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The relationship between increased body mass index and primary venous disease severity and concomitant deep primary venous reflux

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Background: The role of overweight in chronic venous disease is still controversial. The aim of this study was to evaluate the impact of overweight and obesity in chronic primary venous disease in relation to disease severity, using the CEAP and the Venous Clinical Severity Score (VCSS) as well as body weight on the presence of concomitant primary deep venous reflux.

Material: Between October 2005 and September 2010, 1445 consecutive patients (2023 limbs) presenting with duplex ultrasound-confirmed chronic primary venous disease and planned for intervention were evaluated from a database. The patients were classified according to CEAP, the VCSS, and body mass index (BMI; kg/m²), using the World Health Organization definition. Concomitant primary deep venous reflux was evaluated and re-examined following eradication of the superficial reflux.

Results: There were 636 normal weight patients (890 limbs; BMI <25), 526 overweight patients (740 limbs; BMI 25 to 29.9), and 283 obese patients (393 limbs; BMI ≥30 kg/m²). Overweight patients had more incompetent perforators ($P < .001$), hypertension ($P < .001$), and diabetes ($P = .019$) than normal weight patients and higher C class (CEAP classification)

and VCSS ($P < .001$). Obese patients had more incompetent perforators ($P < .001$), hypertension ($P < .001$), diabetes ($P = .004$), and primary deep insufficiency ($P < .001$) than overweight patients as well as higher C class and VCSS ($P < .001$). Correlation between the C class and the VCSS was found excellent ($r = 0.80$). Obese patients had more axial reflux than the two other groups. There was no relationship between disease duration, body weight, and severity within each group. After eradication of superficial reflux, abolition of the deep reflux was lowest among obese patients (13.7%) compared with overweight patients (22.5%).

Conclusions: There was a close relation between body weight and clinical severity of primary venous disease. Both overweight and obesity appear to be a separate risk factor for increased severity in patients with chronic primary venous disease without correlation to disease duration. CEAP and VCSS seem to accurately evaluate disease severity with an excellent correlation between the two scores. Concomitant primary deep venous reflux is more often observed in the obese patients, with less abolishment following eradication of the superficial reflux than observed for normal weight and overweight patients. (*J Vasc Surg: Venous and Lym Dis* 2013;1:239-44.)

Obesity is not only an important health issue in the United States but is also more and more important in Europe, leading to many serious health issues. The role of overweight and obesity in chronic venous disease is still subject to controversy among the community of vascular surgeons. A study by Danielsson et al¹ has demonstrated a positive association between a body mass index (BMI) >25 kg/m² and clinical severity of chronic venous disease. Van Rij and coworkers² have shown that the CEAP clinical staging of venous disease is more advanced

in obese patients than in nonobese patients, but no comparison between normal weight, overweight, and obese patients was performed. Their hypothesis was that an increase in intra-abdominal pressure due to the weight of the abdominal wall and by the mass effect of the fat contained within the abdomen is exercising an increase in pressure in the pelvic veins. This results in a greater reflux, increased vein diameter, and venous pressures.² Increased abdominal pressure in severely and morbidly obese patients also causes an elevated iliofemoral venous pressure, which transmits via incompetent femoral veins, causing venous stasis in the lower limb.³ Obese patients not only have a change in venous flow pattern due to the changes in intra-abdominal pressure but also due to the chronic inflammatory process in the vessel walls. This makes patients suffering from metabolic syndrome also subject to an increase in the risk of deep venous thrombosis.⁴ An increase in BMI also seems to be correlating significantly with the occurrence of post-thrombotic syndrome.⁵

That lifestyle factors play a role in the development of clinically significant venous disease has also been investigated in the Edinburgh vein study, which showed that in both genders, increasing height was in significant relationship with varicose veins.⁶ With an increase in body height, the pressure measured in the veins of the foot increases.

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Increasing BMI seemed to be a risk factor of varicose veins in women only, which was also shown by the Framingham Study, a finding they explain with increased obesity, which leads to more sedentary activities and lower level of physical activity.⁷

The aim of this study was to investigate if there is a direct relationship between increased BMI and primary venous disease severity and concomitant primary deep venous reflux.

METHODS

Study design. This study is a retrospective analysis from a local database of prospectively entered data. The study was approved by the hospital's ethical committee (CER 09-177-DR [NAC 09-060-DR]), and signed patient informed consent was waived.

