

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Adolescent Varicocele: Who Is at Risk?

Philip Kumanov, Ralitsa N. Robeva and Analia Tomova

Pediatrics 2008;121;e53

DOI: 10.1542/peds.2007-0340

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/121/1/e53.full.html>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2008 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



Adolescent Varicocele: Who Is at Risk?

Philip Kumanov, MD, PhD, Ralitsa N. Robeva, MD, Analia Tomova, MD, PhD

Clinical Center of Endocrinology, Medical University-Sofia, Sofia, Bulgaria

The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

OBJECTIVES. Varicocele results from the abnormal dilation of the veins of the pampiniform plexus and is the most common identifiable cause of male infertility. It can develop during puberty and thus affect the testicular growth and function. The aim of this study was to determine the prevalence and the risk factors for the development of the varicocele among Bulgarian boys.

METHODS. In a prospective study, 6200 boys from 5 regions of the country aged 0 to 19 years were evaluated for varicocele. All were clinically healthy. Height, weight, testicular volumes, penile length, and penile circumference were also examined.

RESULTS. Varicocele was found in 4.1% of all investigated boys, whereas in the age group 10 to 19 years, it was 7.9%. After adjustment for age, the negative factors associated with the development of the disorder were height, penile length, and penile circumference, whereas the weight and BMI had a protective role. The prevalence of varicocele demonstrated clear regional differences, and it was found significantly more often among dark-eyed boys. The incidence of the disease increased rapidly during midpuberty.

CONCLUSIONS. The incidence of varicocele is related to some somatometric parameters and with the accelerated pubertal development. Longitudinal studies are needed to clarify better the relations between the adolescent varicocele and puberty.

www.pediatrics.org/cgi/doi/10.1542/peds.2007-0340

doi:10.1542/peds.2007-0340

Key Words

adolescence, varicocele, height, BMI, penile length, puberty

Accepted for publication May 29, 2007

Address correspondence to Philip Kumanov, MD, PhD, Clinical Center of Endocrinology, Medical University-Sofia, 6, Dame Gruev str, 1303, Sofia, Bulgaria. E-mail: phkumanov@lycos.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2008 by the American Academy of Pediatrics

VARICOCELE IS AN abnormal dilation of the veins of the pampiniform plexus of the spermatic cord and represents the most common identifiable cause of male infertility.¹ Many theories have been proposed to explain the mechanism by which the disease disrupts normal testicular function and causes infertility; however, none has been proved and the exact cause remains an enigma.² Interest has focused on adolescents with a varicocele because of the significant improvement of the sperm concentration and motility after varicocele treatment.³ Varicolectomy in the adolescent population has been proposed as a therapeutic intervention both to preserve fertility and to preserve testicular growth.⁴

Several studies have shown relationships between some anthropometric parameters and the incidence of varicocele.⁵⁻⁷ Our previous published study on 1200 boys from the capital of Bulgaria, Sofia, also indicated that some physical and sexual characteristics of the adolescent could influence the development of the venous anomaly⁸; therefore, we decided to analyze the data of 6200 Bulgarian boys from 5 regions of the country and to describe the possible relations between the physical and pubertal development of the children and the prevalence of varicocele.

METHODS

In a population-based, cross-sectional study on the growth and development in Bulgaria were included 6200 white boys who were between 0 (younger than 1 year) and 19 years from all socioeconomic classes and were from 5 regions of the country: Sofia (city), Plovdiv (city) and the adjacent rural area, Varna (city) and the adjacent rural area, Vratsa (town) and the adjacent rural area, and Blagoevgrad (town) and the adjacent rural area. The areas were chosen at random, but they are representative of the country's population and structure. The number of boys for the country and the regions was chosen according to Lwanga and Lemeshow⁹ with assumed prevalence of the disease of 5% and absolute precision of 2%. The children were seen at random in kindergartens, schools, and military units. They all were clinically healthy on the day of examination. An equal number of children were selected from urban and rural areas. Each of the 20 age groups (aged 0–19) had the same number of boys, and all 6200 children were distributed

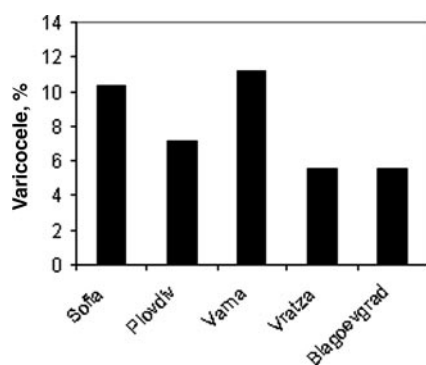


FIGURE 1
Distribution of the prevalence of varicocele (%) in 5 Bulgarian areas.

