

# ADOLESCENT VARICOCELE: IS IT A UNILATERAL DISEASE?

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## ABSTRACT

**Objectives.** To evaluate the incidence of left and right varicocele in adolescents.

**Methods.** The study group consisted of 28 adolescents who underwent evaluation for varicocele at our clinic. In 19 patients, varicocele was detected on routine physical examination, and 9 patients presented with scrotal pain or discomfort. All patients were evaluated by three methods. Physical examination was followed in all cases by contact thermography and venography studies of both testes.

**Results.** The rate of left and right retrograde flow in the spermatic veins by the three methods used was as follows: physical examination 92.8% and 10.7%; contact thermography 100% and 89%; and venography 100% and 85.7%, respectively. Varicocele was not detected by physical examination in 2 (7.2%) of the 28 patients on the left side and in 21 (87.5%) of 24 on the right side.

**Conclusions.** The main finding of this study was that varicocele is a bilateral disease in 85.7% of adolescents. The high percentage of bilateral varicocele in our sample may explain the pathophysiologic mechanism whereby what has traditionally been considered a unilateral disease can produce bilateral testicular dysfunction. The high incidence of subclinical bilateral varicocele may indicate that we should consider varicocele a bilateral disease. The second finding was that only 10% of patients with right varicocele were diagnosed by physical examination and more than 85% were diagnosed by thermography, with confirmation by venography. Therefore, we suggest that thermography and venography should play a major role in the diagnosis of varicocele. UROLOGY 62: 742-747, 2003. © 2003 Elsevier Inc.

Varicocele, or venous dilation of the pampiniform plexus, is due to incompetent or absent valves. It has long been recognized as the most common cause of male infertility in adults.<sup>1-3</sup> The prevalence rate of varicocele is about 15% in healthy men and 40% in men treated in infertility clinics.<sup>4-6</sup> In adolescents, varicocele is usually asymptomatic; therefore, the diagnosis is typically made at routine physical examination. On occasion, a patient will present for evaluation of a scrotal mass or testicular discomfort, such as heaviness or a dull ache after standing all day. Although varicocele detected in adolescents was originally considered a completely innocent finding, most researchers agree today that when varicocele starts

early and persists to adulthood, the damage to the germ cells is greater, as is the testicular atrophy.<sup>3-7</sup> Moreover, Paduch and Niedzielski<sup>3</sup> found that repair in adolescents with moderate and severe varicocele reversed the testicular growth arrest and resulted in catch-up growth within 12 months of treatment. Varicocele is believed to occur mainly on the left side. Skoog *et al.*<sup>7</sup> found that palpable unilateral varicocele occurred on the left side in 85% to 90% of cases. A palpable right varicocele is found in cases of bilateral varicocele in 10% of patients but rarely occurs unilaterally.<sup>8-12</sup>

Recently, a few reports have suggested that the incidence of bilateral varicocele may be underestimated.<sup>13-19</sup> In addition to physical examination, several modalities are currently available for the detection of varicocele, including thermography, color flow Doppler sonography, and venography.<sup>4-7,19-27</sup> The purpose of the present study was to evaluate the incidence of varicocele in adolescents by several methods of examination. To the best of our knowledge, this type of comparison has never been performed in adolescents.

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## MATERIAL AND METHODS

The study group consisted of 28 patients aged 16 to 18 years (mean 17.2) who underwent evaluation for varicocele at our clinic between 1999 and 2002. The ethics committee approved the study, and all the patients' parents gave informed consent before the examinations. In 19 patients, varicocele was detected incidentally on routine physical examination during military recruitment evaluations. The other 9 patients presented with scrotal pain or discomfort. All patients were evaluated by three methods: physical examination, contact scrotal thermography, and venography, which were followed by embolization sclerotherapy of the internal spermatic vein. The indications for treatment were scrotal pain ( $n = 9$ ) and a fear of infertility expressed by the patient or parents ( $n = 19$ ). Embolization sclerotherapy of the spermatic vein was performed after detailed consultation with the patients' parents. Six months after embolization, all patients underwent physical examination and contact scrotal thermography to evaluate for recurrence and complications. All patients were followed up for 8 to 28 months (mean 16) after the procedure.