BMI (kg/m^2) was calculated for all patients, and the patients were designated into either of three BMI groups following the World Health Organization weight categories defined as normal weight (BMI, 18.5-24.9 kg/m^2), overweight (BMI, 25-29.9 kg/m^2), and obese (BMI, >30 kg/m^2).⁸ The BMI used was the BMI calculated at the preintervention consultation, but standard patient history included weight gain or loss retrospectively. None of the patients had significant BMI change following the initial evaluation. During the follow-up interval, no additional interventions were performed in any of the patients, and the type of procedure and weight group did not influence the results.

All patients were classified according to the CEAP classification (clinical, etiological, anatomical, and pathological elements),⁹ as well as the Venous Clinical Severity Score (VCSS).^{10,11} The scores were calculated and registered at the time of presentation and not calculated retrospectively. Disease duration and severity were obtained from patient history and, from those data, it appeared that elevated BMIs preceded the patients' chronic venous insufficiency, particularly the more severe clinical characteristics such as higher C in the CEAP classification.

Inclusion criteria. Between October 2005 and November 2010, 1445 consecutive patients (2023 limbs) who presented with duplex ultrasound-confirmed chronic primary venous disease and planned for eradication of superficial reflux were included in this study. Ten percent of the patients had endovenous laser ablation of the great saphenous vein with no group differences (89 limbs normal weight, 81 limbs overweight, and 35 limbs obese patients). Stab evulsions of marked varicose branches and ligation of grossly incompetent perforators were performed whenever needed, and these additional procedures were equally distributed between the weight groups and the type of main procedure performed. Duplex ultrasound scanning was performed prior to the venous intervention. In patients with any detected deep venous reflux at the time of presentation, the patients were re-examined by Duplex ultrasound (LOGIQe; GE Medical Systems, Glattbrugg, Switzerland) using a standard protocol by the investigator and examined again using the same protocol by the same

investigator at 3 months post-intervention. All duplex scanning was done in the morning before noon, with the patient in standing position. The nonweight-bearing limb was examined.

The greater and smaller saphenous vein, perforating veins, femoral and deep femoral, and popliteal veins were studied. Peak velocity and duration of reflux were recorded during Valsalva maneuver and with manual compression and decompression. Reflux was defined as retrograde flow lasting for more than 0.5 seconds. Deep axial reflux was defined as reflux in both the femoral, deep femoral, and popliteal veins,¹² while all other deep venous reflux was regarded as segmental reflux. Patency of the proximal venous outflow (iliac veins) was evaluated by duplex Doppler only. Concomitant primary deep venous reflux was evaluated and re-examined following eradication of the superficial reflux. Significant change in reflux post-intervention was defined as a decrease or increase of 2 seconds or longer. Change in peak velocity of reflux was defined as a decrease or increase larger than 20 cm/s. There were no exclusion criteria.

Disease duration and severity were obtained from patient history, and from those data, it appeared that elevated BMIs preceded the patients' chronic venous insufficiency, particularly the more severe clinical characteristics such as higher C in the CEAP classification. Only obese patients and patients with previously documented deep venous thrombosis received thrombosis prophylaxis using enoxaparin (40 mg or 60 mg, Clexane; Sanofi-Aventis, Meyrin, Switzerland) subcutaneously 6 hours after the intervention and once daily for 3 days.

Data points for demographics, including concomitant disease such as diabetes and arterial hypertension were recorded, and the thromboembolic risk assessment using the Caprini risk assessment model,¹³ as well as Venous Quality of Life Questionnaire (CIVIQ-2) scores,^{14,15} were registered.

Statistical analysis. Data are presented as mean \pm standard deviation. Continuous variables were analyzed with Student *t*-test and categorical variables using χ^2 test. $P < .05$ was considered statistically significant. The associations between venous disease severity (VCSS and CEAP) and BMI were assessed using the Pearson correlation coefficient.

RESULTS

There were 636 patients (44%) with 890 affected limbs in the group of normal weight, 526 patients (36%) with 740 limbs who were overweight, and 283 patients (20%) with 393 affected limbs who were obese.

Patient demographics and concomitant diseases are presented in Table I.

