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Low body mass index might be a predisposing factor for varicocele recurrence: a prospective study

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Summary

We investigated the possible relationship between body mass index (BMI) score and varicocele recurrence in an infertile patient population. A total of 255 primary infertile male patients (138 with varicocele and 117 for control) were included in this study. Height and weight measurements, clinical examination for varicocele, determination of serum hormone levels and spermiogram were performed in all cases. The BMI score was calculated, and patients with varicocele were operated with subinguinal technique and re-examined for recurrences. The varicocele group had significantly lower weight and the BMI score than the control group ($P < 0.001$). Varicocele recurrences were found in 22 patients (16% of them) after the operations. The BMI score was significantly lower in the recurrent group than in the nonrecurrent and control groups ($P < 0.001$). 73% of the recurrent, 50% of the nonrecurrent and 25% of the control group patients' BMI scores were under 25 kg m^{-2} ($P < 0.001$). In logistic regression analysis, the BMI score was found as a determinant for varicocele recurrence ($P = 0.027$; OR: 1.25). It is concluded that BMI score lower than 25 kg m^{-2} significantly increases the recurrence rate after varicocele operation, and it can be used as an objective indicator for microsurgical varicocelectomy.

Introduction

Varicocele is the most commonly encountered and surgically correctable cause of male infertility. In the male population, the prevalence of varicocele is approximately 15%. Furthermore, 35% of men with primary infertility and 81% of men with secondary infertility have varicocele (Dubin & Amelar, 1971; Gorelick & Goldstein, 1993; Witt & Lipshultz, 1993; Jarow *et al.*, 1996). Moreover, from 75 to 90% of varicoceles are determined on the left side. The incidence of bilateral varicocele is from 15 to 50%; however, the isolated right varicocele is too rare (Handel *et al.*, 2006).

Several factors are accused for the development of varicocele. The anatomical differences between the right and left testicular veins, the absence of competent venous valves in the testicular veins and partial compression of the left renal vein between the aorta and superior mesenteric artery (nutcracker effect) are among the accepted theories (Naughton *et al.*, 2001). Some studies have been performed to investigate the possible relationship between body mass index (BMI) score and varicocele formation most of which have found that prevalence of varicocele decreases with the increasing BMI score or vice versa (Handel *et al.*, 2006; Nielsen *et al.*, 2006; Prabakaran *et al.*, 2006; Gokce *et al.*, 2013).

Various successful techniques have been described for surgical treatment of varicocele. Depending on the used operative technique, the incidence of varicocele recurrence varies from 0.6 to 28% (Homonnai *et al.*, 1980; Kaufman *et al.*, 1983; Goldstein *et al.*, 1992; Marmar & Kim, 1994). Although the exact mechanism for recurrence is not precisely determined, ineffective venous ligation and anatomical variations of venous structures seem to be the main causes of it (Belli, 1998). To the best of our knowledge, there is no study to investigate the effect of the BMI score on varicocele recurrence in literature. Thus, the aim of this prospective study is to investigate any relationship between the BMI score and the varicocele recurrence in the infertile patient population.

Patients and methods

Patient selection

Between January 2006 and December 2010, 291 consecutive primary infertile male patients presented to our

University Hospital Urology clinic and were enrolled to this prospective study. Institutional review board approval was obtained, and all patients were informed about the study. Patients who had the previous history of abdomino-pelvic, retroperitoneal, inguinal or scrotal operations (including previous varicocele repair or orchidopexy) and who gained or lost weight more than 5% at post-operative follow-up period were excluded from the study. Patients who had subclinical varicocele were diagnosed by Doppler ultrasonography, and those who had any kind of hormonal disturbances including hyper- or hypogonadotrophic hypogonadism and hyperprolactinemia were also excluded. Following the exclusion criteria, 255 primary infertile male patients (138 infertile patients with varicocele and 117 infertile patients without varicocele, named as the control group) were found to be eligible for this study, and the data of these patients were taken into consideration.

