Prevalence, Doppler Ultrasound Findings, and Clinical Implications of the Nutcracker Phenomenon in Pediatric Varicoceles

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OBJECTIVE To examine the implications of varicoceles and nutcracker phenomenon (NcP) in a large cohort of adolescent patients. Varicoceles are common in adolescent males, generating concerns regarding etiology and management. At our institution, Doppler ultrasound (US) of the renal vessels is routinely obtained with the goal of assessing for an associated nutcracker phenomenon.

METHODS Between 1/2000 and 3/2017, 182 patients with clinical varicoceles were evaluated with US. Retrospective assessment provided complete data in 137, including maximum varicose vein diameter, testicular measurements, left renal vein velocities at the hilum and impingement point by the superior mesenteric artery, and procedural interventions.

RESULTS NcP was detected in 77 patients (56.2%), who experienced higher venous velocity ratios (8.33 vs 2.87; $P < 0.001$) than those without. Overall, 39 patients (28.5%) had a testicular volume discrepancy >20%, without a significant difference based on the presence or absence of NcP (27.3 vs 30.0%, respectively; $P = 0.36$). Both groups had similar ages at diagnosis, bilateral volume parameters, volume difference, maximum varicose vein sizes, and follow-up duration ($P \geq 0.05$ for all). Intervention was more likely in patients with volume difference >20% ($P = 0.014$). Having NcP was not associated with a higher incidence of initial ($P = 0.59$) or reoperative surgery ($P = 0.73$).

CONCLUSION NcP is common in adolescent patients with a varicocele, but it is not associated with differences in testicular parameters or an increased frequency of initial or reoperative surgery. As such, NcP may have few clinical ramifications as an isolated finding in this patient population, calling into question routine assessment for its presence. UROLOGY 128: 78–83, 2019. © 2019 Elsevier Inc.

Varicoceles in the pediatric and adolescent population are a relatively common phenomenon ranging from 19% to 26% in early to mid-teens.[1] This prevalence persists during transition from pediatric care. In the adult normal male population, they are seen at a rate of approximately 15%, becoming clinically relevant in approximately 40% of men presenting with infertility.[2] Many of these cases are asymptomatic, though some may be associated with esthetic concerns, pain, or discomfort. There is also growing concern that palpable varicoceles can also be associated with future fertility and hormone production problems. This has led to the recommendation that adolescent males with varicoceles be monitored for testicular volume discrepancies (ie, ≥20% compared to the unaffected gonad) with or without semen analyses, and offered varicocele repair if abnormalities are detected.[3,4]

For patients who meet symptomatic or volume-based criteria for varicocele repair, correction centers on interrupting blood flow through the dilated venous system and may be approached via surgery or percutaneous embolization. These approaches are based on the postulated theories behind varicocele development; incompetent venous valve systems and/or anatomical variants such as the nutcracker phenomenon (NcP). The NcP is characterized by left renal vein entrapment, caused by compression of the left renal vein between the aorta and superior mesenteric artery (SMA), causing venous hypertension and development of dilated collateral veins. Clinically, this may manifest as left flank or abdominal pain, varicocele in males, pelvic congestion syndrome in females, hematuria, and/or proteinuria.[5]

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Current management strategies do not consider the presence or absence of a NcP. Moreover, there is limited evidence exploring the left renal vein Doppler ultrasound (US) findings of pediatric and adolescent patients with a varicocele. Given this gap in knowledge, we sought to present data on a systematic analysis of patients with this condition. We also hypothesized that surgical treatment of varicoceles in patients with a NcP would predispose them to recurrence compared to those without. Our primary study objectives were to evaluate the incidence of the NcP in patients with varicoceles confirmed on US at a single-center outpatient urologic population and to compare the descriptive characteristics of patients with vs without a NcP. Our secondary objectives were to investigate whether presence or absence of a NcP was associated with a higher need for initial or recurrent surgery for varicocele repair.

MATERIAL AND METHODS

We performed a retrospective chart review of male patients seen in the urology clinic at a tertiary-care Canadian pediatric hospital, offering care to patients up to the age of 18 years. The institution's research ethics board approved the study protocol prior to data collection and analysis.