In all of the three weight categories, there were significantly more women (65.6%; $P < .0001$) than men (34.7%; $P < .0001$). No other gender difference was observed. There was no significant difference in vein distribution (great saphenous vein and small saphenous vein) or between unilateral and bilateral disease within the different weight categories. The occurrence of incompetent perforators increased in percentage with increasing weight.

Table I. Demographics of 1445 consecutive patients presenting with primary venous insufficiency and planned for eradication of superficial venous reflux in three different weight groups

<i>Variables/groups</i>	<i>Normal weight</i>	<i>P value</i>	<i>Overweight</i>	<i>P value</i>	<i>Obese</i>
Patients, No.	636		526		283
Limbs, No.	890		740		393
Age, years					
Mean ± SD	47.8 ± 15.5	>0.1 ^a	50.1 ± 13.7	>0.1 ^b	50.6 ± 13.2
Range	14-91		15-89		21-87
Female gender	446 (70.1%)	>0.1 ^a	362 (68.8%)	>0.1 ^b	199 (70.3%)
BMI, kg/m ²					
Mean ± SD	22.2 ± 1.9		27.1 ± 1.4		33.5 ± 3.3
Range	15.6-24.9		25.0-29.9		30-47.1
Height, cm					
Mean ± SD	167.3 ± 9.7	>.1 ^a	166.8 ± 9.8	>.1 ^b	166.1 ± 10.3
Unilateral disease	382 (60.1%)	>.1 ^a	312 (59.3%)	>.1 ^b	173 (61.1%)
GSV disease	731 (82.1%)	>.1 ^a	612 (82.7%)	>.1 ^b	310 (78.9%)
SSV disease	106 (11.9%)	>.1 ^a	91 (12.3%)	>.1 ^b	43 (10.9%)
GSV and SSV disease	53 (6.0%)	>.1 ^a	37 (5.0%)	<.002 ^b	40 (10.2%)
Incompetent perforator veins	207 (23.3%)	<.001 ^a	323 (43.7%)	<.001 ^b	02 (51.4%)
Concomitant deep venous reflux	72 (8.1%)	.060 ^a	80 (10.8%)	<.001 ^b	73 (18.6%)
Concomitant disease					
Hypertension	61 (9.6%)	<.001 ^a	100 (19.0%)	<.001 ^b	85 (30.0%)
Diabetes mellitus	12 (1.9%)	.019 ^a	38 (7.2%)	.004 ^a	38 (13.4%)
Mean VTE risk score ± SD	3.5 ± 1.4	<.001 ^a	4.0 ± 1.5	<.001 ^a	4.8 ± 1.8

BMI, Body mass index; GSV, great saphenous vein; SSV, short saphenous vein; SD, standard deviation; VTE, venous thromboembolism.

^aComparison between normal weight and overweight patients.

^bComparison between overweight and obese patients.

Concomitant deep vein reflux increased incrementally with increased BMI from 8.1% (72/890 limbs) and 10.8% (80/740 limbs) to 18.6% (73/393 limbs). The majority of deep reflux observed in all weight categories was short segmental reflux (86.2%), dominantly in the common femoral vein. However, deep axial reflux, although rare, was significantly more frequently seen in the obese group (24.7%; 18/73 limbs) than in the normal and overweight groups (0.9%; 1/72 + 12/80 limbs; *P* < .001). There were no patients with duplex Doppler-

diagnosed proximal vein obstruction or stenosis in this series.

Overweight and obese patients suffered significantly more from hypertension and diabetes than normal weight patients. Mean venous thromboembolism risk assessment scores significantly increased incrementally with increased BMI and so did mean quality-of-life scores. The differences in quality-of-life scores were mainly related to limitations of activity (Table II). There was no relationship between disease duration, body weight, and severity within each group.

Table II. Pretreatment C class of the CEAP classification and varicose VCSS and CIVIQ-2 distribution in 1445 consecutive patients with primary chronic venous insufficiency in three weight groups: normal weight, overweight, and obese