### PHYSICAL EXAMINATION

Patients were examined in a warm room after standing for 5 minutes. The scrotal contents were examined, including volume, position, and consistency of the testes and epididymis. Each spermatic cord was palpated in the standing position and during the Valsalva maneuver. The findings were graded according to the system of Dubin and Amelar<sup>16</sup> as follows: grade 1, varicocele palpable only during the Valsalva maneuver; grade 2, varicocele palpable in standing position; and grade 3, varicocele detectable by visual scrutiny alone. To prevent interobserver bias, the same experienced senior andrologist performed all the examinations.

### CONTACT SCROTAL THERMOGRAPHY

Contact thermography was performed with the patient upright and undressed, after remaining 5 minutes at room temperature of not less than 22°C. The penis was taped to the abdominal wall and the genital region was exposed. The investigator then brought the scrotum forward with both hands to apply the Varicoscreen, a flexible thermostrip liquid crystal film (Amsaten, De Pinte, Belgium) containing heat-sensitive liquid crystals. The screen scale ranges from 31.3°C to 35.3°C, with a color change every 0.8°C. In the healthy male, the temperature of the scrotal skin is symmetrically distributed and does not exceed 32.5°C, corresponding to a brown or reddish color change on the screen. In men with varicocele, the temperature is higher (32.5°C to 35.3°C) and the color changes to dark green, violet, or blue; the last two are diagnostic. A temperature differential of 0.8°C or more, encompassing at least 25% of the area of one hemiscrotum is considered suspicious of varicocele. We also compared the scrotal temperature distribution patterns of the two sides and the intensity and extension of the hyperthermia in the standing position and during the Valsalva maneuver.

### VENOGRAPHY AND PERCUTANEOUS SCLEROTHERAPY

Venography was performed as part of percutaneous sclerotherapy of the internal spermatic vein (ISV). The procedure was performed by an experienced interventional radiologist in an interventional radiology suite using digital fluoroscopic imaging and a 45°/90° tilt table (Polystar, Siemens, Germany). The tilt table is important for entering competent valves; in conjunction with various breathing maneuvers, it encourages antegrade flow in the ISV and allows passage of the catheter.

Vascular access was obtained by way of the right common femoral vein using a 6F vascular sheath catheter and a 3F

coaxial infusion catheter (Cook, Bjaeverskov, Denmark). The guiding catheter was advanced into the inferior vena cava (IVC) and from there into the left renal vein. Injection of contrast material (Ultravist 300, Schering AG, Berlin, Germany) in the left renal vein demonstrated passive reflux along the ISV into the pampiniform testicular plexus. Then, an attempt was made to catheterize the ISV superselectively using the 3F catheter. If successful, the 3F catheter was advanced under fluoroscopic control to the pelvic fossa. If the left ISV could not be entered, the patient was placed in the 5% to 10% Trendelenburg position, and deep inspiration and mild coughing were used as maneuvers to pass the upper valve. Inguinal reflux of the ISV was documented and quantified by injection of a bolus of iodinated contrast material diluted with heparinized saline solution (Ultravist 300). Before sclerotherapy, occlusion of the ISV in the inguinal canal was performed by the patient; a limited venographic series was used to confirm adequate occlusion. This prevented intratesticular reflux of the sclerosant and also washout of the sclerosant by incoming blood flow. Spasm of the ISV was induced by movement of the catheters to achieve occlusion of the ISV renal vein orifice, which was partially occluded by the indwelling guiding catheter. Then, 3 to 4 mL of sclerosant (Ethanolamine Oleate 5%, Medeva Pharma, Lancashire, UK) was injected forcefully into the ISV in the pelvic region, with the catheter being withdrawn for the last part of the bolus. This was followed by 1 to 2 mL of contrast material to flush the catheter. If no technical difficulties were encountered in superselective catheterization, the 3F catheter was retracted to the upper ISV.

After 5 to 10 minutes of continuous digital compression of the groin, with intermittent aspiration of the ISV after 5 minutes, the success of sclerotherapy was assessed by a repeated venographic injection. Any previously nonapparent collateral vessels that might reestablish ISV reflux were treated with additional sclerosant, up to a maximum of 10 mL per side.