Physical examinations

Physical examinations, including weight and height measurements, were performed by a single examiner (SG). Spermatic cord examinations were performed in a warm room, and the patients were at supine and standing position, both with and without the Valsalva manoeuvre. The severity of varicocele was classified as small (grade I – palpable only with the Valsalva manoeuvre), medium (grade II – palpable without the Valsalva manoeuvre, but not visible) and large (grade III – easily visible through the scrotal skin without the Valsalva manoeuvre) according to the standard grading system stated by Dubin & Amelar (1970). Varicoceles were diagnosed only by physical examination. Patients with varicocele were also asked for the presence of scrotal pain related to varicocele.

Calculation and categorisation of BMI score

The BMI score was defined and calculated using the mathematical formula of weight (kg)/height $(m)^2$. According to National Institute of Health definition, patients with a BMI score of <25 kg m^{-2} were categorised as normal weight, those with a BMI score of 25–30 kg m^{-2} as overweight and those with a BMI score more than 30 kg m^{-2} as obese (NIH, 1998).

Hormonal examinations and sperm analysis

After physical examination, morning blood samples were obtained from all subjects, and serum follicle-stimulating hormone (FSH), luteinising hormone (LH), prolactin (PRL) and total testosterone (T) levels were measured. All serum samples were analysed using chemiluminescence assays (UniCel DXI 800; Beckman Coulter Inc., Miami, FL, USA).

To determine the sperm parameters, all subjects were asked to give their semen samples in two different periods for analysis using the semen analysis method. Semen samples were obtained by masturbation after three to 5 days of sexual abstinence. Samples were examined within 1 h of collection, and after liquefaction, standard semen parameters (volume, concentration, motility and morphology) were determined according to World Health Organization guidelines (WHO, 1999). The total motile sperm count (TMSC) was calculated with the following formula: semen volume × sperm concentration per millilitre × per cent motility/100.

Operation technique

All patients with varicocele were operated using conventional subinguinal varicocelectomy technique by a single surgeon (SG). Briefly, under spinal/regional anaesthesia, a 2–3 cm skin incision was made below the external inguinal ring. The testicle was delivered into the operative field, and all dilated external spermatic and gubernacular veins were ligated and divided. Thereafter, the spermatic cord was found; external and internal spermatic fasciae were opened in the longitudinal direction. The spermatic artery and lymphatics were identified and preserved as much as possible. The vas deferens and its vessels were also preserved. All dilated internal spermatic veins were ligated and divided.

Post-operative follow-up

All subjects who underwent varicocelectomy were re-examined for any post-operative complications such as varicocele recurrence, hydrocele formation, haematoma and testicular atrophy at early (1 month) and late (at least 6 months) post-operative periods. The same pre-operative *physical examination* criteria were used for the diagnosis of the varicocele recurrences.

Statistical analysis

The SPSS 13.0 statistical software package (SPSS Inc., Chicago, IL, USA) was used to analyse all of the data. Categorical variables were compared using chi-square test, and continuous variables were compared using independent-samples *t-test* and ANOVA *post hoc* Tukey's HSD test. A binary logistic regression analysis was performed to determine the association between varicocele recurrence and BMI score, testicular pain, serum hormone levels and pre-operative sperm parameters. As height and weight were components of the BMI score, these parameters were not included into the regression model to avoid

their confounding effect. Alpha level was set at 0.05, and all of the tests used were two-tailed. A *P*-value <0.05 was considered as significant.

Results

The overall follow-up period was 9.2 ± 2.4 (range from 6 to 16) months. The demographic information of study groups is presented in Table 1. Mean age, height, weight and BMI score of overall patients were 32.0 ± 6.2 years, 174.5 ± 6.5 cm, 78.5 ± 10.4 kg and 25.7 ± 3.0 kg m^{-2} respectively.