<i>Variables/groups</i>	<i>Normal weight</i>		<i>Overweight</i>		<i>Obese</i>	
	<i>N = 636 patients</i>	<i>P value</i>	<i>N = 526 patients</i>	<i>P value</i>	<i>N = 283 patients</i>	<i>P value</i>
	<i>N = 890 limbs</i>		<i>N = 740 limbs</i>		<i>N = 393 limbs</i>	
Mean CEAP score	2.41 ± 0.96	<.001 ^a	3.13 ± 1.07	<.001 ^b	4.12 ± 0.9	<.001 ^b
Range	2-6		2-6		2-6	
C2	727 (81.7%)	<.001 ^a	229 (31.0%)	<.001 ^b	11 (2.8%)	<.001 ^b
C3	83 (9.3%)	<.001 ^a	220 (29.7%)	<.001 ^b	65 (16.5%)	<.001 ^b
C4	61 (6.9%)	<.001 ^a	239 (32.2%)	<.001 ^b	262 (66.75)	<.001 ^b
C5	4 (0.4%)	.002 ^a	16 (2.2%)	.007 ^b	21 (5.3%)	.007 ^b
C6	15 (1.7%)	<.001 ^a	36 (4.9%)	.017 ^b	34 (8.7%)	.017 ^b
Mean varicose VCSS	6.28 ± 3.52	<.001 ^a	8.01 ± 3.96	<.001 ^b	10.82 ± 4.37	<.001 ^b
Mean CIVIQ-2 score	17.1 ± 3.6	<.001 ^a	22.8 ± 3.2	<.001 ^b	0.3 ± 2.0	<.001 ^b

CIVIQ-2, Venous Quality of Life Questionnaire; VCSS, Venous Clinical Severity Score.

^aComparison between normal weight and overweight patients.

^bComparison between overweight and obese patients.

As for the severity of the chronic venous disease, overweight and obese patients had increasingly higher CEAP class and clinical severity score than normal weight patients, with an incremental increase with increased BMI (Table II). In the obese group, significantly more patients were in C class 5 and 6 compared with overweight and normal weight patients. With increased BMI, the mean VCSS was also incrementally increased and so was the mean quality-of-life score.

There was a very good correlation between the C class of CEAP and the VCSS in all three weight categories (Fig 1).

All patients underwent eradication of their superficial reflux, and postoperative complications were few. Hematomas/bruising were significantly more often observed in the obese group compared with normal weight and overweight patients. There was also a trend toward more wound groin infection in patients treated surgically in the obese group (Table III).

Following eradication of the superficial reflux, patients with preoperative deep reflux were re-examined by duplex Doppler 3 months following eradication of superficial reflux. During the follow-up interval, no additional interventions were performed in any of the patients, and the type of procedure and weight group did not influence the results.

More of deep reflux was abolished post-intervention in normal weight patients (34.4%; 25/72 limbs) and overweight patients (22.5%; 18/80 limbs) than what was observed in the obese patients (13.7%; 10/73 limbs). When comparing normal weight and obese patients, this difference was highly statistically significant ($P = .003$; Fig 2). No limbs with preinterventional axial reflux showed abolishment of the deep reflux in all weight categories.

DISCUSSION

In the present study, we were able to show that there is a close relationship between BMI and the clinical severity, classified with the CEAP and the VCSS. We are therefore suggesting that increasing body weight may be independently involved in primary venous disease. Even though overweight and obesity correlated in this series with clinical severity, whether this is a risk factor or not cannot be determined in the present study.

In addition, an excellent correlation between CEAP classification and VCSS was demonstrated. The following aspects of the VCSS score improved following the intervention—pain edema and induration—but usage of compression stockings did not improve.

Increased intra-abdominal pressure could be part of the explanation for the correlation of BMI and increasing severity of primary venous disease, such as first mentioned by Danielsson et al.¹ That obese patients have an increase in intra-abdominal pressure was also shown by Sugerma et al,¹⁶ who investigated urinary bladder pressure in morbidly obese patients under general anesthesia who were undergoing bypass surgery. They found that there was an increase in sagittal abdominal diameter that was associated with an increase in intra-abdominal pressure

