Differences in Biochemical Markers and Body Mass Index Between Patients With and Without Varicocele

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Background: Varicocele is characterized by abnormal tortuosity and dilatation of the veins of the pampiniform plexus within the spermatic cord and is one of the causes of male infertility. This study aimed to evaluate the differences in biochemical markers and body mass index (BMI) between patients with and without varicocele.

Methods: Between January 2004 and June 2009, 102 patients with varicocele (Group A) were evaluated. Ninety-five age-matched male patients who did not have varicocele were selected as controls (Group B). Varicocele was diagnosed by physical examination and confirmed by Doppler ultrasonography. The range of ages was between 18 and 50 years old. BMI, testosterone, serum alkaline phosphatase, calcium, lactic dehydrogenase, inorganic phosphate, γ-glutamine transpeptidase, uric acid, albumin, iron, cholesterol, triglyceride, alanine aminotransferase, and aspartate aminotransferase levels were measured for all the subjects.

Results: The mean age was 35.4 years in group A and 36.5 years in group B. Of the 102 patients in group A, 20 were grade 1 varicocele, 55 were grade 2 and 27 were grade 3. The BMI (mean ± SD) of patients with varicocele (22.8 ± 3.2) was significantly lower than that of patients without varicocele (24.9 ± 4.1). Patients with varicocele had significantly lower serum levels of cholesterol than patients without varicocele (176.5 ± 31.1 *vs.* 187.7 ± 42.1 mg/dL). There were no significant differences for the other biochemical markers between the groups. Patients with grade 3 varicocele had a lower BMI than patients with grades 1 and 2 varicocele, but this was not significant. No significant differences were found for the other biochemical markers among the patients with grade 1, 2 or 3 varicocele.

Conclusion: Patients with varicocele had significantly lower serum levels of cholesterol than those without varicocele. In addition, the prevalence of varicocele was higher in patients with a lower BMI. Our findings suggest that patients with a greater BMI may have advantages in relieving the nutcracker phenomenon, which causes significant varicoceles. [*J Chin Med Assoc* 2010;73(4):194–198]

Key Words: biochemical markers, body mass index, testosterone, varicocele

Introduction

Varicocele is characterized by abnormal tortuosity and dilatation of the veins of the pampiniform plexus within the spermatic cord and is one of the causes of male infertility. The prevalence of varicocele is approximately 15–20% in the general population and 30–40% in infertile men.[1] Furthermore, approximately 69–81% of men with secondary infertility have varicocele.[2,3] Levinger et al proposed that varicocele prevalence is increased over time and the risk of incidence is approximately 10% for each decade of life.[4] The definite etiology of varicocele is still unknown. Kumanov et al suggested that weight and body mass index (BMI) have a protective role, and height, penile length and penile circumference were negative factors in the

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development of varicocele in 6,200 boys aged 0–19 years.[5] Delaney et al demonstrated that patients with varicocele are significantly taller and heavier than age-matched controls.[6] Nielsen et al reported that varicoceles are less likely to be diagnosed among obese men.[7]

The role of testosterone in the pathophysiology of varicocele is not established and testosterone might induce relaxation of the human internal spermatic vein.[8] Sheriff showed that there was increased cholesterol and glyceride in the testes of patients with bilateral varicocele compared with those in controls.[9] Odabas et al suggested that the levels of lactic dehydrogenase (LDH) were higher in the spermatic vein than those in the peripheral vein.[10]

Other than findings on age, BMI and testosterone levels, there is limited information about the correlation between biochemical markers and varicocele. Therefore, we conducted this prospective study to evaluate differences between patients with and without varicocele with regard to BMI, testosterone levels and serum biochemical markers including hemoglobin, alkaline phosphatase (Alk-p), calcium, LDH, inorganic phosphate, γ-glutamine transpeptidase, uric acid, albumin, iron, cholesterol (Cho), triglyceride (TG), alanine aminotransferase, and aspartate aminotransferase levels. We also wished to determine possible risk factors in the pathogenesis of varicocele.

