Varicocele and Nutcracker Syndrome

Sonographic Findings

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Objective. Varicocele is a vascular lesion commonly associated with infertility. Its etiology is only partly understood; hence, the purpose of the study was to establish its correlation with intrinsic anatomic differences and nutcracker syndrome. ***Methods.*** A total of 93 patients with varicocele and 76 patients without varicocele were enrolled. The diagnosis of varicocele was based on physical examination, followed by sonographic evaluation of the hilar portion and aortomesenteric portion (AMP) of the left renal vein (LRV). The anteroposterior diameter in millimeters and peak flow in centimeters per second in each region were measured. ***Results.*** A total of 28 patients with the nutcracker syndrome were identified in the study group (30.10%), and 2 were identified in the control group (2.63%). The mean diameters of the hilar portion and AMP of the LRV were significantly different in varicocele-affected patients compared with the control group ($P < .0001$ for both). The mean peak velocities in the hilar portion and AMP were significantly different in patients with varicocele ($P < .0001$). Patients with varicocele and nutcracker syndrome did not have a significant difference in either the hilar or AMP diameter compared with patients with varicocele without nutcracker syndrome. They had a significant difference in both the hilar and AMP peak flow velocity ($P = .0001$ for both). ***Conclusions.*** Our findings indicate that nutcracker syndrome is a frequent finding in varicocele-affected patients and should be routinely excluded as a possible cause of varicocele. In addition, intrinsic anatomic differences in the AMP and hilar portion of the LRV could be directly responsible for the onset of varicocele. ***Key words:*** nutcracker syndrome; renal hemodynamics; sonography; varicocele.

Abbreviations
AMP, aortomesenteric portion; ANOVA, analysis of variance; LRV, left renal vein

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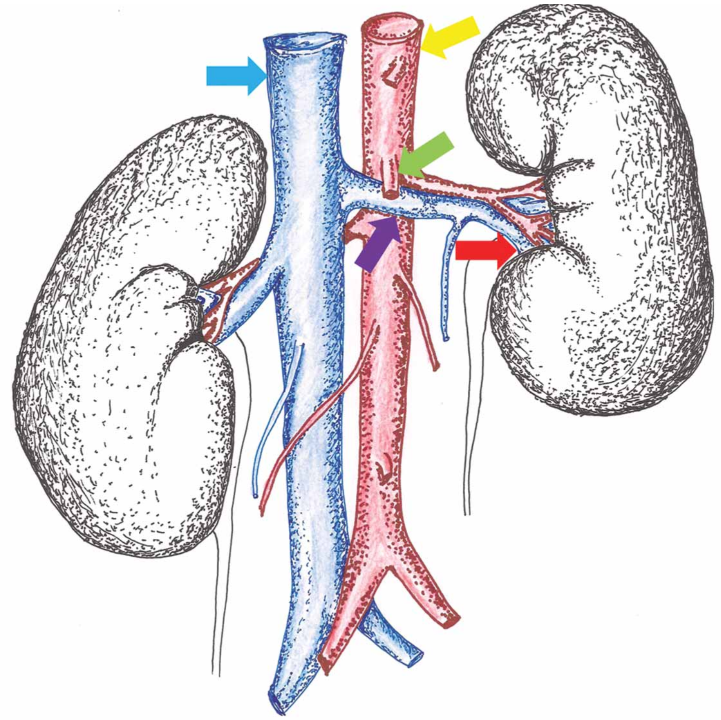
Although the causes of infertility in men are of various characters and origins (eg, developmental defects and exposure to harmful agents), a substantial proportion, especially secondarily infertile men, have the clinically detectable and correctable vascular abnormality varicocele.

Despite various theories, the underlying cause of varicocele remains enigmatic. The role of intrinsic anatomic differences between the left and the right renal vein drainage systems has been implicated in the development of this condition. A greater length of the left internal spermatic vein in comparison with the right system and higher venous pressure on the left side caused by the junction of the left internal spermatic vein with the left renal vein (LRV) at a right angle are the most commonly considered factors because they lead to subsequent propagation of the elevated pressure to the left scrotal vein[1] and possibly determine the onset of varicocele.