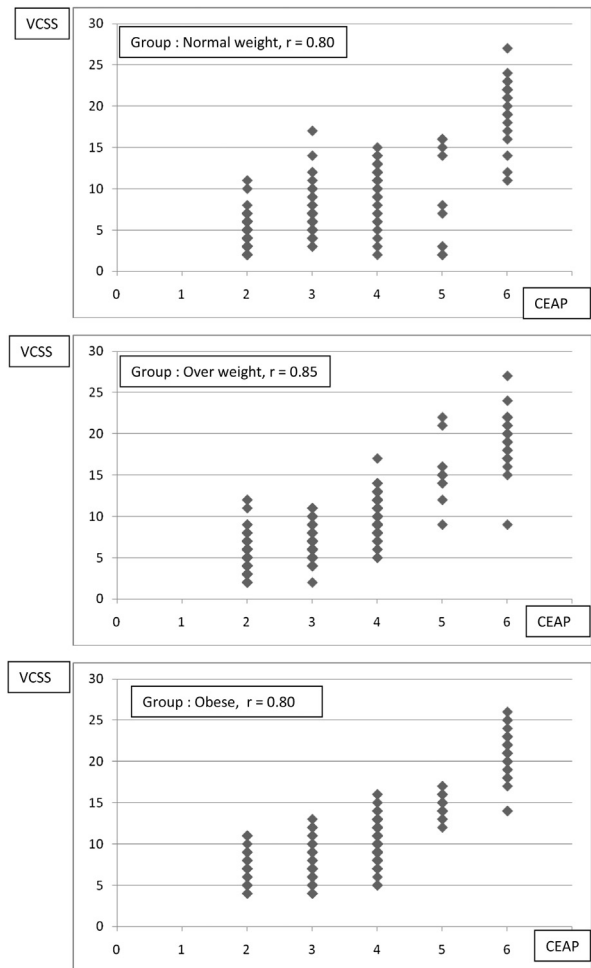


Fig 1. Correlation between CEAP classification, C class, and varicose Venous Clinical Severity Score (VCSS) in different weight categories, normal weight, overweight, and obese in 2023 limbs undergoing eradication of superficial venous reflux.

more so than the waist/hip ratio. In the same line of findings, Willenberg et al¹⁷ were able to show that lower limb venous flow parameters differ significantly between healthy obese and nonobese individuals, which supports the mechanical role of abdominal adipose tissue. In our patient population, increasing weight was not only associated with an elevated VCSS but also with other obesity-related problems such as hypertension and diabetes. Sugerma et al¹⁸ found that severe venous stasis disease was associated with significantly greater weight, BMI, male gender, age, comorbidity, and surgical risk. After gastric bypass surgery, the weight loss corrected the venous stasis disease as well as the other obesity-related problems in almost all patients. We therefore conclude that weight loss could be the first line of treatment to correct venous stasis disease and other obesity-related problems before any venous surgery is planned. However, if weight loss cannot be achieved, with or without gastric bypass surgery, venous surgery

Table III. Postinterventional complications following eradication of superficial reflux in 1445 patients and 2023 limbs in relation to patients' weight: normal weight, overweight, or obese

Variables/groups	Normal weight		Overweight		Obese
	N = 636 patients		N = 526 patients		N = 283 patients
	N = 890 limbs	P value	N = 740 limbs	P value	N = 393 limbs
Wound infection	1 (0.2%)	>1 ^a	1 (0.4%)	.08 ^b	6 (2.1%)
Hematoma/bruising	106 (11.9%)	.920 ^a	90 (12.2%)	.035 ^b	67 (17.0%)
Superficial localized phlebitis	22 (2.5%)	>1 ^a	19 (2.6%)	.111 ^b	16 (4.1%)
Transient paresthesia	8 (0.9%)	>1 ^a	7 (1.0%)	>1 ^b	4 (1.0%)
Deep vein thrombosis	1 (0.1%)	>1 ^a	0 (0.0%)	>1 ^b	0 (0.0%)

Mean ± standard deviation.

^aComparison between normal weight and overweight patients.

^bComparison between overweight and obese patients.

should not be refused. More frequent use of endovenous saphenous ablation is advocated in the obese group of patients to decrease post-treatment complication. Even when eradication of superficial reflux was performed, weight loss seems to be an important issue, since obese patients were found to have a significantly higher incidence of concomitant deep venous reflux with a poorer degree of abolishment of the deep reflux compared with normal weight patients. One reason for poorer rate of deep reflux abolishment in the obese group could be the higher incidence of deep axial reflux as earlier discussed by Labropoulos et al and others.^{1,12,19} It may appear that 3 months of follow-up is too short, but in a study by Puggioni et al, a short time following eradication of the superficial reflux was shown with a possibility of continued improvement by time, even though it must be taken into consideration that over time, with current duplex scanning, reproducibility decreases.¹²

Besides raised intra-abdominal pressure, there is another important factor that may be playing into the development of venous stasis disease, which is the reduced physical activity in obese patients. The lack of use of the calf

muscle reduces its blood pumping activity and therefore contributes to a stasis in the lower limb venous system. Although obese patients seem to have a relatively larger muscle mass in their calf muscle and a better calf muscle pump performance, their daily activity is reduced compared with the nonobese.² Other factors such as sleep apnea syndrome, cor pulmonale, and chronic heart failure may also be considered to be playing a role in the obese patient group. However, only a few obese patients in our series had sleep apnea syndrome (21 patients) or cor pulmonale (10 patients), and none was in chronic heart failure. Another confounding factor for limb edema could be leg arthritis, which could worsen the edema. None of the patients in our series had documented arthritis.