There were no statistically significant differences between the primary varicocele and control groups regarding age and height ($P = 0.131$ and $P = 0.396$ respectively). However, the primary varicocele group had significantly lower weight and BMI score than the control group ($P < 0.001$ and $P < 0.001$ respectively). 54% of the patients in the primary varicocele and 25% of the control subjects had BMI scores <25, whereas 42% of patients with primary varicocele and 62% of the control subjects had BMI scores between 25 and 30 kg m^{-2} (Table 1). These differences were found statistically significant ($P < 0.001$). Two groups were similar with regard to serum FSH, LH, prolactin and testosterone levels ($P = 0.159$, $P = 0.234$, $P = 0.191$ and $P = 0.335$ respectively). However, pre-operative sperm motility, morphology and TMSC in primary varicocele groups were significantly higher than in the control group ($P < 0.001$, $P < 0.001$ and $P < 0.002$ respectively).

Table 1 Patients' characteristics

	Overall	Primary varicocele	Primary infertile (control)	*P*-value
Patients (*n*)	255	138	117	–
Age (year)				
Range	18–45	18–45	18–45	0.131*
Mean ± SD	32.0 ± 6.2	32.6 ± 6.7	31.2 ± 5.4	
Height (cm)				
Range	155–190	155–190	158–184	0.396*
Mean ± SD	174.5 ± 6.5	174.8 ± 6.8	174.1 ± 6.2	
Weight (kg)				
Range	55–107	55–105	60–107	<0.001*
Mean ± SD	78.5 ± 10.4	75.8 ± 9.7	81.6 ± 10.4	
BMI (kg m^{-2})				
Range	17.5–34.9	17.5–34.9	21.1–34.7	<0.001*
Mean ± SD	25.7 ± 3.0	24.8 ± 2.9	26.9 ± 2.9	
Cat. BMI *n* (%)				
BMI < 25	103 (40)	74 (54)	29 (25)	<0.001†
BMI 25–30	131 (52)	58 (42)	73 (62)	
BMI > 30	21 (8)	6 (4)	15 (13)	
Varicocele (%)				
Bilateral	–	24 (17)	–	–
Grade I	–	30 (22)	–	
Grade II	–	76 (55)	–	
Grade III	–	32 (23)	–	
Testicular pain	–	34 (25)	–	–
Serum FSH (mIU ml^{-1})	7.3 ± 3.2	7.5 ± 3.9	7.0 ± 1.9	0.159*
Serum LH (mIU ml^{-1})	5.8 ± 2.2	6.0 ± 2.7	5.7 ± 1.4	0.234*
Prolactin (ng ml^{-1})	9.2 ± 2.6	9.4 ± 2.8	9.0 ± 2.3	0.191*
Testosterone (ng dl^{-1})	514.7 ± 112.0	508 ± 127.5	522.0 ± 90.3	0.335*
Spermiogram				
Volume (ml)	3.1 ± 1.0	3.2 ± 0.9	3.0 ± 1.0	0.080*
Count (million ml^{-1})	9.1 ± 7.2	9.3 ± 6.7	8.9 ± 7.8	0.654*
Motility (%)	16.4 ± 12.2	19.7 ± 12.6	12.4 ± 10.6	<0.001*
Morphology (%)	15.8 ± 12.1	18.6 ± 12.6	12.6 ± 10.8	<0.001*
TMSC (million ml^{-1})	6.4 ± 6.5	7.6 ± 6.8	5.1 ± 5.8	<0.002*

TMSC, total motile sperm count.

*Independent *t*-test was used for comparison of continuous variables.

†Chi-square test was used for comparison of categorical variables.

After the subinguinal varicocelectomy operation, varicocele recurrences occurred in 22 (16%) patients. Nonrecurrent, recurrent and control group patients' data are summarised in Table 2. There were no statistically significant differences in these three groups regarding age and height ($P = 0.498$ and $P = 0.732$ respectively). However, weight and BMI score of recurrent varicocele group were significantly lower than in the other groups ($P < 0.001$ and $P < 0.001$ respectively). 73% of the recurrent, 50% of the nonrecurrent and 25% of the control group patients' BMI scores were under 25 kg m^{-2}. Additionally, 27% of the recurrent, 45% of the nonrecurrent and 62% of the control group patients' BMI scores were between 25 and 30 kg m^{-2}, and these differences were found statistically significant ($P < 0.001$). Serum LH, prolactin, testosterone levels and TMSC were similar in all groups ($P = 0.089$, $P = 0.482$, $P = 0.184$ and $P = 0.078$ respectively); however, serum FSH levels were higher in the recurrent group than in the other groups ($P = 0.002$). Sperm motility and morphology were found to be better in the nonrecurrent group ($P < 0.001$ and $P < 0.001$ respectively). In logistic regression model, only the BMI score was found as a determinant for varicocele recurrence ($P = 0.027$; OR: 1.25, CI: 0.66–0.96) (Table 3).