in the respective age groups according to the completed age at the day of examination. The children were included in the specified groups until their number reached the previously fixed number in the design of the study.⁹

All children were investigated by only 1 experienced examiner (Dr Kumanov) to reduce the interobserver error. The presence of varicocele was determined by palpation. The boys were examined in the standing position with the help of Valsalva maneuver when appropriate after the age of 7. The boys with new-found cases were sent to specialized hospitals for verification. The height, weight, pubic hair distribution, testicular volume (mL), and penile length (cm) were also measured and recorded. A Prader orchidometer was used to determine testicular volume. The pubic hair was described according to Tanner stages.¹⁰ The height of the children was measured with an anthropometer (Siber Hegner, Zürich, Switzerland). The stretched length of the flaccid penis was measured from the base of penis (the pubopenile skin junction) to the top of the penis excluding prepuce, and penile circumference was measured at the base of penis close to pubic hair with a measuring tape. In obese children, the low-abdominal adipose tissue was shifted manually to 1 side to measure penile length and circumference. BMI was calculated according to the formula body weight in kg/height in squared meters. Eyes and hair color were described in 513 children who were chosen at random. Hair color was grouped into the following categories: blond, brown, brown-black, and reddish. Eye color was assessed in the following categories: dark-eyed (black-brown and brown) and light-eyed, which included mixed, blue, and gray-green. All of the boys

TABLE 1 Significant factors influencing the varicocele in adolescent boys

Factor	OR	95% CI	P
Age	1.055	1.008–1.104	.022
Height	1.018	1.008–1.028	<.001
Penile length	1.158	1.083–1.238	<.001
Penile circumference	1.182	1.096–1.275	<.001
Dark eye color	2.007	1.032–3.904	.040
Dark hair color			NS

OR indicates odds ratio; CI, confidence interval; NS, nonsignificant.

TABLE 2 Factors Related to the Development of Varicocele After Adjustment for Age

Factor	OR	95% CI	P
Weight	0.985	0.972–0.997	.016
Height	1.024	1.008–1.041	.004
BMI	0.898	0.856–0.943	<.001
Left testicular volume	0.927	0.894–0.962	<.001
Right testicular volume			NS
Penile length	1.231	1.114–1.360	<.001
Penile circumference	1.255	1.127–1.397	<.001

and/or their parents consented to the examination. The study was approved by the institutional review board of the Clinical Center of Endocrinology, Medical University (Sofia, Bulgaria).

The statistical analyses were performed with SPSS for Windows 11.0 (SPSS Inc, Chicago, IL). Frequency analyses, descriptive statistics, χ^2 tests, and logistic regression were used where appropriate.

RESULTS

The prevalence of varicocele among all investigated children was 4.1%. Only left-sided varicocele was found. The presenting complaint was asymptomatic in almost all affected boys. The frequency of the disease was extremely low in boys who were younger than 10 years (0.22%) and increased rapidly in the age group 10 to 19 years (7.9%); therefore, the analyses of the influencing factors were made with the data of the latter age group ($n = 3100$). The distribution across the 5 investigated regions is shown in Fig 1. Significant differences in the prevalence of varicocele between the areas were found ($P = .009$); however, no significant difference was established between the children from rural and those from urban regions ($P > .05$).

According to the logistic regression analyses, the age of the boys was positively related to the development of varicocele, as well as penile length, penile circumference, and height of the children (Table 1). From the 513 randomly investigated children, 342 were dark-eyed and the other 171 were light-eyed. It is interesting that the dark eye color also increased the risk for the anomaly (Table 1). No relationship was found with hair color. After adjustment for age, the height, penile length, and circumference remained positively related to the incidence of varicocele, whereas BMI and weight became significant protective factors (Table 2). Penile length was

TABLE 3 Penile Length as a Factor Influencing Varicocele Prevalence in Adolescent Boys in Different Tanner Stages

Tanner Stage	OR	95% CI	P
1	3.474	2.026–5.955	<.001
2	2.145	1.533–3.000	<.001
3	1.686	1.220–2.330	.002
4			NS
5			NS
6			NS

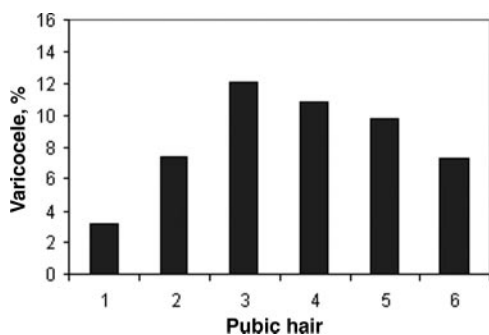


FIGURE 2
Distribution of the prevalence of varicocele (%) according to Tanner stage of pubic hair.