Another theory regarding the absence or incompetency of internal spermatic valves leading to reflux of blood and an increase in hydrostatic pressure is currently considered obsolete because recent studies have shown intact valves in men affected with clinical varicocele as well as absent valves in men without this condition.[2] The last suspected factor in the genesis of varicocele is the so-called nutcracker phenomenon (or nutcracker syndrome), characterized by compression of the LRV between the abdominal aorta and the superior mesenteric artery (Figure 1). This condition also leads to retrograde blood flow from the LRV into the internal spermatic vein and may hence be manifested as varicocele in men.[3–9]

The purpose of this study was to evaluate the quantitative and hemodynamic parameters of the LRV in patients with and without varicocele by conducting a comparative analysis and to assess the presence of nutcracker syndrome in both groups and related differences in anatomic and sonographic findings.

Figure 1. Anatomic structures related to nutcracker syndrome. Blue arrow indicates inferior vena cava; yellow arrow, abdominal aorta; green arrow, superior mesenteric artery; purple arrow, AMP of the LRV; and red arrow, hilar portion of the LRV.



Materials and Methods

Study Participants

This case-control study was conducted between May 2008 and July 2009 at the Department of Radiology of Imam Khomeini Government Hospital after Institutional Review Board and Ethics Committee approval was obtained. It is the only urology clinic in the city, determining the single-center character of the study.

A total of 169 consecutive patients (93 from an outpatient urology clinic and 76 from the general clinic of a tertiary referral hospital) were referred by a urologist to the Department of Radiology for Doppler sonographic evaluation of the LRV and suspected varicocele. The relative homogeneity of the patient population was due to the fact that army service is compulsory in Iran, and because patients with grade 2 or higher varicocele are exempted, clinical conditions of the military recruits have to be carefully examined. The purpose of the study and procedures involved in participation were fully explained to eligible patients, and informed consent was obtained from all participants. Patients were divided into 2 groups: a study group consisting of 93 patients with varicocele and a control group consisting of 76 patients without varicocele. Exclusion criteria included patients with previous surgical ligation of varicocele, pyelonephritis, heart failure, the presence of a mass in the renal parenchyma, additional urologic symptoms, epididymitis, orchitis, and the presence of a scrotal mass.

Diagnostic Procedure

The diagnosis of varicocele was based on physical examination conducted at the urology clinic, and all lesions were subsequently stratified by a differential grading scale: grade 1 represents small varicocele palpable only during the Valsalva maneuver; grade 2 varicocele is of medium size and palpable in the standing position without the Valsalva maneuver; and grade 3 is detectable visually through the scrotal skin and is characterized by a pampiniform plexus diameter of greater than 3 mm detected with sonography.[1]

Sonographic Evaluation

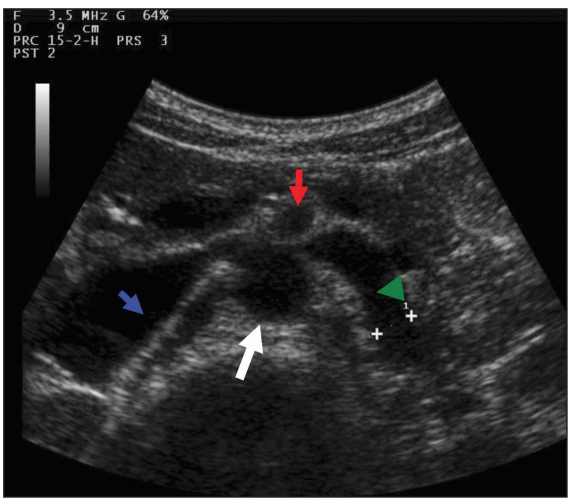
A single radiologist (A.M.) with 6 years of experience performed the sonographic examination.

The radiologist first performed sonography of the renal vein followed then by a sonographic examination of varicocele.