All varicocele recurrences were detected on the left side (12 patients with grade II and 10 patients with grade I varicocele). Varicocele grade changes in the recurrent group are shown in Table 4. Haematoma or testicular atrophy was not observed in the operated group during the follow-up period. Mild or moderate hydroceles developed in eight patients (6%). Among all recurrent varicocele subjects ($n = 22$), six patients were reoperated using the same varicocelectomy technique. The other patients did not accept the reoperation, and some of them were referred to assisted reproductive technique centres.

Table 2 Clinical characteristics of three subgroups

Characteristics	Groups			*P*-value
	Nonrecurrent varicocele	Recurrent varicocele	Primary infertile (control)	
Patients (*n*)	116	22	117	–
Age (year)				
Range	18–45	18–43	18–45	0.498*
Mean ± SD	32.6 ± 6.8[a]	32.5 ± 6.7[a]	31.2 ± 5.4[a]	
Height (cm)				
Range	155–190	163–188	158–184	0.732*
Mean ± SD	174.8 ± 6.9[a]	175.1 ± 6.5[a]	174.1 ± 6.2[a]	
Weight (kg)				
Range	55–105	60–84	60–107	<0.001*
Mean ± SD	76.6 ± 10.0[a]	71.3 ± 6.5[b]	81.7 ± 10.4[c]	
BMI (kg m^{-2})				
Range	19.6–34.9	17.5–27.3	21.1–34.7	<0.001*
Mean ± SD	25.1 ± 2.9[a]	23.3 ± 2.3[b]	26.9 ± 2.9[c]	
Cat. BMI *n* (%)				
BMI < 25	58 (50)	16 (73)	29 (25)	<0.001†
BMI 25–30	52 (45)	6 (27)	73 (62)	
BMI > 30	6 (5)	0 (0)	15 (13)	
Testicular pain (%)	28 (24)	6 (27)	–	0.789†
Serum FSH (mIU ml^{-1})	7.1 ± 3.3[a]	9.6 ± 5.9[b]	7.0 ± 2.0[a]	0.002*
Serum LH (mIU ml^{-1})	5.8 ± 2.5[a,b]	6.8 ± 3.5[b]	5.7 ± 1.4[a]	0.089*
Prolactin (ng ml^{-1})	9.4 ± 2.7[a]	9.6 ± 3.3[a]	9.0 ± 2.3[a]	0.482*
Testosterone (ng dl^{-1})	502.0 ± 126.9[a]	542.3 ± 128.1[a]	522.0 ± 90.3[a]	0.184*
Spermiogram				
Volume (ml)	3.3 ± 0.9[a]	2.98 ± 0.9[a]	3.0 ± 1.0[a]	0.356*
Count (million ml^{-1})	9.52 ± 7.0[a]	7.9 ± 5.1[a]	8.9 ± 7.8[a]	0.515*
Motility (%)	20.3 ± 12.9[a]	16.5 ± 10.6[a,b]	12.4 ± 10.6[b]	<0.001*
Morphology (%)	18.9 ± 13.0[a]	16.6 ± 10.0[a,b]	12.6 ± 10.8[b]	<0.001*
TMSC (million ml^{-1})	7.9 ± 6.9[a]	5.8 ± 6.1[a]	5.1 ± 5.8[a]	0.078*

TMSC, total motile sperm count.

*Analysis of variance and *post hoc* Tukey's HSD test was used for comparison of continuous variables.

