

The Influence of Body Mass Index on Lower Extremity Vein Diameters at Different Levels in Healthy Population

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Abstract

Background: To investigate changes in the size of the deep and superficial venous systems associated with body mass index (BMI), gender, age, in patients without venous insufficiency including the effects of posture.

Methods: Healthy individuals who had no previous diagnosis of venous insufficiency were evaluated with an ultrasound device with a duplex option. The left and right deep and superficial venous systems were scanned both supine and upright positions by the same two radiologists. All clinical findings, BMI and age were recorded for each subject.

Results: Two-hundred ninety-eight patients were included in the study. The patients' mean age and BMI were 49.94 ± 13.19 years (range 19-76), BMI was 24.91 ± 4.0 kg/m² (range 18-38) respectively. The difference between upright and supine positions vein diameters were statistically significant ($p < 0.01$). There were no significant differences between overweight and normal participants in terms of femoral and saphenous vein diameters ($p > 0.05$). The proximal diameter of the great saphenous vein was significantly lower in overweight patients (Table 2). When the patients were analyzed according to BMIs the right femoral vein diameters, the diameters of proximal part and distal two parts of the right great saphenous vein, and left proximal small saphenous vein diameters were significantly higher in patients whose BMI values were between 35-39.99 (obese-class II) ($p < 0.001$).

Conclusions: In conclusion we found both lower limbs' vein diameters were significantly larger in upright position either superficial and deep systems, however the relationship between age and BMI was not significant. Further longitudinal studies are needed to clarify the influence of anatomic variances in subjects with obese healthy veins.

Key words: Chronic Venous Disease, Risk Factors, Age, Obesity, Lower Extremity, Vein Diameter.

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INTRODUCTION

Chronic venous disease (CVD) is one of the most common disorders in many countries. The etiology is probably multifactorial. Obesity has been suggested as one of the risk factors for CVD, or an aggravating factor rather than the primary cause of CVD (1, 2).

Obesity can significantly affect the development of metabolic syndrome with a cluster of cardiovascular risk factors (3). It is thought to predispose individuals to venous stasis, which is a trigger of both deep vein thrombosis and CVI (4, 5).

The venous system of the lower extremity is anatomically divided into a deep and superficial system, but functionally it is accepted as one unit. Both systems communicate with each other by means of perforating veins and through the confluence of the great and small saphenous vein (6). Determination of the physiological adaptations of vein size and volume increase associated with the standing position has been insufficiently described. The details of the anatomy of the venous system are particularly relevant and have recently become even more significant because of the surgical interest in this vein as an approach to each in situ bypass procedure; hence, accurate knowledge of this system has provided a major advance in the simplification of such procedure (7).

In this study, we aimed to investigate changes in the size of the deep and superficial venous systems associated with body mass index (BMI), gender, age, in patients without venous insufficiency including the effects of posture.

MATERIALS AND METHODS

The study protocol was approved by the Acbadem University, Ethics Committee (Date: 26.07.2018, No: 2018-11/9). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients who were employed at the hospital gave informed consent to the study protocol. Healthy individuals who had no previous diagnosis of venous insufficiency were included in our study. While the patients were being evaluated, they were questioned whether they had any complaints in the lower limb or not. Complaints such as pain, numbness, itchiness, heaviness, burning and cramps were recorded. Measurements were done in the mid-day (9:30-15:00). The left and right deep and superficial venous systems were scanned both in supine and upright position by the same two radiologists. All clinical complaints, body mass index (BMI) and age were recorded for each subject. BMI was calculated

as the patient's weight (kg) /height (m²). Classifications for BMI were used according to the NIH and the World Health Organization (WHO) for White, Hispanic, and Black individuals. BMIs were classified as; severely underweight - BMI less than 16.5kg/m², underweight - BMI under 18.5 kg/m², normal-weight - BMI greater than or equal to 18.5 to 24.9 kg/m², overweight – BMI greater than or equal to 25 to 29.9 kg/m², obesity – BMI greater than or equal to 30 kg/m². obesity class I – BMI 30 to 34.9 kg/m², obesity class II – BMI 35 to 39.9 kg/m², obesity class III – BMI greater than or equal to 40 kg/m² also referred to as severe, extreme, or massive obesity (8, 9).