In the present study, no significant proximal vein stenosis or obstruction was observed using duplex Doppler, which could be a third cause for deep venous reflux. However, minor outflow vein obstruction cannot be completely ruled out since neither intravascular ultrasound nor phlebography examinations were performed in this series of patients. In a recent study, Raju and Neglen reported that as high as 89% of obese patients had primary or post-thrombotic iliac vein lesions seen by intravascular ultrasound, which is in contrast to our findings.²⁰

The literature is controversial on the subject of gender difference in the prevalence of venous stasis disease and its severity. Most studies have found that venous stasis disease is more prevalent in women than in men.²¹ Other studies have reported no gender difference in the prevalence rates.²² In contrast, in the Edinburgh Vein Study, the prevalence of varicose veins was higher in men.⁶ However, we found that there were significantly more women in all of the three weight categories. In this present study, we did not randomize the population studied. Instead, we analyzed the data of consecutive patients who consulted for their primary venous disease and were planned for intervention regarding their superficial reflux. In the present study as in other publications with the same finding, there could be a selection bias because women may be more aware of their varicose veins than men and will more easily consult and undergo surgical treatment and may therefore

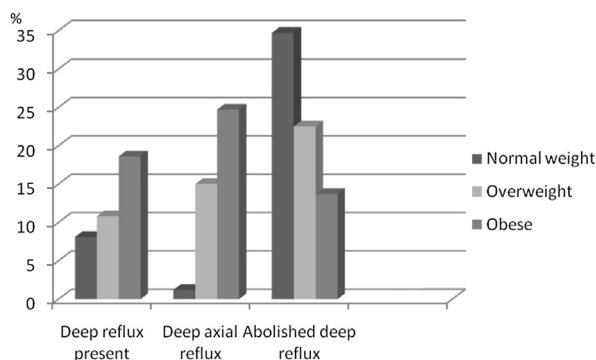


Fig 2. Percent concomitant deep venous reflux, deep venous axial reflux, and abolishment of deep reflux 3 months after eradication of superficial reflux for three different weight categories of patients with primary venous disease.

be more readily selected for these studies. As Robertson et al²³ pointed out in their epidemiological research, the variation in the prevalence of varicose veins in men and women in the studies examined by the authors, reflect differences in variability of study population including age, race, and gender, methods of measurement, and disease definition. The fact that the results had not been adjusted for age may especially contribute to the observed gender differences. Whether increased BMI is more of a risk factor for varicose veins in women than in men, which had been described by the Edinburgh Vein Study,⁶ cannot be confirmed with our study setup and needs to be further investigated.

BMI is the body weight in relation to the total body surface. It is known that people with the same BMI but different heights have different venous pressure in the venous system of their lower limb. One could argue, therefore, that the variation we saw in clinical severity with increasing BMI is not due to the weight but rather due to the difference in height between the patients. Body height significantly influences venous pressure with an increase in pressure in upright resting position.^{6,24} However, in our series, there was no significant difference in height of the patients in the various weight categories. The BMI is used in studies investigating the prevalence of obesity. The World Health Organization categories allow the differentiation between normal weight, overweight, and obese weight categories. It is a precise score, and we were the first to investigate between three weight categories.

In conclusion, our study has demonstrated that overweight and obese patients had an increase in clinical severity of primary venous disease and more concomitant deep venous reflux with less abolishment of their deep reflux following eradication of the superficial reflux than do normal weight patients.

AUTHOR CONTRIBUTIONS

Conception and design: JC

Analysis and interpretation: JC

Data collection: LV

Writing the article: LV, JC

Critical revision of the article: GG

Final approval of the article: JC, GG, LV

Statistical analysis: JC

Obtained funding: Not applicable

Overall responsibility: JC

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