†Chi-square test was used for comparison of categorical variables.

[a,b,c]Statistically significant difference present among three study subgroups.

Table 3 Results of binary multivariate logistic regression analysis used to determine the association between varicocele recurrence and study variables

						95% CI for OR	
	B	SE	Wald	*P*	OR	Lower	Upper
BMI	−0.219	0.099	4.898	0.027	1.25	0.662	0.975
Testicular pain	−0.164	0.583	0.079	0.778	1.18	0.271	2.660
FSH	0.118	0.077	2.332	0.127	1.13	0.967	1.309
LH	−0.018	0.110	0.027	0.869	1.02	0.792	1.217
Prolactin	0.038	0.097	0.156	0.693	1.04	0.860	1.255
Testosterone	0.003	0.002	2.754	0.097	1.01	0.999	1.007
Sperm count	−0.003	0.058	0.002	0.960	1.00	0.890	1.117
Sperm motility	−0.041	0.053	0.610	0.435	1.04	0.865	1.065
Sperm morphology	0.031	0.050	0.369	0.544	1.03	0.934	1.138

Table 4 Varicocele grade changes in recurrent group

Pre-operative grades	Post-operative recurrence grades		
	Grade 3	Grade 2	Grade 1
Grade 3 (*n*: 6)	0	5	1
Grade 2 (*n*: 13)	0	7	6
Grade 1 (*n*: 3)	0	0	3
Total (*n*: 22)	0	12	10

Discussion

Varicocele, dilatation of the pampiniform plexus or internal spermatic venous system that drains the testicle, is a common problem in urology practice. Although several theories have been asserted to explain the pathogenesis of varicocele development, the exact mechanism is still unknown. Some studies have been performed to investigate the role and effects of somatometric parameters (height, weight and BMI score) on varicocele formation. In one study, the authors retrospectively reviewed the data of 43 adolescent male (mean age 14.3, range 11–19) patients with varicocele and found that patients with varicocele were taller and heavier than the age-matched controls, although the BMI score was not different (Delaney *et al.*, 2004). In another study about this issue, the researchers evaluated the somatometric data of 2106 men (667 men were evaluated for infertility and 1439 men for erectile dysfunction) and showed that there was a statistically significant inverse relationship between the BMI score and the presence of a varicocele. They also showed that there was no significant association between height and varicocele diagnosis in either subgroup or the overall study population (Nielsen *et al.*, 2006). Similar to these studies, Handel *et al.* (2006) evaluated the data of 3213 infertile male patients and found that the prevalence of varicocele decreased with increasing BMI score for all varicocele grades. Additionally, Gokce *et al.* (2013) investigated the association of left varicocele with somatometric parameters (BMI score and height) and found that the probability of having varicocele increased with higher height and lower BMI score. Interestingly, they also showed that a one-unit decrease in the BMI score caused a 1.08 times increase of the probability of having varicocele. Our results are consistent with Nielsen's, Handel's and partly Gokce's studies. We found that there was no association between height and varicocele presence. On the other hand, we observed an inverse relationship between varicocele presence and weight or BMI score. Mean weight and BMI score of patients with varicocele were significantly lower than in those without varicocele.

Persistent or recurrent varicocele after operation is an important problem in urology practice. Ineffective venous ligation, anatomical variations and persistence of patent collateral veins missed at the first repair are the main causes of recurrence (Belli, 1998). In one study, the authors investigated the mechanism of persistence or recurrence of varicocele after surgical repairment by examining the venographic anatomy. They found that the majority of patients (65%) had duplications draining into a single left gonadal vein. Duplications were found most commonly in the pelvis and in the inguinal canal (Bahren classifications type 3) (Bähren *et al.*, 1983). They also detected that communications with other retroperitoneal veins, including the renal hilar, lumbar, iliac and circumaortic renal vein, were relatively uncommon (Sze *et al.*, 2008). Similar to this result, some other researchers reported that 85% of duplications were determined in the middle or lower parts of the gonadal vein (Murray *et al.*, 1986). Yet, in contrast to these studies, Tefekli *et al.* (2001) determined 78% incidence of Bahren classification type 0 anatomy (no evidence of venous reflux on venography) in a series of recurrent varicoceles detected by scrotal colour Doppler ultrasonography and concluded that selective internal spermatic venography was neither necessary nor sufficient in the evaluation of recurrent varicocele. Additionally, Moon *et al.* (2012) investigated the possible mechanisms that could play a role in recurrence after varicocelectomy using angiography, and they found that 64% of patients with recurrent varicocele had a patent internal spermatic vein. The authors also concluded that patent internal spermatic or collateral veins might be the cause of recurrence after varicocelectomy.