Methods

Patients

From January 2004 to June 2009, 102 patients with varicocele (Group A) were included for evaluation for this study. Ninety-five male patients who did not have varicocele were selected as controls (Group B). All of the 197 patients were normal, healthy young to middle-aged males. They were from the outpatient Department of Urology or had received a regular physical check-up at the hospital. Varicocele was diagnosed by physical examination and confirmed by Doppler ultrasonography. Varicocele grades were defined as: grade 1, palpable only with the Valsalva maneuver; grade 2, palpable without the Valsalva maneuver; and grade 3, visible from a distance.[11] Patients with subclinical varicocele were excluded from the study. The range of ages was between 18 and 50 years old. BMI, and testosterone, Alk-p, calcium, LDH, inorganic phosphate, glutamine transpeptidase, uric acid, albumin, iron, Cho, TG, alanine aminotransferase, aspartate aminotransferase and hemoglobin levels were measured in all of the patients (normal ranges: BMI < 25, normal weight; BMI ≥ 25 and < 30, overweight; BMI ≥ 30, obese; testosterone, 241–827 ng/dL; Alk-p, 100–280 U/L; calcium, 8.1–10.7 mg/dL; LDH, 95–213 U/L; inorganic phosphate, 2.1–4.7 mg/dL; glutamine transpeptidase, 8–60 U/L; uric acid, 2.5–7.2 mg/dL; albumin, 3.7–5.3 g/dL; iron, 35–200 μg/dL; Cho, 125–240 mg/dL; TG, 20–200 mg/dL; alanine aminotransferase, 0–40 U/L; aspartate aminotransferase, 5–45 U/L; hemoglobin, 12–16 g/dL). Patients with poor control of diabetes mellitus, hypertension or other systemic disease or BMI < 15 or > 40 were excluded from the study.

Patients were examined in a warm room while standing up and the scrotum was inspected and palpated. All the patients received Doppler ultrasonography of the scrotum. All the patients signed informed consent, and the study was approved by the Institutional Review Board of Taipei City Hospital.

Statistical analysis

The Mann-Whitney U test and Kruskal-Wallis test were used for statistical analysis, with $p < 0.05$ considered statistically significant.

Results

The mean age was 35.4 years in group A and 36.5 years old in group B. Data for age, BMI, testosterone levels and biochemical markers for patients in both groups, and different grades of varicocele are shown in Tables 1 and 2. There were no significant differences in age between the patients of groups A and B and among the patients with different grades of varicocele (grades 1, 2 and 3). Of the 102 patients in group A, 19.6% were grade 1, 53.9% were grade 2 and 26.5% were grade 3. The BMI of patients with varicocele was significantly lower ($p = 0.03$) than that in patients without varicocele (Table 1). Patients with varicocele had lower serum levels of Cho, TG and testosterone and higher serum levels of LDH and Alk-p than patients without varicocele, but only Cho was significantly different ($p = 0.03$, Table 1). There were no significant differences in the other biochemical markers between the patients of groups A and B (Table 1).

Patients with grade 3 varicocele had a lower BMI than patients with grades 1 and 2 varicocele, but this was not significantly different (Table 2). Patients with grade 3 varicocele had lower serum levels of Cho and testosterone and higher serum levels of LDH and Alk-p than patients with low grade varicocele (grades 1 and 2), but this was not significant. There were no significant differences in any of the other biochemical markers among the patients with grades 1, 2, and 3 varicocele (Table 2).