Sonography of the LRV was performed with the patient in a supine position using a MyLab 50 ultrasound system (Esaote SpA, Genoa, Italy) equipped with a broadband 3.5- to 5-MHz curvilinear transducer. The anteroposterior diameters of the LRV at the hilar portion (Figure 2) and aortomesenteric portion (AMP, the portion of the LRV between the aorta and superior mesenteric artery; Figure 3) were measured in millimeters. Peak velocities in the LRV were also measured at identical locations in centimeters per second (Figures 4 and 5). The Doppler angle was less than 60°, and wall filters were set to minimum. A sample volume of 6 to 8 mm was used to cover the range of movement of the LRV between the pulsating aorta and superior mesenteric artery for the measurement of the Doppler spectra of the AMP, and a sample volume of 2 to 4 mm was used for the Doppler spectral measurement of the hilar portion.

The peak velocity ratio between the AMP and hilar portion of the LRV was calculated, and a hilar portion peak velocity greater than 5-fold the AMP peak velocity was considered diagnostic of the nutcracker phenomenon.[10] In this study, the resistive index of interlobar arteries bilaterally was also calculated.

Figure 2. Diameter of the hilar portion of the LRV (white calipers). Green arrowhead indicates main renal vein, white arrow, aorta; red arrow, superior mesenteric artery; and blue arrow, inferior vena cava.



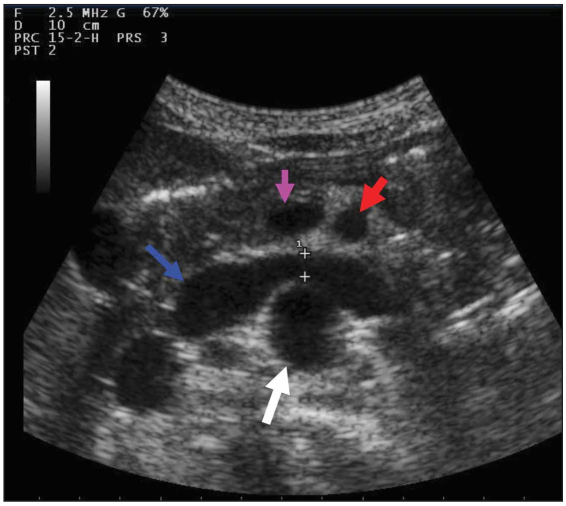
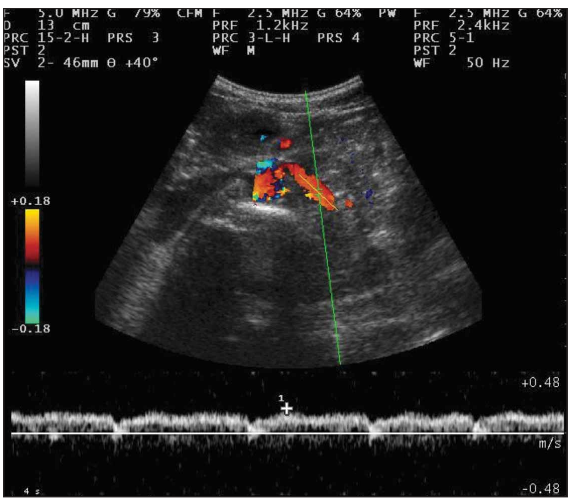


Figure 3. Diameter of the AMP of the LRV (white calipers). Purple arrow indicates superior mesenteric vein; red arrow, superior mesenteric artery; blue arrow, inferior vena cava; and white arrow, aorta.

Statistical Analysis

Statistical analysis was performed using SPSS version 16 software (SPSS Inc, Chicago, IL). The statistical calculation was performed by using a t test, a paired t test, and analysis of variance (ANOVA). $P \leq .05$ was considered statistically significant.

Figure 4. Velocity in the hilar portion of the LRV.



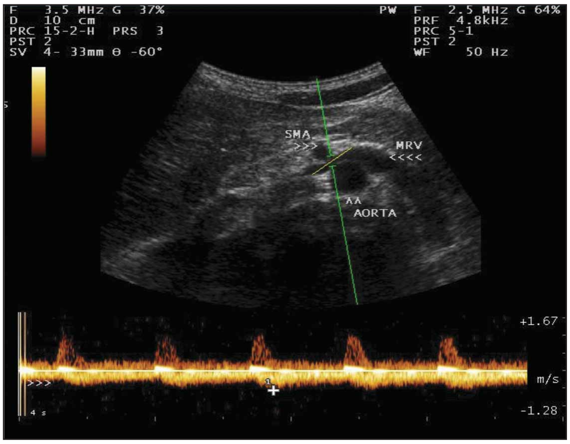


Figure 5. Velocity in the AMP of the LRV. MRV indicates main renal vein; and SMA, superior mesenteric artery.