When ISV occlusion was confirmed and no collateral vessels remained, the catheters were withdrawn into the left renal vein, and a semierect (up to 60°) left renal venogram was obtained to confirm the lack of reflux and additional collateral veins. For the diagnosis and treatment of right-sided varicocele, a right-sided ISV guiding catheter (a variation of the "Simmons" shape, Cook) was advanced into the IVC, and a right renal venogram was performed with the patient in the semierect position. When injection of contrast material (Ultravist 300) in the IVC demonstrated passive reflux along the ISV into the pampiniform testicular plexus, a diagnosis of right varicocele was made. The right ISV orifice was identified using gentle probing with a soft-tipped catheter guide or with the 3F coaxial infusion catheter. If the ISV orifice was competent, tilt-table and patient maneuvers were used to pass the upper valve. After sclerotherapy of the right ISV, using the same technique as on the left, with confirmation of ISV occlusion and absence of collateral filling, the catheters were withdrawn, the sheath was removed, and digital compression was applied to the puncture site for 5 minutes to ensure homeostasis. The patient was observed during the next hour and discharged home with specific instructions for immediate post-procedural follow-up. These included digital compression of the puncture site whenever the patient was not supine, bed rest for the first 4 hours, ample fluid intake, and nonsteroidal anti-inflammatory analgesics (not aspirin).

## RESULTS

On physical examination, 26 (92.8%) of 28 patients were found to have left varicocele of varying degrees, and 3 patients (10.7%) had right varicocele of varying degrees.

We defined subclinical varicocele as varicocele detected by scrotal thermography or venography but not by clinical examination. Subclinical varicocele was noted on the left side in 2 patients (7.1%) and on the right side in 21 (87.59%). The corresponding findings for the other methods were as follows: contact thermography, 28 patients (100%) with left varicocele and 25 (89.3%) with right varicocele (1 patient had a false-positive result); and venography, 28 (100%) and 24 (85.7%), respectively. Twenty-four patients (85.7%) underwent bilateral ISV embolization and only 4 (14.3%) unilateral left ISV embolization. The overall technical success was 100%. On follow-up, physical examination and contact thermography revealed recurrence in 2 patients (7.1%) on the left side. Two patients reported postprocedural inguinal pain and testicular discomfort, which were relieved after 24 hours. No major complications occurred.

### COMMENT

Varicocele was recognized as a reversible cause of male infertility in 1952. Thereafter, the early detection and treatment of varicocele in adolescents was introduced as a preventive measure against infertility. Early studies reported that the size of the varicocele had no relationship to the testicular tissue damage, semen pathologic findings, or improvement in semen quality after varicocelectomy.<sup>11,15</sup> Dubin and Amelar<sup>11</sup> reported that the size of the varicocele did not correlate with the adverse effects of varicocele repair, which led to good results whether the grade was 1, 2, or 3. Vereecken and Boeckx<sup>8</sup> in a study of 374 patients who underwent varicocele repair found that the preoperative semen analysis did not correlate with varicocele size and that all semen parameters improved postoperatively with an increase in left testicular volume. Lyon and associates<sup>9</sup> reported a similar negative correlation of varicocele grade and testicular size in 30 adolescents with left-sided varicocele. These findings indicated that even subclinical varicocele may have significant pathophysiologic potential and that varicocele in adolescents can lead to alterations in the testicular parenchyma.<sup>3</sup>

The reference standard method of small varicocele detection is testicular venography, which is based on the finding that retrograde flow can be provoked only in patients with varicocele.<sup>4,7</sup> Contact thermography is also noninvasive, simple, and reliable, with a high sensitivity and specificity.<sup>4</sup> In our study, both these modalities together demonstrated incidence rates of 100% for left varicocele and 85.7% for right varicocele.

However, many of the studies on the incidence of adolescent varicocele in urologic published reports<sup>3,5,7</sup> used only physical examination. Skoog *et*

*al.*<sup>7</sup> reported that palpable unilateral varicocele occurred on the left side in 85% to 90% of patients and bilateral varicocele in 10%. Greenbaum *et al.*,<sup>10</sup> in a survey of 21,529 healthy adolescents, found varicocele in 1478 subjects (6.86%); about 90% were on the left side and 10% were bilateral. These findings for physical examination agree with our results after physical examination, for which 26 (92.8%) of the 28 patients had left varicocele and 3 (10.7%) had right varicocele. However, when we added contact scrotal thermography and venography, considered the reference standard for diagnosis,<sup>7</sup> we found that 24 patients (85.7%) had bilateral varicocele and only 4 (14.2%) had unilateral left varicocele.