a predictive factor for the development of varicocele for boys in the first to third Tanner stages, whereas subsequently it was not related to the presence of the anomaly (Table 3). The prevalence of varicocele according to Tanner stages of pubic hair is shown in Fig 2. The prevalence of varicocele was greatest at pubic hair stage 3. There were significant differences in the prevalence of varicocele between Tanner stages 1 and 2 ($P < .001$) and 2 and 3 ($P = .016$). Between stages 3 and 4 and stages 4 and 5, differences in the prevalence of varicocele were not significant. The left testicular volume in boys with varicocele became smaller in comparison with those in healthy boys after the age of 14, whereas the volumes of the right testis remained similar. The relationships between left testicular volume, age, and Tanner pubic stage are shown in Fig 3.

DISCUSSION

Varicocele could be defined as an abnormal tortuosity and dilation of the veins of the pampiniform plexus.¹¹ The predominance of left-sided varicocele and the unique anatomy of left testicular vein are the base for several theories explaining the cause of the disease. The “nutcracker effect” is thought to occur when the left renal vein is compressed between the superior mesenteric artery and aorta, proximal of the point where the left testicular vein runs in it. The subsequent increase of

the hydrostatic pressure could result in varicocele formation. Other potential causes for the development of varicocele in the adolescent are the incompetent venous valve system, the increased arterial blood flow to the testis at puberty exceeding the venous capacity, and the elevated levels of nitric oxide in plexus pampiniformis.¹¹ The genetic susceptibility is also important, considering that 50% of first-degree relatives and >70% of brothers of men with varicocele also had a palpable varicocele.¹²

The incidence of the abnormality in older adolescents varies between 12.4% and 17.8%, with an average of 14.2%.¹¹ Our results demonstrated low prevalence of adolescent varicocele among Bulgarian boys (7.9%) for the age group 10 to 19 years. Similar low frequency was described in geographically closed populations on the Balkan Peninsula: among Greece adolescents, varicocele was detected in only 98 (3%) of 3047 school boys,¹³ whereas in Turkish boys aged 11 to 19 years, the prevalence of the disease was 11.02%.¹⁴ In addition, our results described significant regional differences. The prevalence of varicocele was highest in the areas of Sofia and Varna, which are the largest cities of the country and lowest in the areas of much smaller towns of Vratza and Blagoevgrad. The differences could be genetically determined, and a role of environmental factors is less likely in view of the regional economic development and manufacturing. We speculate that lifestyle factors, such as food intake, or differences in physical development could play a role.

Recent studies discussed the protective role of higher BMI and/or weight on the development of varicocele⁶⁻⁸ as well as the negative influence of height.^{5,15} Our results also showed that the age, height, penile length, and penile circumference of the boys could favor the development of varicocele, whereas weight and the BMI may have protective influence.

We speculate that the accelerated growth spurt and pubertal development could affect the incidence of the adolescent varicocele. The rapid growth could lead to decreased angle of the superior mesenteric artery with the aorta and thus to the “nutcracker effect” and respectively to higher hydrostatic pressure in the plexus pam-

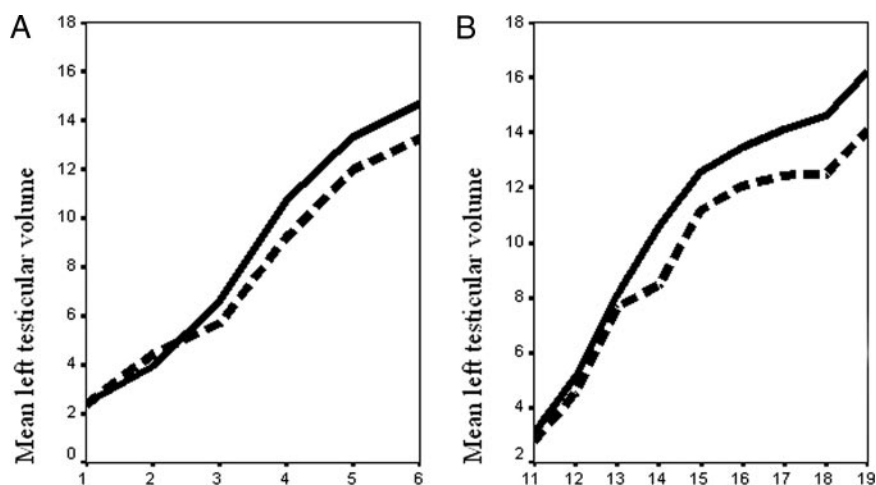


FIGURE 3
Left testicular volume according to age and Tanner pubic hair stage in children with varicocele (dashed line) and in healthy boys (solid line).