The patients with symptoms on the right or left sides were excluded and the participants with symptoms in both lower extremities were enrolled in the study.

The superficial system, great saphenous vein was evaluated as a) sapheno-femoral junction (SFJ) distal to terminal valve (2 cm), b) mid-thigh c) knee level d) midleg (below medial trochanter 10 cm), e) 1 cm proximal to medial malleolus. Small saphenous vein was evaluated as 1) sapheno-popliteal junction 1cm distal 2) mid leg 3) 1 cm proximal to medial malleolus. Deep venous system was measured as (a) femoral vein (FV) proximal to the orifice of the great saphenous vein (b) the proximal section of the FV about 1–2 cm distal to the orifice of the deep FV and (c) the distal section of the FV about 20 cm distal to the orifice of the deep FV were used for scanning (7).

The ultrasound machine (Logic S8, GE, NewYork, USA) with a 38 mm linear transducer (6–13 MHz) and the duplex option was used. The mean diameter for each measuring position was calculated by assessing both minimum and maximum diameter (cross measurement) with B-mode sonography. Besides their estimated anatomical location, veins were identified by being compressed by brief transducer pressure and through differentiation with color duplex sonography. The diagnosis of reflux was based on the detection of reverse flow induced by Valsalva's maneuver of the ½ proximal limb and by augmentation maneuver of the ½ distal lower extremity. Reflux longer than 0.5 s for the great saphenous vein and longer than 1 second for the femoral vein was considered as insufficiency. Eighteen patients were excluded because of pathological reflux. Intraobserver variation was tested under same conditions for five subjects. Interobserver variation was tested for six subjects by re-measuring the FVD in raw digital ultrasound images) with the analyze-tool image processing program.

Statistical Analysis

SPSS 26.0 (IBM Corporation, Armonk, New York, United States) program was used in the analysis of variables. The suitability of univariate data to normal distribution was evaluated by Kolmogorov-Smirnov test and Shapiro-Wilk Francia test. Mann-Whitney U test was used with Monte Carlo simulation technique in comparing two independent groups to quantitative data. For the comparison of duplicate measurements of dependent quantitative variables, Wilcoxon Signed Ranks Test was used with Monte Carlo simulation. Kendall's tau-b test was used to examine the correlations of variables with each other. Quantitative variables are mean \pm SD in tables. (standard deviation), Median (Percentile 25% / Percentile 75%) and Median (Minimum / Maximum), while categorical variables were shown as n (%). Variables were examined at a 95% confidence level, and a p value of less than 0.05 was considered significant.

RESULTS

Two-hundred ninety-eight patients (173 female, 125 male) were included into the study. The patients mean age was 40.94 ± 13.19 years (range 19-76). The mean height and weight of the patients were 167.41 ± 9.16 cm and 70.04 ± 13.24 kg respectively. The mean BMI was 24.91 ± 4.0 kg/m² (range 18-38). The median diameter of the middle position (proximal FV) distal to the orifice of the deep FV of right and left limbs measured 9 mm and 10 mm in supine position (range: 8-10 mm) and 13 mm (range 11-15) and 12 mm in upright position respectively. A mean diameter increases of 33% for the right limb and 20% for the left limb in upright position. The distal level (distal FV) diameters of right and left limbs were 6 mm and 5.6 mm in supine position and 7 mm and 6.5 mm in upright position which means an increase of 16% and 18% respectively. The difference between upright and supine positions' vein diameters were found statistically significant ($p < 0.01$). Diameters of the femoral vein and the great saphenous vein of both lower limbs in the different levels of all studied subjects were summarized in Table 1.