Results

A total of 169 patients (93 with varicocele, study group; and 76 without varicocele, control group) were enrolled in the study. The mean ages ± SD of the participants were 22 ± 3.6 years in the study group and 22 ± 3.9 years in the control group (t test: $P < .9$; $t = 0.103$), showing that the patients were age matched. A total of 28 patients with nutcracker syndrome were identified in the study group (30.10%), and 2 were identified in the control group (2.63%).

The mean diameters of the hilar portion of the LRV were 7.38 ± 1.19 mm (range, 5–11 mm) in the study group and 6.11 ± 0.97 mm (range, 4–9 mm) in the control group, which represented a significant difference between the groups (t test: $P <.0001$; $t = 7.42$). The mean diameters of the AMP of the LRV were 1.63 ± 0.54 mm (range, 0.8–32 mm) in the study group and 2.29 ± 0.46 mm (range, 1.4–3.5 mm) in the control group, which also showed a significant difference between the groups (t test: $P < .0001$; $t = –8.33$; Table 1 and Figure 6).

The mean peak velocities in the hilar portion of the LRV were 20.49 ± 3.77 cm/s in the study group and 25.66 ± 4.29 cm/s in the control group (t test: $P < .0001$; $t = –8.31$). The mean peak velocities in the AMP were 87.91 ± 22.79 cm/s in the study group and 63.89 ± 15.94 cm/s in the control group. The mean peak velocities were significantly different between the study and control groups in the hilar portion and AMP (t test: $P < .0001$; $t = 8.04$; Table 1 and Figure 7).

Patients with varicocele and nutcracker syndrome (28 patients identified within the case group) did not have a significant difference in either the hilar or AMP diameter in comparison with patients with varicocele without nutcracker syndrome (65 patients; t test: $P = .16$; $t = 1.41$; $P = .08$; $t = 1.78$, respectively). Also, with respect to varicocele grading, no significant difference was observed in this subgroup of patients (Table 2). However, they showed a significant difference in both the hilar and AMP peak flow velocities ($P = .0001$ for both).

The resistive indices were 0.619 for the left kidney and 0.5914 for the right kidney. Although both values were within the normal range (0.54–0.70), they were significantly different when comparing both kidneys (paired t test: $P < .007$; $t = 7.55$).

Table 1. Doppler Sonographic Parameters of the LRV in the Varicocele and Control Groups

Parameter	Varicocele Group (n = 93)	Control Group (n = 63)	P
Diameter, mm			
Hilar	7.38 ± 1.19	6.11 ± 0.97	<.0001
AMP	1.63 ± 0.54	2.29 ± 0.46	<.0001
Velocity, cm/s			
Hilar	20.49 ± 3.77	25.66 ± 4.29	<.0001
AMP	57.91 ± 22.79	63.89 ± 15.94	<.0001

Discussion

Varicocele is a vascular lesion defined as an abnormally dilated and serpiginous pampiniform venous plexus within the scrotum,[1] characterized by retrograde flow in the internal spermatic vein.[11] Its presence is most commonly detected on the left side.[1] The association between varicocele and male infertility was first proposed in the 19th century,[12] and varicocele constitutes the most common surgically correctable cause of subfertility and infertility in men.[13]

The prevalence of varicocele in the general male population is 15%,[14] yet nearly two-thirds of men with this condition remain fertile.[2] However, in infertile men, the frequency of varicocele is reported to reach up to 35% to 40%[15–17] and up to 80% in men with secondary infertility.[12] The suggested cause of infertility is not known despite arduous research but is believed to be related to a higher testicular temperature because the "cooling" of arterial blood in testicular arteries via the encircling pampiniform plexus and countercurrent heat exchange mechanism is abolished.[2] Moreover, recent studies have shown that varicocele is associated with sperm DNA damage,[18] and varicocele repair results in improved semen quality in up to 80% of infertile men.[18,19]

In addition to infertility, varicocele of younger ages is associated with failure of testicular development,[12] testicular atrophy, and Leydig cell dysfunction.[12] Adequate treatment has been reported to reverse testicular atrophy in adolescents,[20–23] underscoring the importance of early accurate diagnosis and treatment of varicocele.