Study Population

Using ISYS software, a proprietary radiologic database software which searches the text in radiologic reports since January 2000, the keywords "varicocele" and "nutcracker" were used separately to identify male patients assessed between January 2000 and March 2017 with a clinically significant (ie, symptomatic or visible or palpable on physical exam) left-sided varicocele who had undergone scrotal US as well as a focused renal vessel Doppler US to assess for NcP (Fig. 1). Based on previous literature, NcP was defined as present when the ratio between the left renal vein velocity at the impingement point by the SMA and the left renal vein at the hilum was greater than 4.8.[6-10]

Collected data included maximum diameter of the varicose veins, testicular volume measurements, left renal vein velocities at the hilum and impingement point by the SMA, the decision to proceed with any type of corrective intervention, as well as the need for redo surgery. Surgical modalities were chosen based on surgeon preference. Testicular volume was calculated using the formula length × width × height × 0.71.[11] Percent difference in testicular volume was calculated as 100 × (right testicular volume − left testicular volume)/right testicular volume.[4] No semen analysis data were available for the included patients.

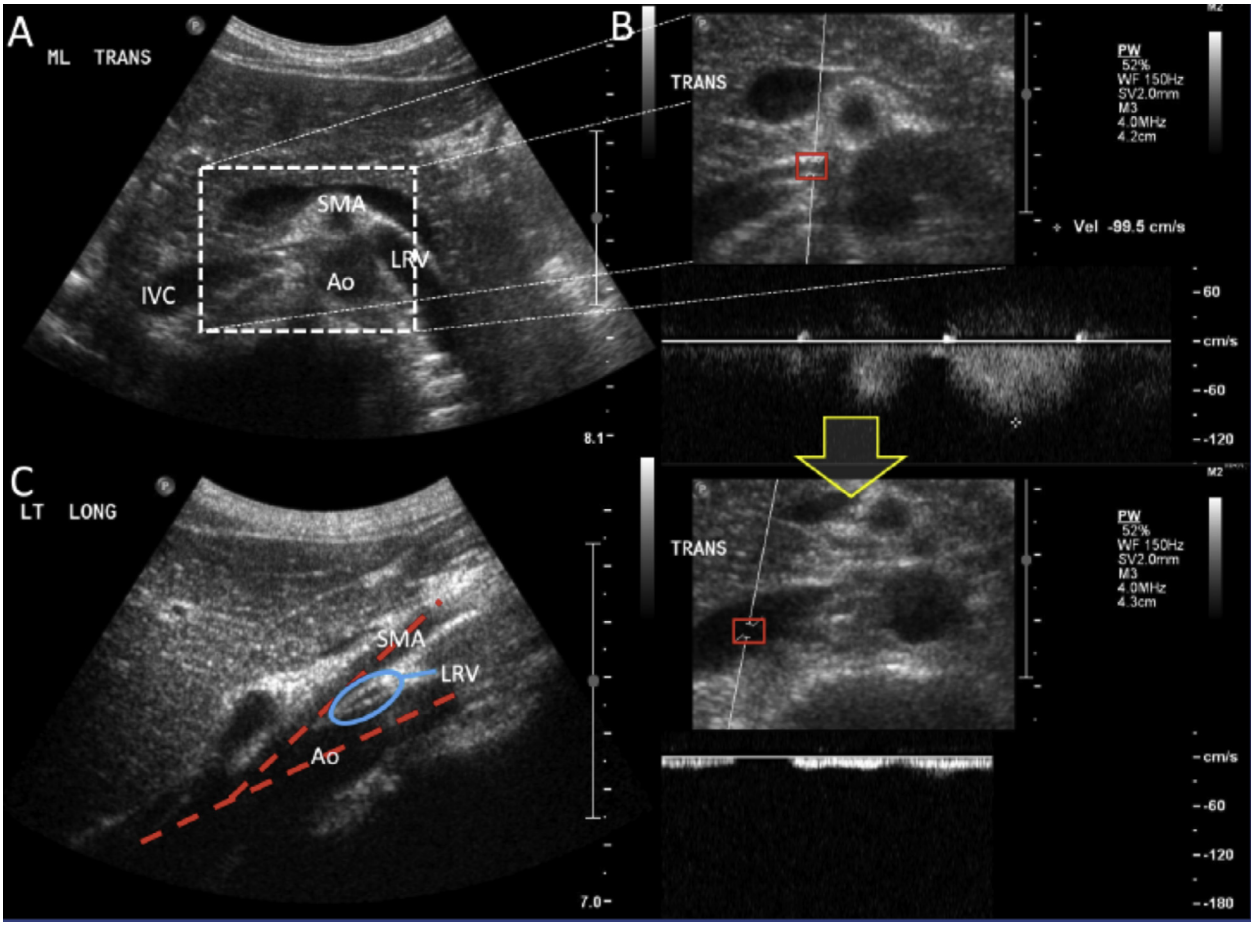

Figure 1. Doppler US findings in patients with NcP. (A) Extrinsic compression of the left renal vein (LRV) between the aorta (Ao) and superior mesenteric artery (SMA). (B) Doppler waveform at the level of extrinsic compression and outside the area of impingement. (C) Sagittal view demonstrating the "Nutcracker anatomy" with the LRV compressed between the SMA and Ao. IVC, inferior vena cava. (Color version available online.)