Table 1. Both extremities comparison of the vein diameters at supine and upright position

		Supine Position	Upright	P
		Med (Q1 / Q3)	Med (Q1 / Q3)	
Right				
	Femoral Vein-1	9 (8 / 10)	13 (11 / 15)	<0.001
	Femoral Vein-2	7.5 (6.5 / 8.5)	10 (8.8 / 12)	<0.001
	Femoral Vein-3	6 (5 / 7)	7 (6 / 9)	<0.001
	Great Saphenous Vein-1	4.5 (4.3 / 5)	5.7 (5.2 / 6.4)	<0.001
	Great Saphenous Vein -2	4 (3.8 / 4.5)	5.2 (4.8 / 6)	<0.001
	Great Saphenous Vein -3	3.6 (3.2 / 4)	4.8 (4.4 / 5.5)	<0.001
	Great Saphenous Vein -4	3 (2.8 / 3.5)	4.2 (3.9 / 5)	<0.001
	Great Saphenous Vein -5	2.2 (2 / 3)	3.8 (3.5 / 4.4)	<0.001
	Small Saphenous Vein -1	3.6 (3.3 / 4)	4.1 (3.5 / 4.5)	<0.001
	Small Saphenous Vein -2	2.95 (2.5 / 3.3)	3.15 (2.6 / 3.6)	<0.001
	Small Saphenous Vein -3	2.3 (2 / 2.5)	2.5 (1.9 / 2.8)	0.001
Left				
	Femoral Vein-1	10 (9 / 12)	12 (9.8 / 14)	<0.001
	FemoraVein-2	8 (6.6 / 9)	9 (7.5 / 11)	<0.001
	FemoraVein-3	5.6 (5 / 6.8)	6.5 (5.5 / 8)	<0.001
	Great Saphenous Vein -1	5.1 (4.8 / 5.5)	5.2 (4.7 / 5.5)	0.004
	Great Saphenous Vein -2	4.5 (4.3 / 4.9)	4.6 (4.2 / 5)	0.031
	Great Saphenous Vein -3	4.1 (3.7 / 4.4)	4.1 (3.6 / 4.5)	0.145
	Great Saphenous Vein -4	3.5 (3.2 / 3.8)	3.55 (3 / 4)	0.479
	Great Saphenous Vein -5	2.8 (2.6 / 3.2)	3 (2.5 / 3.5)	0.446
	Small Saphenous Vein -1	3.4 (3 / 3.8)	3.42 (3.3 / 3.6)	0.018
	Small Saphenous Vein -2	2.8 (2.3 / 3.2)	2.9 (2.7 / 3.1)	<0.001
	Small Saphenous Vein -3	2.1 (1.7 / 2.6)	2.4 (2.2 / 2.5)	<0.001
Wilcoxon Signed Ranks Test (Monte Carlo), Med.: Median, Q1: Percentile 25%, Q3: Percentile 75%				

There were no significant differences between overweight and normal participants in terms of femoral vein diameters at supine position ($p>0.05$). The proximal diameter of the great saphenous vein was significantly lower in overweight patients (Table 2). When the patients were analyzed according to BMI levels, the right femoral vein

diameters, the diameters of proximal level and distal two level of the right great saphenous vein and left proximal small saphenous vein diameters were significantly higher in patients whose BMI values were between 35-39.99 (obese-class II) ($p<0.001$) (Table 3)