Varicocele is substantially prevalent among infertile men.[1,17,24,25] Although the direct effect of varicocele on infertility has been proposed to be controversial in the past, recently it has been shown that the semen profile, testicular volume, and hormonal level are substantially different in patients with varicocele,[26] and microsurgical varicocelectomy has a beneficial effect on human sperm DNA integrity.[18] Its effect on male fertility underpins the importance of early diagnosis and prompt treatment of this disease.[27]

The main diagnostic and grading approach toward varicocele depends on physical examination, which is associated with many limitations and namely low sensitivity in comparison with imaging techniques.[28] In cases in which physical examination is not achievable (eg, obese patients and low-grade varicocele) or the diagnosis is equivocal, ancillary trans-scrotal sonography with color flow Doppler imaging is the test of choice.

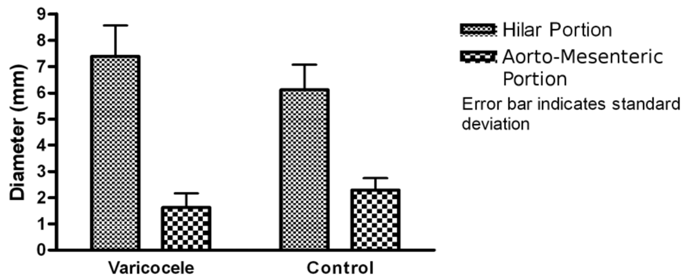


Figure 6. Diameters of the LRV portions in the study and control groups.

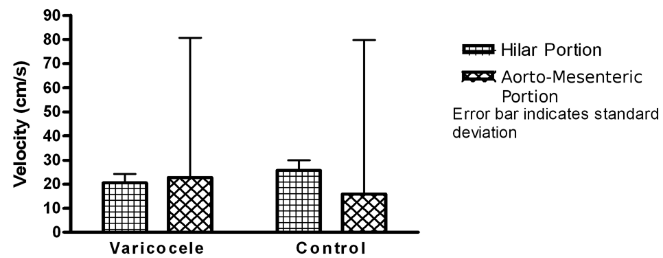


Figure 7. Mean peak velocities in the study and control groups.

The nutcracker phenomenon, first reported more than 50 years ago,[29] is most commonly manifested by left flank and abdominal pain, usually but not implicitly accompanied by macroscopic or microscopic haematuria.[3] Compression of the LRV in the fork between the abdominal aorta and proximal superior mesenteric artery causes left renal venous hypertension, which subsequently leads to the development of collateral veins with intrarenal and perirenal varicosities close to calyceal fornices.[30,31] If the septum separating the veins from the collecting system ruptures, this leads to hematuria, which is mostly of an intermittent yet often severe character.[32]

Table 2. Comparison of Hilar and AMP Diameters and Velocities Between Patients With Different Varicocele Grades

Grade	Patients, n	Velocity, cm/s	ANOVA	Diameter, mm	ANOVA
Hilar					
1	30	21.23 ± 3.66	F = 0.89, P = .41	7.38 ± 1.19	F = 0.06, P = .79
2	40	20.30 ± 3.85		7.40 ± 1.26	
3	23	20.35 ± 3.85		7.33 ± 1.06	
AMP					
1	30	84.17 ± 22.68	F = 0.74, P = .48	1.64 ± 0.55	F = 0.84, P = .36
2	40	88.50 ± 19.45		1.60 ± 0.54	
3	23	91.76 ± 28.08		1.71 ± 0.56	

During the past 2 decades, there have been accumulating reports relating proteinuria and the nutcracker phenomenon. This was observed primarily in children,[10,33–34] and reports among adults followed.[35,36] The nutcracker phenomenon should be considered in the differential diagnosis of patients with inexplicable persistent or intermittent hematuria and proteinuria.[37] In addition to hematuria, proteinuria, and varicocele, often asymptomatic nutcracker syndrome may result in ovarian vein syndrome, LRV hypertension, and pelviureteral varices.[38]