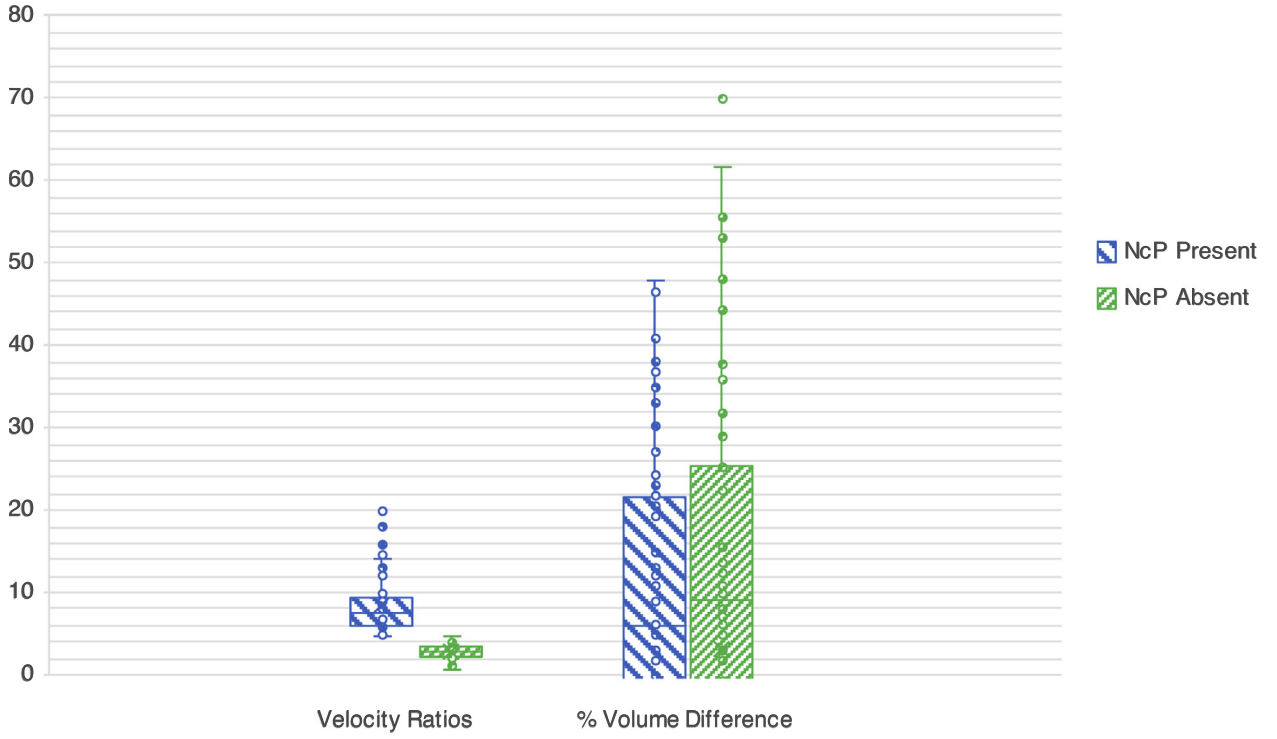

Figure 2. Comparison of renal vein velocity ratios at SMA and testicular volume differences in patients with and without NcP. (Color version available online.)

Inclusion Criteria

Male patients up to and including 18 years of age with a documented presence of a clinical left-sided varicocele who underwent scrotal US and renal Doppler evaluation for NcP were included. Measurement of varicose vein diameter, testicular parameters to calculate testicular volume, and renal vein velocities proximal to and at the point of impingement by the SMA were required for inclusion.

Exclusion Criteria

Patients were excluded if there was missing or limited documentation, if a varicocele was not identified as clinically present in documentation, and/or if there were incomplete Doppler US analyses (ie absent venous velocities at the SMA and left renal hilum).