Table 2. The comparison of vein diameters and complaints at upright position

Upright Position	Right			Left		
	Femoral Vein-1	Great Saphenous Vein-1	Small Saphenous Vein -1	Great Saphenous Vein-1	Small Saphenous Vein-1	Femoral Vein-1
	Med (Q1 / Q3)	Med (Q1 / Q3)	Med (Q1 / Q3)	Med (Q1 / Q3)	Med (Q1 / Q3)	Med (Q1 / Q3)
Gender						
Female	13 (12 / 15)	5.6 (5.2 / 6.3)	4 (3.4 / 4.5)	5.2 (4.6 / 5.5)	3.4 (3.3 / 3.7)	12 (10.5 / 14)
Male	13 (11 / 15)	5.9 (5.3 / 6.4)	4.2 (3.5 / 4.5)	5 (4.8 / 5.5)	3.4 (3.3 / 3.6)	12 (9.6 / 14)
p	0.370	0.079	0.295	0.566	0.292	0.328
BMI						
Normal	12.5 (10 / 14)	5.6 (5.1 / 6.3)	4.3 (3.4 / 4.6)	5.5 (5 / 5.6)	3.4 (3.3 / 3.6)	11 (9.5 / 13)
Overweight	13 (12 / 15)	5.7 (5.2 / 6.4)	4 (3.5 / 4.5)	5.1 (4.6 / 5.5)	3.4 (3.3 / 3.6)	12 (9.8 / 14)
p	0.154	0.438	0.375	0.003	0.596	0.106
Patients without pain	12.1 (11 / 14)	5.5 (5.1 / 6.3)	4.05 (3.5 / 4.4)	5.2 (4.5 / 5.5)	3.4 (3.3 / 3.6)	11 (9.4 / 13)
Patients with pain	13 (12 / 15)	5.85 (5.35 / 6.45)	4.1 (3.5 / 4.5)	5.2 (4.8 / 5.5)	3.45 (3.3 / 3.6)	13 (11 / 14)
p	0.002	0.008	0.518	0.853	0.043	<0.001
Patients without heaviness	13 (12 / 14)	5.5 (5.2 / 6.3)	4 (3.3 / 4.5)	5 (4.6 / 5.5)	3.4 (3.3 / 3.6)	12 (9.4 / 13)
Patients with heaviness	13 (11 / 16)	6.2 (5.3 / 6.5)	4.1 (3.7 / 4.5)	5.3 (4.8 / 5.5)	3.4 (3.3 / 3.7)	12.5 (10.8 / 14)
p	0.089	0.017	0.147	0.022	0.455	0.013
Patients without burning	13 (11 / 14)	5.6 (5.2 / 6.4)	4.1 (3.4 / 4.5)	5.2 (4.5 / 5.5)	3.4 (3.3 / 3.6)	12 (9.8 / 13)
Patients with burning	14 (12 / 15)	5.8 (5.3 / 6.5)	4 (3.5 / 4.5)	5.2 (5 / 5.5)	3.5 (3.3 / 3.7)	12.8 (10 / 14)
p	0.021	0.056	0.526	0.108	0.027	0.121
Patients without itchiness	13 (11 / 14)	5.7 (5.2 / 6.4)	4.1 (3.5 / 4.5)	5.2 (4.7 / 5.5)	3.4 (3.3 / 3.6)	12 (10.5 / 14)
Patients with itchiness	14 (12 / 15)	5.7 (5.3 / 7)	4 (3.5 / 4.3)	5 (4.7 / 5.3)	3.5 (3.3 / 3.7)	12.4 (8.6 / 14)
p	0.024	0.078	0.236	0.020	0.262	0.541
Patients without cramps	13 (11 / 14)	5.7 (5.2 / 6.3)	4.1 (3.5 / 4.5)	5.2 (4.6 / 5.5)	3.4 (3.3 / 3.6)	12 (10.5 / 14)
Patients with cramps	14 (12 / 15)	5.5 (5.25 / 6.9)	3.85 (3.25 / 4.45)	5.2 (4.8 / 5.4)	3.4 (3.3 / 3.6)	12 (8.6 / 14)
p	0.005	0.382	0.082	0.793	0.665	0.358

Mann Whitney u test (Monte Carlo), Med.: Median, Q1: Percentile 25%, Q3: Percentile 75%