In this study, we mainly investigated the possible effect of the BMI score on varicocele recurrence. The prevalence of varicocele recurrence significantly increased with

decreasing BMI scores. Moreover, we also determined that one-unit decrease in the BMI score caused a 1.25 times increased risk of varicocele recurrence using a logistic regression model. The veins that were normal or not prominent at the time of varicocelectomy might become dilated after the operation, especially in patients with BMI scores lower than 25 kg m^{-2}. Overall, our results suggest that a BMI score lower than 25 kg m^{-2} might be a predisposing factor for varicocele recurrence. We can also propose that the microsurgical subinguinal varicocelectomy technique, which has a nearly ten times lower recurrence rate than the conventional subinguinal technique, should be used to decrease the recurrence rate, especially in patients having a low BMI score; so, a low BMI score can be used as an objective indicator for microsurgery. However, to propose it precisely, randomised studies are required to compare the result of microsurgical subinguinal varicocelectomy with conventional subinguinal varicocelectomy regarding BMI score and recurrence rate. We can also propose that patients with low BMI scores should be evaluated with greater emphasis for recurrence after conventional subinguinal varicocelectomy, as the probability of recurrence rate is higher. The results of this study also showed that patients with recurrence had lower weight than other groups. Increased nutcracker effect or compression of the left renal vein due to decreased adipose tissue between the superior mesenteric artery and aorta or decreased adipose tissue at retroperitoneal area which could play a cushion effect for pressure could play a role for recurrence in these patients. This could also be a factor why all recurrences were found to exist on the left side.

There are some limitations for this study. First of all, the number of recurrent varicocele patients was relatively small. Therefore, we could not offer an exact suggestion. Yet, we hope this study can give some new ideas for further researchers to investigate the underlying anatomical/somatometric mechanisms or risk factors (e.g. testicular volume, scrotal temperature, occupation of patients, length of internal spermatic vein and some Doppler ultrasonographic parameters) that can play a role in varicocele recurrence in a larger population. Secondly, we did not use any invasive radiological techniques such as venography to evaluate patients with recurrence. As venographic investigation is an invasive method and may have some serious complications, we have not performed this investigation method for the evaluation of recurrent patient population. Thirdly, we used the BMI score for measuring the per cent of body fat. Although hydrodensitometry, dual-energy X-ray absorption and magnetic resonance imaging techniques provide more accurate information about retroperitoneal fat content, these techniques are more expensive, and it has been shown that none of these techniques offers any benefits to the patients or physicians in terms of altering the clinical management (He *et al.*, 2003; Delaney *et al.*, 2004). Finally, genetic aberrations may be one of the aetiological factors for infertility in varicocele patients, and this might also cause varicocele recurrence; however, the genetic status of patients with varicocele is not within the scope of this study.

The present study indicates that there is a significant inverse relationship between BMI score and varicocele presence. The results of this investigation also show that the prevalence of varicocele recurrences significantly increased with decreasing BMI scores, especially in patients whose BMI scores were lower than 25 kg m^{-2}. It seems that a low BMI score might be a predisposing factor for varicocele recurrence and can be an objective indicator for microsurgical subinguinal varicocelectomy. Further comparative, haemodynamic (Doppler ultrasonographic), radiological and genetic studies are needed for better clarification of the possible mechanisms.

Conflict of interest

The authors declare that they have no conflict of interest.

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