piniformis.⁵ In this case, the increased adipose tissue could protect the left renal vein from compression.⁷ Moreover, the accelerated pubertal development with growth spurt and increased androgen secretion may explain the relationship of penile size and varicocele; however, common vasoactive factors could induce rapid development of the penile vascular system and a simultaneous dilation of the venous plexus, which is a possible explanation for the observed relationship with penile size occurring in the early stages of the pubertal development. The role of nitric oxide might be discussed, because inducible nitric oxide synthase was found to be overexpressed in the varicocele testes.¹⁶

Increased adipose tissue in the spermatic cord leads to decreased detection of varicocele, but the decrease in varicocele prevalence as a function of BMI regardless of varicocele grade suggests that this explanation is less likely⁷; however, it is not clear whether the protective role of weight resulted from the increased adipose or muscle tissue. Moreover, both of them depend on the individual physical activity, which could affect the incidence of the varicocele per se. A high incidence of the disease was observed in athletes; in addition, physical activity might represent an aggravating factor for spermatogenesis in affected sportsmen with varicocele.^{17,18}

Varicocele is very rare in Bulgarian prepubertal boys and increased rapidly with the development of pubic stages 2 to 3. The disorder becomes most frequent during midpuberty; thereafter, the prevalence remains constant. The increase in testicular perfusion at puberty may unmask an underlying abnormality in the internal spermatic venous system and thus result in the presence of varicocele.¹⁹ Perhaps the rapid increase of height, penile length, and penile circumference that accompanies the exaggerated pubertal development reflects the imbalance in action of different endocrine and paracrine growth factors and therefore acts as a negative factor for the incidence of varicocele in genetically susceptible boys.

Our results showed that in children with varicocele, the left testicular volume became significantly smaller than that in healthy boys after the age of 14. Similarly, Skoog et al²⁰ summarized that it is during the rapid growth of the testes, between 11 and 16 years of age, that a volume discrepancy between the 2 testes became clinically apparent in the adolescent with a varicocele, and the loss of testicular volume is accompanied by a decrease in the sperm count. Consequently, early diagnosis of the disease is important for the prevention of sperm impairment and infertility.

To the best of our knowledge, this study showed for the first time that dark eye color is a risk factor for the development of varicocele; therefore, it is difficult to find an acceptable explanation. The iris color was not a risk factor for other conditions that also were investigated by us, such as gynecomastia and cryptorchidism. More studies among male adolescents and adults are required to confirm and clarify or to reject this finding. The relationship between some diseases and iris pigment have been described previously in animals and humans. The association between blue eye color and deafness in white

cats, known as the feline homolog of the human Waardenburg syndrome, was described in the early 1970s. Although the pleiotropic gene effect has been suggested, the precise hereditary mechanisms are not yet fully understood.²¹ Likewise, significantly more patients with type 1 diabetes were blue-eyed in comparison with healthy control subjects, but the explanation of the possible predisposition is still under debate.²²

As far as we know, this is the largest cross-sectional study on adolescent varicocele. The entire physical examination of all of the boys was done by only 1 investigator, thereby excluding the interobserver bias; however, our study has a few limitations. Varicocele was screened only by palpation without using Doppler sonography or thermography. Testicular volumes were measured only by an orchidometer. Use of ultrasound in our large population-based study was not practically feasible. Moreover, for mostly ethical reasons, we did not ask adolescents to give semen for analyses. Another limitation was the cross-sectional design of the study. Testes in normal boys are known to have different growth rates throughout adolescence, so a single measurement at 1 point in time may not capture the true abnormality. The low incidence of varicocele may also be attributable to the examination at a single point in time, which underlines the need for longitudinal studies. Nevertheless, our study has revealed some significant findings that could facilitate future research on varicocele.

CONCLUSIONS

This study analyzed the risk factors for the development of varicocele among a large cohort of Bulgarian adolescents. After adjustment for age, the negative factors for the development of the disorder were height, penile length, and penile circumference, whereas weight and BMI showed a protective role. The prevalence of varicocele demonstrated clear regional differences, and it was found more often among dark-eyed boys. The incidence of the disease increased rapidly during midpuberty. Longitudinal studies are needed to clarify the relations between the adolescent varicocele and pubertal development. Only the early finding and treatment of the disorder could prevent additional complications.