We believe that physical examination for varicocele has several disadvantages, including a limited capacity to detect blood flow changes and a risk of significant interphysician variability. Furthermore, physical examination alone may be inadequate to diagnose small or subclinical varicoceles. In our study, physical examination failed to detect 7.2% of the left varicoceles and about 90% of the right varicoceles that were detected with the more sensitive diagnostic modalities. This partly explains the difference between our findings on the incidence of right varicocele and those of earlier studies.<sup>4-9</sup> Our findings are supported by several published reports. In 1986, McClure and Hricak<sup>13</sup> used ultrasonography to detect subclinical varicocele in 50 infertile men, of whom 25 had palpable left-sided varicocele and 3 had palpable right-sided varicocele. All these cases were confirmed by sonographic examination. In addition, sonography detected subclinical varicoceles in 9 men on the left side and 21 men on the right side, indicating that 70% of the patients had bilateral varicocele. Using thermography, Chatel and associates<sup>17</sup> noted evidence of bilateral varicocele in 60% of 178 patients, and, using venography, Gonzalez and associates<sup>14</sup> reported a 61% rate in 39 patients.

Bigot and Chatel<sup>15</sup> found spermatic venous insufficiency to be almost as frequent on the right side as on the left (60% versus 76%). In a large study of 870 varicocelectomies performed between 1980 and 1981, Cockett *et al.*<sup>18</sup> found bilateral varicoceles in 57% of cases. In 65% of the new patients presenting with left varicocele, right varicocele was also found. The investigators suggested that these findings could explain the failure of left varicocelectomy to restore spermatogenesis and improve fertility in many patients. This assumption was supported by the study of Scherr and Goldstein,<sup>19</sup> showing significantly greater improvement in semen parameters for bilateral than for unilateral repair. Their findings implied that even small, unre-

paired varicoceles continue to have a detrimental effect on bilateral testicular function. In a more recent study, Abdulmaaboud and associates<sup>20</sup> reported bilateral varicocele in 42% of 301 infertile patients.

We believe that our use of thermography, together with the more invasive and accurate technique of venography, may account for the high incidence of right-sided and bilateral varicocele found in our sample. Therefore, we believe that contact thermography along with physical examination should be part of the routine evaluation for varicocele.

Our findings also agree with the autopsy data of Ahlberg and coworkers,<sup>21</sup> who documented an absence of valves in 40% of left spermatic veins and 23% of right ones, favoring a mechanical explanation for the predominance of left-sided varicocele. Accordingly, Wishahi<sup>22</sup> reported on absence of valves in both spermatic veins in 40 men.

Several theories of the pathophysiologic effect of ISV dilation on spermatogenesis have been advanced to explain how a unilateral anatomic anomaly could produce a bilateral testicular dysfunction. One theory is based on the findings of Zorngniotti and MacLoed<sup>23</sup> that testicular and scrotal temperatures are increased in patients with varicocele. Goldstein and Eid<sup>24</sup> documented an elevation in intratesticular temperature in 28 men with varicocele. These findings confirm the results of animal studies revealing an elevation of intratesticular temperature associated with varicocele. The higher testicular temperature apparently interferes with the production of chromatin by DNA polymerase, leading to abnormal morphology and poor sperm motility.<sup>25</sup> In our study, we documented bilateral elevation of contact scrotal temperature in 85.7% of the patients.

The high incidence of varicocele on the left side compared with the right is often attributed to the "nutcracker phenomenon." This theory claims that compression of the left renal vein by the superior mesenteric artery increases the pressure in the vein, with consequent dilation of the spermatic vein. However, we suggest that this accounts for only a small part of the difference in the incidence between the left and right sides and that there is an additional explanation. The spermatic vein arises anatomically from the pampiniform plexus near the deep inguinal ring. The left spermatic vein ends in the left renal vein, and the right vein ends in the IVC.<sup>26</sup> Therefore, the left spermatic vein is a few centimeters higher than the right one and has a higher hydrostatic pressure. This causes varicocele to be detected more often on the left side.