Table 1. Age, serum biochemical markers, testosterone and BMI in groups A and B*

	A ($n=102$)	B ($n=95$)	$p^{\dagger}$
Age (yr)	35.4 ± 9.6	36.5 ± 10.5	0.76
Alk-p (U/L)	128.5 ± 42.6	121.5 ± 40.5	0.09
Calcium (mg/dL)	8.9 ± 0.2	8.8 ± 0.2	0.79
LDH (U/L)	128.9 ± 22.9	122.8 ± 21.1	0.09
IP (mg/dL)	3.1 ± 0.4	3.2 ± 0.5	0.32
γ-GT (U/L)	31.2 ± 12.1	29.1 ± 10.5	0.43
Uric acid (mg/dL)	6.0 ± 1.5	6.1 ± 1.9	0.83
Albumin (g/dL)	3.6 ± 0.4	3.7 ± 0.5	0.86
Iron (μg/dL)	77.8 ± 29.2	81.2 ± 32.7	0.55
Cholesterol (mg/dL)	176.5 ± 31.1	187.7 ± 42.1	0.03
Triglyceride (mg/dL)	140.5 ± 85.2	166.7 ± 93.5	0.06
ALT (U/L)	25.4 ± 11.2	26.5 ± 12.5	0.89
AST (U/L)	26.2 ± 10.5	28.2 ± 11.7	0.75
Hemoglobin (g/dL)	14.2 ± 1.8	14.5 ± 1.9	0.77
Testosterone (ng/dL)	332.5 ± 104.6	399.4 ± 193.1	0.06
BMI (kg/m^2)	22.8 ± 3.2	24.9 ± 4.1	0.03

**Data presented as mean ± standard deviation; †statistical analysis by Mann-Whitney U test. A = group A, with varicocele; B = group B, without varicocele; Alk-p = alkaline phosphatase; LDH = lactic dehydrogenase; IP = inorganic phosphate; γ-GT = γ-glutamine transpeptidase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index.*

Table 2. Age, serum biochemical markers, testosterone and BMI according to different grades of varicocele*

	Grade 1 ($n=20$)	Grade 2 ($n=55$)	Grade 3 ($n=27$)	$p^{\dagger}$
Age (yr)	36.1 ± 9.7	34.9 ± 9.3	35.3 ± 9.5	0.69
Alk-p (U/L)	122.3 ± 43.4	125.5 ± 41.6	133.6 ± 43.1	0.08
Calcium (mg/dL)	8.9 ± 0.3	8.9 ± 0.2	8.8 ± 0.3	0.63
LDH (U/L)	124.1 ± 21.9	128.4 ± 22.5	133.9 ± 23.2	0.07
IP (mg/dL)	3.0 ± 0.4	3.1 ± 0.5	3.2 ± 0.4	0.46
γ-GT (U/L)	30.8 ± 12.4	31.1 ± 12.0	31.6 ± 11.8	0.65
Uric acid (mg/dL)	6.1 ± 1.6	6.0 ± 1.4	5.9 ± 1.4	0.54
Albumin (g/dL)	3.7 ± 0.5	3.6 ± 0.4	3.6 ± 0.5	0.89
Iron (μg/dL)	78.2 ± 29.3	77.7 ± 29.1	76.5 ± 28.9	0.67
Cholesterol (mg/dL)	183.3 ± 31.9	175.5 ± 31.2	169.4 ± 30.5	0.09
Triglyceride (mg/dL)	137.1 ± 83.5	141.2 ± 84.2	145.3 ± 87.2	0.09
ALT (U/L)	25.6 ± 11.9	25.3 ± 11.2	25.1 ± 11.1	0.69
AST (U/L)	26.0 ± 15.7	26.1 ± 10.4	27.1 ± 11.2	0.75
Hemoglobin (g/dL)	14.2 ± 1.7	14.0 ± 1.5	14.3 ± 1.9	0.45
Testosterone (ng/dL)	352.2 ± 99.5	325.5 ± 101.6	300.1 ± 145.1	0.06
BMI (kg/m^2)	23.7 ± 3.4	22.7 ± 3.1	21.7 ± 3.0	0.06

**Data presented as mean ± standard deviation; †statistical analysis by Kruskal-Wallis test. Alk-p = alkaline phosphatase; LDH = lactic dehydrogenase; IP = inorganic phosphate; γ-GT = γ-glutamine transpeptidase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index.*

Discussion

Tsao et al showed that the prevalence and severity of varicoceles is inversely correlated with obesity, which indicates that obesity may result in a decreased nutcracker effect.[12] Handel et al reported that the prevalence of varicocele decreases with increasing BMI, and the reason for this is that increased adipose tissue decreases compression of the left renal vein and prevents detection due to adipose tissue in the spermatic cord.[13] In the present study, patients with varicocele had a lower BMI than normal age-matched controls, but patients with grade 3 varicocele did not have a significantly lower BMI than patients with lower-grade varicocele. The different etiology between our study and that of Tsao et al may be because patients in the previous study were young males serving in the army, which was different from our patients, but the etiology needs further evaluation.