Statistical Analysis

Non-normally distributed continuous variables (age at diagnosis, testicular volume, maximum varicose vein diameter, venous velocity at SMA, venous velocity ratio between narrowed and hilar renal veins, testis volume difference, and follow-up) were compared using the Mann-Whitney *U* test. The chi-square and Fisher's exact tests were used to compare the differences in undergoing initial or reoperative surgery for patients with testicular volume differences ≥20% or <20% and for patients with and without a NcP. Analyses were conducted using SPSS software, version 25 (IBM Corp, Armonk, NY).

RESULTS

From January 2000 to March 2017, 182 boys were diagnosed with a left-sided varicocele (confirmed on testis US) and were also evaluated with renal vessel Doppler US. Twenty-two patients were excluded due to incomplete data, leaving 137 patients for analysis. No patients were excluded for subclinical varicoceles. Average age at diagnosis of varicocele was 13.6 years (range 9-18 years) and mean follow-up was 25 months (range 0-77 months), with 19 patients lost to follow-up, and the remaining having a minimum of 2 months of follow-up.

NcP was detected in 77 patients (56.2%). As expected, these individuals experienced significantly higher renal vein velocities at the SMA (1.58 vs 0.91 m/s; $P < 0.001$) and significantly higher velocity ratios (8.33 vs 2.87; $P < 0.001$) than those without NcP (Fig. 2).

Patients with and without NcP had similar ages at diagnosis, testicular volumes, maximum size of varicose veins, volume difference (Fig. 2), and follow-up ($P \geq 0.05$ for all). Overall, 39 patients (28.5%) had a testicular volume discrepancy greater than 20%. Surgical intervention was more frequent in patients with a testicular volume difference greater than 20% ($P = 0.014$); however, there was no significant difference in patients undergoing initial surgery based on the presence or absence of NcP (25.5 vs 21.9%, respectively; $P = 0.59$).

Of those patients who underwent surgery and required additional surgery for varicocele recurrence, more had initially undergone microsurgical ligation (ML, 87.5%) vs laparoscopic mass ligation (LL, 0%) or embolization (E,12.5%), though overall ML was also the most common technique, comprising 64.6% of the initial surgeries (Fig. 3). This difference was not statistically significant ($P = 0.13$). There was no association between the presence of a NcP and the selected corrective intervention (Fig. 3). Four patients with NcP and 4 patients without NcP underwent 1 or more reoperative procedures for recurrent varicoceles. The diagnosis of a NcP was not associated with a higher incidence of initial ($P = 0.59$) or reoperative surgery ($P = 0.73$; Fig. 4).