The diagnostic procedure considered the reference standard for establishing the diagnosis of nutcracker syndrome is invasive selective left renal phlebography with measurement of the pressure gradient between the LRV and inferior vena cava (pressure in the LRV – pressure in inferior vena cava ≥3 mm Hg is considered a cutoff value for the diagnosis of the nutcracker syndrome[39]). The sonographic diagnostic criterion consists of a peak flow velocity ratio between the AMP and hilar portion of the LRV of greater than 5.[40,41] Investigations regarding the use of noninvasive sonographic imaging for the confirmation of the nutcracker phenomenon in children and adults have been performed previously.[10,11,42–44] The scope of this study focused on quantitative description and hemodynamic evaluation of the LRV and on the presence of the nutcracker phenomenon (compression of the LRV between the aorta and superior mesenteric artery)[1,4–7,9–10] to establish auxiliary diagnostic leads in the determination of the cause of varicocele using noninvasive sonography.

Quantitative and Hemodynamic Parameters of the LRV

Our results showed a significant difference in tested parameters in the LRV between patients with varicocele and the control group. The mean diameters of the LRV were significantly different between the study and control groups in both locations examined (hilar portion and AMP; $P < .0001$), which is in accordance with previous reports.[11] A greater diameter in the hilar portion was observed in the varicocele group, but this was reversed in the AMP, where the greater diameter was observed in the control group. The mean peak velocities in both the hilar portion and AMP were lower in the study group than in the control group. The fact that velocity increases inversely proportionally to the LRV diameter indicates that the onset of varicocele may be directly related to intrinsic anatomic differences. Our explanation is that the resistance of the LRV changes in the AMP (which is beyond the junction with the left internal gonadal vein), and if the diameter of this portion is diminished, the resistance increase leads to further pressure elevation, and propagation of the pressure increment may be the underlying cause of varicocele in this patient group.

Quantitative and Hemodynamic Parameters and Nutcracker Syndrome

Patients with peak velocity ratios of greater than 5 between the hilar portion and AMP were considered to have the nutcracker phenomenon. We identified 28 patients in the study group and 2 patients in the control group. This subgroup of patients showed no difference in the diameter of either of the LRV portions, but the difference in the peak flow velocities between those groups was significant ($P = .0001$ for both). Impingement of the LRV between the aorta and superior mesenteric artery leads to renal vein hypertension, which manifests itself as varicocele in select patients, and increased pressure may also lead to a change in flow velocity, as observed in the sonographic measurements.

Summary

To our knowledge, a quantitative assessment of the nutcracker syndrome prevalence among patients with varicocele has not been reported previously. The proportion of patients with varicocele that had sonographic findings indicative of the nutcracker phenomenon (>30%) was surprisingly high. Parallel to this, only 2 patients among the 76 control patients also had this condition.

Because nutcracker syndrome is treatable mainly surgically, we thus recommend routine sonographic evaluation of the LRV in all patients with varicocele to exclude nutcracker syndrome as the underlying cause. If left undiagnosed or untreated, hypertension in the LRV may lead to further symptoms (such as hematuria), and once-treated varicocele may reappear in the future.

A limitation of our study was that magnetic resonance imaging, computed tomography, or venography was not used as a reference standard to confirm or exclude the diagnosis of nutcracker syndrome. Also, measurement of the LRV parameters was conducted only on patients in a supine position, and it was measured in only one location of the portion. In addition, only one sonographer conducted the sonographic evaluations.

In conclusion, our findings show that nutcracker syndrome may be the cause of varicocele in a high proportion of patients (30%), and varicocele may arise due to intrinsic anatomic differences represented by a substantially smaller diameter of the AMP of the LRV, leading to higher resistance and subsequently elevated pressure in the internal gonadal vein. With respect to the high number of patients in our study, we recommend that these parameters be routinely examined in patients with varicocele to confirm or exclude nutcracker syndrome as the direct cause of varicocele and to evaluate the anatomic characteristics of the patients to be able to predict possible reoccurrence of varicocele or treatment (such as a renal vein stent). This approach may represent treatment of the direct cause of varicocele and thus may prevent varicocele reoccurrence. Further studies are needed to establish precise diameter cutoff values of the AMP and hilar portion of the LRV to identify patients that may directly benefit from surgical treatment.