## CONCLUSIONS

The present study had two major findings. First, what was traditionally considered a predominantly unilateral anatomic abnormality apparently has a strikingly high incidence of bilaterally (85.7%). A high incidence of bilateral varicocele could explain the high rates of bilateral testicular dysfunction. The second finding was that only 10% of patients with right varicocele were diagnosed by physical examination and more than 85% were diagnosed by thermography with confirmation by venography. Therefore, we suggest that thermography and venography should play a major role in the diagnosis of varicocele.

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#### EDITORIAL COMMENT

This is a unique and important study; unique because venography, “reference standard,” was used in each instance to confirm the presence of a varicocele, and important because the diagnostic maneuvers used, contact thermography and venography, diagnosed a strikingly high frequency of bilaterality when only a unilateral varicocele was clinically suspected. Using a percutaneous retrograde venographic technique, these authors demonstrated that 85% of their patients had bilateral varicoceles present when the clinical examination had only indicated that one side was involved. Previous reports and these authors’ experience indicate that ISV reflux can only occur when the ISV valves are incompetent, resulting in a varicocele. This study, therefore, offers additional evidence to the findings already suggested by others cited that varicoceles are in fact often a bilateral disease. These patients underwent the “reference standard” of testing, allowing for objective validation of their findings, as well as validation of the accuracy of the other diagnostic modalities used.

This concept raises many unique and important issues. First, the data suggest that most males with varicoceles may have bilateral disease. Second, the findings may explain why a relatively large number of men have sustained significant semen and fertility abnormalities after an apparently successful unilateral varicolectomy and why better improvement in semen parameters has been found in some studies after bilateral repair. Third, the apparently high degree of clinical correlation between ultrasonography and thermography with ISV venography suggests that these modalities (with specific attention to the right side) should be used as a routine part of the

diagnostic evaluation. Fourth, if a larger amount of corroborative data is obtained confirming the results indicated in the present study, routine screening for bilateral disease may become the standard of care in treating all patients with varicoceles. A large cooperative prospective multicenter study could easily obtain sufficient appropriate data within a few years to answer this question.

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#### REPLY BY THE AUTHORS

In response to the first point. The bilaterality of varicocele was well confirmed in our more than 700 adult patients by screening with US color flow Doppler, thermography (highly sensitive), and retrograde venography followed by sclerotherapy.

Studies have shown that male fertility is preserved with only one healthy testis. Therefore, oligoteroasthenospermia (OTA) indicates a bilateral testicular dysfunction. This poses an enigma to clinicians: How can left varicocele cause bilateral testicular dysfunction? Although in some of the cases there exists an intertesticular venous connection that transfers heat and toxic material (vasoconstrictors-prostaglandins and norepinephrine) into the testicular tissue from one side to the other, this explains the phenomenon only partially. We believe the answer lies in our finding, in adolescents and adults, that varicocele is a bilateral disease. As such, in patients with OTA, how can treatment only of the left side heal also the right one? It seems that the correlation between varicocele and male infertility remains an obscure subject even after 50 years of treatment and the results seem to be fluctuating and unstable. However the clinical reality is now much clearer.

In May 2003, *The Lancet* published a meta-analysis of seven prospective randomized studies conducted in the last two decades suggesting that “varicocele repair does not seem to be an effective treatment for male subfertility.”<sup>1</sup> We were not surprised by the stated findings, considering that the vast majority of patients were treated according to the usual practice, on the left side only. Our calculations showed that only about 20%—that is, those who did not have right varicocele—received complete treatment. Until now, the bilaterality of varicocele has gone largely unrecognized. Therefore, the findings of the meta-analysis do not reflect the realistic clinical picture, and thus they have no clinical or statistical connection to reality. One of the studies reported a high rate of pregnancy after varicocele treatment as compared to an untreated group (Madgar *et al*<sup>2</sup>), but the other six studies failed to repeat this result and proved that repair of varicocele (left side), or medical consultation only without treatment, yield the same results. This is representative of the discrepant, confusing and often hit-or-miss handling of varicocele in the medical literature to date. It also explains why most infertile men are not examined for varicocele in IVF units, which is a product of the growing split phenomena between the urologists and andrologists on the one hand and the gynecologists on the other hand, on issues concerning infertility/fertility.

Our study suggests that the bilaterality of varicocele may have been missed because it is impossible to palpate right varicocele in more than 90% of cases. This issue will be treated in our next study.