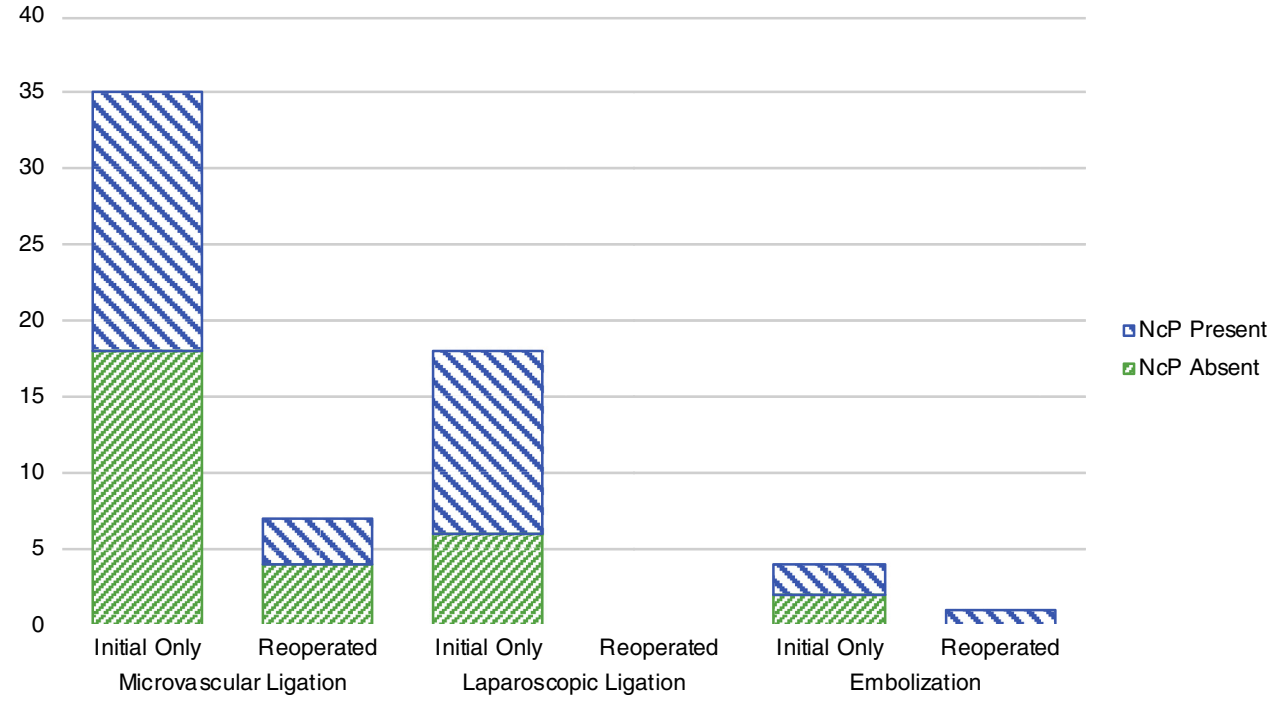

Figure 3. Distribution of surgical techniques employed, characterization of NcP, and need for one surgery or recurrent surgery among patients undergoing surgery for varicocele. (Color version available online.)

DISCUSSION

The exact prevalence of NcP in the general population remains largely unknown. Given the variability of associated symptoms and diagnostic criteria, it has been challenging to precisely define its epidemiology. Previous studies, however, have documented the association between varicoceles — a more readily understood condition — and NcP.[12] In a recent, relatively large case-control study, Mohamadi et al reported a 30.10% prevalence of NcP in young adult patients with varicocele compared to 2.63% in age-matched patients without varicocele.[5] Their findings were some of the first to call attention to

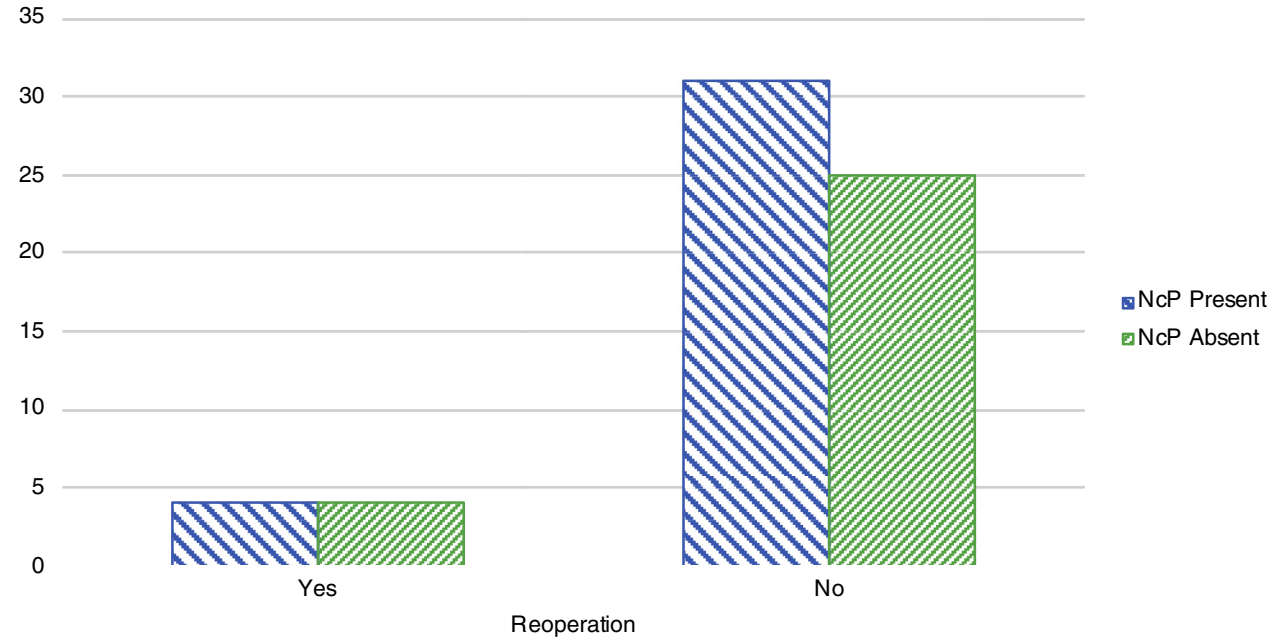

Figure 4. Distribution of need for reoperative intervention for varicocele based on presence or absence of NcP. (Color version available online.)

the potential association between NcP and varicoceles in adult men without fertility concerns (as they were mostly diagnosed during fitness assessment for military service). Interestingly, based on their findings, these authors recommended routine Doppler assessment of the left renal vein in asymptomatic patients with varicoceles based on the theoretical implications in terms of need for surgical intervention and risk for recurrence.