References

1. Tanagho EA, Smith DR, McAninch JW. Smith's General Urology. New York, NY: McGraw-Hill Medical; 2008.
2. Sandlow JI. Do varicoceles really affect male fertility? Sexuality Reprod Menopause 2004; 2:219–221.
3. Ahmed K, Sampath R, Khan MS. Current trends in the diagnosis and management of renal nutcracker syndrome: a review. Eur J Vasc Endovasc Surg 2006; 31:410–416.
4. Carl P, Stark L, Ouzoun N, Reindl P. Venous pressure in idiopathic varicocele. Eur Urol 1993; 24:214–220.
5. Mali WP, Oei HY, Arndt JW, Kremer J, Coolsaet BL, Schuur K. Hemodynamics of the varicocele, part II: correlation among the results of renocaval pressure measurements, varicocele scintigraphy and phlebography. J Urol 1986; 135:489–493.
6. Zerhouni EA, Siegelman SS, Walsh PC, White RI. Elevated pressure in the left renal vein in patients with varicocele: preliminary observations. J Urol 1980; 123:512–513.
7. Braedel HU, Steffens J, Ziegler M, Polsky MS, Platt ML. A possible ontogenic etiology for idiopathic left varicocele. J Urol 1994; 151:62–66.
8. Kim SH, Park JH, Han MC, Paick JS. Embolization of the internal spermatic vein in varicocele: significance of venous pressure. Cardiovasc Intervent Radiol 1992; 15:102–107.
9. Buschi AJ, Harrison RB, Norman A, et al. Distended left renal vein: CT/sonographic normal variant. AJR Am J Roentgenol 1980; 135:339–342.
10. Kim SH, Cho SW, Kim HD, Chung JW, Park JH, Han MC. Nutcracker syndrome: diagnosis with Doppler US. Radiology 1996; 198:93–97.
11. Kim WS, Cheon JE, Kim IO, et al. Hemodynamic investigation of the left renal vein in pediatric varicocele: Doppler US, venography, and pressure measurements. Radiology 2006; 241:228–234.
12. Mohammed A, Chinegwundoh F. Testicular varicocele: an overview. Urol Int 2009; 82:373–379.
13. Gunderman RB. Essential Radiology: Clinical Presentation, Pathophysiology, Imaging. Vol 14. New York, NY: Thieme; 1998.
14. Beddy P, Geoghegan T, Browne RF, Torreggiani WC. Testicular varicoceles. Clin Radiol 2005; 60:1248–1255.
15. Jarow JP. Effects of varicocele on male fertility. Hum Reprod Update 2001; 7:59–64.
16. Dubin L, Amelar RD. Varicocelectomy: 986 cases in a twelve-year study. Urology 1977; 10:446–449.
17. Greenberg SH, Lipshultz LI, Wein AJ. Experience with 425 subfertile male patients. J Urol 1978; 119:507–510.
18. Zini A, Blumenfeld A, Libman J, Willis J. Beneficial effect of microsurgical varicocelectomy on human sperm DNA integrity. Hum Reprod 2005; 20:1018–1021.
19. Agarwal A, Deepinder F, Cocuzza M, et al. Efficacy of varicocelectomy in improving semen parameters: new meta-analytical approach. Urology 2007; 70:532–538.
20. Paduch DA, Niedzielski J. Repair versus observation in adolescent varicocele: a prospective study. J Urol 1997; 158: 1128–1132.
21. Sayfan J, Siplovich L, Koltun L, Benyamin N. Varicocele treatment in pubertal boys prevents testicular growth arrest. J Urol 1997; 157:1456–1457.
22. Laven JS, Haans LC, Mali WP, te Velde ER, Wensing CJ, Eimers JM. Effects of varicocele treatment in adolescents: a randomized study. Fertil Steril 1992; 58:756–762.
23. Yamamoto M, Hibi H, Katsuno S, Miyake K. Effects of varicocelectomy on testis volume and semen parameters in adolescents: a randomized prospective study. Nagoya J Med Sci 1995; 58:127–132.
24. Akbay E, Cayan S, Doruk E, Duce MN, Bozlu M. The prevalence of varicocele and varicocele-related testicular atrophy in Turkish children and adolescents. BJU Int 2000; 86:490–493.