ACKNOWLEDGMENTS

This study was supported by the Medical University-Sofia.

We express our gratitude to Prof Mircho Vukov for statistical evaluation of the data.

REFERENCES

1. Kass E. Adolescent varicocele: current concepts. *Semin Urol.* 1988;2:140-145
2. Kass E. The management of the asymptomatic varicocele in adolescence. *Probl Urol.* 1990;4:690-704
3. Cayan S, Akbay E, Bozlu M, et al. The effect of varicocele repair on testicular volume in children and adolescents with varicocele. *J Urol.* 2002;168:731-734
4. Salzhauer E, Sokol A, Glassberg K. Paternity after adolescent varicocele repair. *Pediatrics.* 2004;114:1631-1633

5. Delaney D, Carr M, Kolon T, Snyder H, Zderik S. The physical characteristics of young males with varicocele. *BJU*. 2004;94:62–64
6. Nielsen ME, Zderic S, Freedland SJ, Jarow JP. Insight on pathogenesis of varicocele: relationship of varicocele and body mass index. *Urology*. 2006;68:392–396
7. Handel LN, Shetty R, Sigman M. The relationship between varicoceles and obesity. *J Urol*. 2006;176:2138–2140
8. Prabakaran S, Kumanov Ph, Tomova A, Hubaveshki S, Agarwal A. Adolescent varicocele: association with somatometric parameters. *Urol Int*. 2006;77:114–117
9. Lwanga SK, Lemeshow S. *Sample Size Determination in Health Studies: A Practical Manual*. Geneva, Switzerland: World Health Organization; 1991
10. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. *Arch Dis Child*. 1970;45:13–23
11. Paduch D, Skoog S. Current management of adolescent varicocele. *Rev Urol*. 2001;3:120–133
12. Raman J, Walmsley K, Goldstein M. Inheritance of varicocele. *Adult Urol*. 2005;65:1186–1189
13. Stavropoulos NE, Mihailidis I, Hastazeris K, et al. Varicocele in schoolboys. *Arch Androl*. 2002;48:187–192
14. Akbay E, Cayan S, Doruk E, Duce M, Bozlu M. The prevalence of varicocele-related testicular atrophy in Turkish children and adolescents. *BJU*. 2000;86:490–493
15. May M, Taymoorian K, Beutner S, et al. Body size and weight as predisposing factors in varicocele. *Scand J Urol Nephrol*. 2006;40:45–48
16. Santoro G, Romeo C, Impellizzeri P, et al. Nitric oxide synthase patterns in normal and varicocele testis in adolescent age. *Br Urol Int*. 2001;88:967–973
17. Di Luigi L, Gentile V, Pigozzi F, Parisi A, Gianetti D, Romanelli F. Physical activity as a possible aggravating factor for athletes with varicocele: impact on the semen profile. *Hum Reprod*. 2001;16:1180–1184
18. Di Luigi L, Romanelli F, Pigozzi F, et al. Role of sport medicine in andrological prevention. *Med Sport*. 1994;47:665–670
19. Sawczuk I, Hensle T, Burbige K, Nagler H. Varicoceles: effect on testicular volume in prepubertal and pubertal males. *Urology*. 1993;41:466–468
20. Skoog SJ, Roberts K, Goldstein M, Pryor J. The adolescent varicocele: what's new with an old problem in young patients? *Pediatrics*. 1997;100:112–122
21. Geigy CA, Heid S, Steffen F, Danielson K, Jaggy A, Gaillard C. Does a pleiotropic gene explain deafness and blue irises in white cats? *Vet J*. 2007;173:548–553
22. Ziegler AG, Baumgartl HJ, Ede G, et al. Low-pigment skin type and predisposition for development of type I diabetes. *Diabetes Care*. 1990;13:529–531

Adolescent Varicocele: Who Is at Risk?
Philip Kumanov, Ralitsa N. Robeva and Analia Tomova
Pediatrics 2008;121:e53
DOI: 10.1542/peds.2007-0340

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/121/1/e53.full.html
References	This article cites 21 articles, 5 of which can be accessed free at: http://pediatrics.aappublications.org/content/121/1/e53.full.html#ref-list-1
Citations	This article has been cited by 1 HighWire-hosted articles: http://pediatrics.aappublications.org/content/121/1/e53.full.html#related-urls
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Genitourinary Tract http://pediatrics.aappublications.org/cgi/collection/genitourinary_tract
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://pediatrics.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://pediatrics.aappublications.org/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2008 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