Our study of pediatric and adolescent male patients with clinically significant left-sided varicoceles identified a high prevalence of NcP (56.2%). This finding highlights the frequent association between the presence of a varicocele and the NcP in this population. Previous smaller studies have suggested a similar pattern. For example, Kim et al found a high rate of NcP in a small number of pediatric patients with varicoceles, based on hemodynamic and sonographic parameters.[13] Taken together, these data support the hypothesis that abnormal-elevated venous pressures caused by extrinsic compression of the left renal vein between the aorta and the superior mesenteric artery stimulate the development of collateral flow, which includes retrograde drainage into the left gonadal vein.[5]

Though there is no evidence to support its practice, the reported high prevalence of NcP among patients with varicoceles has led some practitioners to recommend obtaining routine sonographic evaluation of the left renal vein in all patients with varicoceles to exclude NcP as a predisposing condition. Unfortunately, there is a paucity of evidence to support or dispute this practice. Our study is the first to demonstrate that the presence of NcP is not associated with a higher incidence of undergoing initial ($P = 0.59$) or reoperative surgery ($P = 0.73$) for varicocele repair, and thus that NcP may not predispose patients to a higher risk of surgical failure. While further studies are needed to corroborate our findings, we conclude that there is no clear additional benefit to routinely investigating a pediatric varicocele patient with an abdominal US to exclude underlying NcP, as in our study, the presence of NcP did not impact clinical outcomes. Even though there is little risk in obtaining a Doppler US of the renal vessels, the added imaging time and cost has an impact on resource utilization, an issue that is important as we consider the current climate of cost-containment. The presented data provide an interesting, common pathophysiological finding that enjoys modest clinical value in routine practice. It may remain important in selected cases, such as patients with other symptoms consistent with NcP, multiple varicocele recurrences or possible extrinsic compression by a retroperitoneal mass.

Management of pediatric and adolescent varicoceles remains one of the most controversial topics in pediatric urology. According to the American Urological Association recommendations, varicoceles in these patients warrant intervention if there is objective evidence of reduced ipsilateral testicular size or semen abnormalities.[14] Other organizations, such as the European Association of Urology, raise concerns about possible overtreatment of adolescent varicoceles, proposing that observation alone may be unlikely to result in future fertility problems.[15] Despite a lack of universal consensus about management guidelines, it can be agreed that the goals of pediatric varicocele management are to address any bothersome symptoms, optimize testicular function for future fertility and address potential esthetic concerns caused by the appearance of a large varicocele. Interestingly, as data suggest that young patients with a nutcracker syndrome may spontaneously resolve, the presence of a NcP may be associated with varicocele resolution in some patients.[16] Future studies may consider this as an outcome of interest.

There is literature that supports a correlation between poor ipsilateral testicular growth and higher varicocele grade.[17] We initially hypothesized that due to the higher venous velocities and subsequent venous pressure found in NcP, the varicose veins would have been of greater diameters and consequently of greater grade, thus impacting ipsilateral testicular volumes. In our results, however, patients with NcP did not have significantly larger varicose veins or larger discrepancies in testicular volumes vs patients without NcP. Considering that total testicular volume is predictive of total motile sperm count in adolescents, extrapolating our findings may suggest that NcP is not a predictor of worse preoperative fertility status.[18] Further research evaluating semen parameters in adolescents with NcP and varicoceles continues to be warranted.

Our study is limited by its retrospective nature. Because the study was conducted in a single institution, our cohort is relatively small, yet comparable to other retrospective pediatric varicocele studies. Additionally, the duration of follow-up and number of patients lost to follow-up may have underestimated the number of varicocele recurrences. Although possible, it is unlikely that these patients would seek care at other pediatric institutions based on the referral patterns and characteristics of our health care system. While larger, prospective studies with longer term follow-up would help provide stronger evidence regarding the impact and necessity of diagnosing NcP, our study calls attention to the limited value of assessing for its presence in routine clinical practice.

CONCLUSION

NcP is a common finding in boys and young men with varicoceles. Fortunately, the presence of NcP does not appear to be associated with a higher likelihood of initial or reoperative surgery. Based on our study, radiological diagnosis of a NcP has few clinical ramifications as an isolated finding in the presence of clinical left-sided varicocele, and thus may not warrant systematic evaluation for its presence.

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