We found that obese or overweight ($BMI \geq 25$) patients might have higher serum levels of Cho and TG than normal subjects ($BMI < 25$). Sultan Sheriff demonstrated a marked increase in lipids, Cho and TG in the testis of varicocele patients and the etiology may have been due to non-utilization of Cho for androgen biosynthesis.[14] In this study, patients with varicocele had significantly lower serum levels of Cho than patients without varicocele, but no significant difference was found for TG, which might be due to the large standard deviation (Table 1). However, there were no significant differences in Cho and TG among patients with different grades of varicocele (Table 2), and the reason needs further investigation. Obesity can mask the clinical detection of varicocele. Therefore, we used Doppler ultrasonography to confirm the diagnosis of varicocele and excluded those patients with subclinical varicocele.

Kumanov et al demonstrated that gynecomastia is negatively correlated with BMI.[15] Low serum follicle-stimulating hormone and high testosterone are good prognostic factors for varicocelectomy.[16] Ishikawa and Fujisawa showed that the vasodilatory effect of testosterone is decreased in high grade varicocele and they suggested that serum free testosterone will be increased after varicocele repair.[17] Ghosh and York have reported that testosterone levels are lower and Alk-p levels are higher in the testis of varicocele-created rats.[18] In our study, patients with varicocele had lower serum levels of testosterone and higher serum levels of Alk-p than patients without varicocele. In addition, patients with grade 3 varicocele had lower serum levels of testosterone and higher serum levels of Alk-p than patients with low grade varicocele. Both parameters did not reach statistical significance, and the reason might be due to a large standard deviation for testosterone and Alk-p levels. Therefore, the role of testosterone and Alk-p in patients with varicocele needs further evaluation; however, we did not measure follicle-stimulating hormone in this study. Our previous study showed that more free radicals might be generated in varicocele veins than in the corresponding peripheral veins in patients with varicocele, because 8-hydroxy-2′-deoxyguanosine levels of leukocyte DNA in spermatic veins are higher than in the corresponding peripheral veins in these patients.[19] Yesilli et al showed that LDH and malondialdehyde levels are greater in the sperm of infertile men with varicocele, but the levels of LDH and malondialdehyde does not decrease after varicocelectomy.[20] In the present study, serum levels of LDH were higher in patients with varicocele than in patients without varicocele. Furthermore, higher serum levels of LDH were found in patients with high-grade varicocele than in patients with lower-grade varicocele. Neither of these findings was statistically significant. Therefore, the effect of LDH in patients with varicocele needs further evaluation.

Our findings suggest that an increase in body fat might be associated with relieving the nutcracker phenomenon of the superior mesenteric artery to the left renal vein. However, this study had some limitations. First, we did not compare the change in severity of varicocele in the same individual as BMI changed over time. Second, we did not use other imaging studies, such as computed tomography or magnetic resonance imaging, to demonstrate the relationship between visceral fat and the region of the superior mesenteric artery, left renal vein and aorta. Third, the case numbers were small from an epidemiological view, because all of the subjects needed to have data for biochemical markers, which restricted the patient numbers. Therefore, we need to include more cases in future studies.

In conclusion, patients with varicocele might have significantly lower serum levels of cholesterol than patients without varicocele. In addition, our findings support the hypothesis that patients with a greater BMI may have advantages in relieving the nutcracker phenomenon causing significant varicoceles, but further studies are required to clarify this issue.

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