25. Clarke BG. Incidence of varicocele in normal men and among men of different ages. JAMA 1966; 198:1121–1122.

26. Pasqualotto FF, Lucon AM, de Góes PM, et al. Semen profile, testicular volume, and hormonal levels in infertile patients with varicoceles compared with fertile men with and without varicoceles. Fertil Steril 2005; 83:74–77.

27. Richter F, Stock JA, LaSalle M, Sadeghi-Nejad H, Hanna MK. Management of prepubertal varicoceles: results of a questionnaire study among pediatric urologists and urologists with infertility training. Urology 2001; 58:98–102.

28. Zumrutbas A, Resorlu B, Yesil M, Yaman O. Is the presence of venous reflux really significant in the diagnosis of varicocele? Int Urol Nephrol 2008; 40:983–987.

29. Ragazzi M, Milani G, Edefonti A, Burdick L, Bianchetti M, Fossali E. Left renal vein entrapment: a frequent feature in children with postural proteinuria. Pediatr Nephrol 2008; 23:1837–1839.

30. Russo D, Minutolo R, Iaccarino V, Andreucci M, Capuano A, Savino FA. Gross hematuria of uncommon origin: the nutcracker syndrome. Am J Kidney Dis 1998; 32:E3.

31. Hanna HE, Santella RN, Zawada ET Jr, Masterson TE. Nutcracker syndrome: an underdiagnosed cause for hematuria? SD J Med 1997; 50:429–436.

32. Tanaka H, Waga S. Spontaneous remission of persistent severe hematuria in an adolescent with nutcracker syndrome: seven years' observation. Clin Exp Nephrol 2004; 8:68–70.

33. Shintaku N, Takahashi Y, Akaishi K, Sano A, Kuroda Y. Entrapment of left renal vein in children with orthostatic proteinuria. Pediatr Nephrol 1990; 4:324–327.

34. Lee SJ, You ES, Lee JE, Chung EC. Left renal vein entrapment syndrome in two girls with orthostatic proteinuria. Pediatr Nephrol 1997; 11:218–220.

35. Wang L, Yi L, Yang L, et al. Diagnosis and surgical treatment of nutcracker syndrome: a single-center experience. Urology 2009; 73:871–876.

36. Oteki T, Nagase S, Hirayama A, et al. Nutcracker syndrome associated with severe anemia and mild proteinuria. Clin Nephrol 2004; 62:62–65.

37. Ekim M, Ozcakar ZB, Fitoz S, et al. The "nutcracker phenomenon" with orthostatic proteinuria: case reports. Clin Nephrol 2006; 65:280–283.

38. Park YB, Lim SH, Ahn JH, et al. Nutcracker syndrome: intravascular stenting approach. Nephrol Dial Transplant 2000; 15:99–101.

39. Nishimura Y, Fushiki M, Yoshida M, et al. Left renal vein hypertension in patients with left renal bleeding of unknown origin. Radiology 1986; 160:663–667.

40. Cho BS, Choi YM, Kang HH, Park SJ, Lim JW, Yoon TY. Diagnosis of nutcracker phenomenon using renal Doppler ultrasound in orthostatic proteinuria. Nephrol Dial Transplant 2001; 16:1620–1625.

41. Vehaskari VM. Mechanism of orthostatic proteinuria. Pediatr Nephrol 1990; 4:328–330.

42. Stavros AT, Sickler KJ, Menter RR. Color duplex sonography of the nutcracker syndrome (aortomesenteric left renal vein compression). J Ultrasound Med 1994; 13:569–574.

43. Takebayashi S, Ueki T, Ikeda N, Fujikawa A. Diagnosis of the nutcracker syndrome with color Doppler sonography: correlation with flow patterns on retrograde left renal venography. AJR Am J Roentgenol 1999; 172:39–43.

44. Graif M, Hauser R, Hirshebein A, Botchan A, Kessler A, Yabetz H. Varicocele and the testicular-renal venous route: hemodynamic Doppler sonographic investigation. J Ultrasound Med 2000; 19:627–631.