that standing Doppler US would be more sensitive in demonstrating the nutcracker phenomenon. Romero-Villegas et al. [13] stated that PVR measurement with standing Doppler US would show the nutcracker phenomenon with the best sensitivity and specificity by analyzing Doppler US results in patients with intermittent hematuria of unknown cause. Unlu et al. [4] also showed that the Doppler measurements while standing defined the nutcracker phenomenon better than those performed in the supine position without a sharp threshold. In our study, a significant increase was observed in both PVR and DR values while standing. As a result of this, the rate of nutcracker phenomenon when standing up has more than doubled, reaching almost 90% with different threshold values. These high rates are not surprising when varicocele is considered a manifestation of nutcracker syndrome. We think that ultrasonic measurements while standing are necessary to resolve the causes of varicocele.

Many studies have shown an inverse relationship between BMI and varicocele frequency and grade [14, 15]. This has been attributed to the fact that as the BMI increases, the adipose tissue around the renal vein increases and prevents compression, and the fat tissue makes it difficult to examine the spermatic cord [16]. In our study, we also found an inverse relationship between the varicocele grade and BMI. Almost all children with a BMI below the 5th percentile had a grade 3 varicocele. However, no significant difference was found in ultrasonographic measurements between these underweight children and the others.

Orthostatic proteinuria is one of the symptoms of nutcracker syndrome [1]. It is usually a benign finding and does not require treatment. Park et al. [2] showed that DR and PVR were increased in patients with orthostatic proteinuria compared to healthy volunteers. The mean DR was reported as 5.31 and PVR as 5.21 in cases with proteinuria. Proteinuria was found in 6 cases with the dipstick test, and DR and PVR rates were 5.12 and 5.27, respectively, which were very close to the aforementioned study. Although the mean velocity and diameter ratios in both supine and standing cases were higher in these 6 cases compared to the others, no significance was found. However, we think that this difference can be demonstrated statistically by conducting studies with a larger number of cases.

Limitations

The most important limitations of our study are its retrospective nature and the lack of a control group, which may both cause bias. Performing both standing and supine ultrasonic measurements and comparing them with different parameters such as BMI, proteinuria, and varicocele grade are the strengths of our study.

Conclusion

Doppler ultrasonography in the standing position is superior to that performed in the supine position in detecting the nutcracker phenomenon in patients with varicocele. Furthermore, in almost all cases with varicocele, the Doppler US detected the nutcracker phenomenon at the standing position, based on every threshold value. Future randomized controlled studies with

Doppler US at the standing position may reveal that the nutcracker phenomenon might be the main cause of varicocele.

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