Table 3. The comparison of vein diameters according to BMI

		BMI					p	
		15-19.99	20-24.99	25-29.99	30-34.99	35-39.99		
		Med.(Q1/Q3)	Med.(Q1/Q3)	Med.(Q1/Q3)	Med.(Q1/Q3)	Med.(Q1/Q3)		
Right	Femoral							
		Vein 1	13 (10 / 14)	13 (11 / 14)	13 (12 / 15)	15 (13 / 17)	17 (17 / 17)	<0.001*
		Vein 2	10 (9 / 10)	10 (8 / 11)	10 (8 / 11)	13 (11 / 15)	15.5 (13 / 16)	<0.001*
		Vein 3	7 (6 / 8)	7 (6 / 9)	7 (6 / 9)	12 (8 / 12)	12 (11 / 12)	<0.001*
	Great Saphenous							
		Vein 1	5.6 (5.2 / 6.3)	5.65 (5.2 / 6.3)	5.7 (5.2 / 6.4)	6 (5.3 / 6.8)	7.5 (6.8 / 7.5)	<0.001*
		Vein 2	5.2 (4.8 / 5.7)	5.15 (4.8 / 5.8)	5.2 (4.7 / 6)	5.5 (5 / 6)	5.6 (5.2 / 6.2)	0.196
		Vein 3	4.6 (4.5 / 5.4)	4.8 (4.5 / 5.4)	4.8 (4.3 / 5.5)	4.5 (4.5 / 5.5)	5.5 (3.6 / 5.5)	0.889
		Vein 4	4.4 (4 / 5)	4.25 (4 / 4.9)	4.3 (4 / 5.1)	4 (3.8 / 4.2)	3.5 (3 / 3.5)	<0.001*
		Vein 5	4 (3.5 / 4.5)	3.8 (3.5 / 4.5)	4 (3.5 / 4.5)	3.5 (3.2 / 3.8)	3 (2.5 / 3)	<0.001*
	Small Saphenous							
		Vein 1	3.8 (3.4 / 4.7)	4.2 (3.5 / 4.5)	3.9 (3.6 / 4.4)	4 (3.5 / 4.5)	4.5 (3.3 / 4.5)	0.839
		Vein 2	2.9 (2.5 / 3.5)	3.2 (2.6 / 3.6)	3.1 (2.6 / 3.5)	3.6 (3 / 4)	4 (2.8 / 4)	0.014
		Vein 3	2.5 (1.7 / 2.6)	2.35 (1.8 / 2.8)	2.4 (1.8 / 2.6)	3 (2.5 / 3)	3.25 (2.5 / 3.5)	<0.001*
	Left	Femoral						
		Vein 1	11 (7.9 / 12)	12 (9 / 13)	12 (10.4 / 14)	17 (13 / 18)	14 (14 / 14)	<0.001*
		Vein 2	7.5 (6 / 9)	8.35 (7.5 / 10)	9 (7.6 / 10.5)	15 (11 / 15)	13 (12 / 13)	<0.001*
		Vein 3	5.5 (5 / 7)	6.5 (5.5 / 7.5)	6.5 (5.5 / 7.7)	12 (8 / 13)	10 (9 / 10)	<0.001*
Great Saphenous								
		Vein 1	5.4 (5 / 5.7)	5.1 (4.5 / 5.5)	5.2 (4.8 / 5.5)	5.4 (5 / 5.5)	5.05 (4.5 / 5.3)	0.147
		Vein 2	4.8 (4.2 / 5.2)	4.5 (4 / 4.9)	4.6 (4.2 / 5.1)	5 (4.4 / 5)	4.65 (4 / 5)	0.278
		Vein 3	4.3 (3.6 / 4.7)	4.1 (3.5 / 4.5)	4.1 (3.5 / 4.6)	4 (4 / 4.3)	4.25 (3 / 4.5)	0.867
		Vein 4	3.9 (3.2 / 4.2)	3.5 (3 / 4)	3.8 (3 / 4)	3.5 (3.3 / 3.7)	3.45 (2.5 / 3.7)	0.364
		Vein 5	3.1 (2.7 / 3.8)	2.9 (2.5 / 3.5)	3 (2.6 / 3.5)	3 (3 / 3.2)	3 (2 / 3)	0.278
Small Saphenous								
		Vein 1	3.4 (3.3 / 3.8)	3.4 (3.3 / 3.6)	3.4 (3.3 / 3.6)	3.8 (3.3 / 3.8)	4.15 (3.3 / 4.5)	0.012*
		Vein 2	2.9 (2.6 / 3.3)	2.8 (2.6 / 3.1)	2.9 (2.7 / 3.1)	3.2 (2.8 / 3.5)	3.6 (2.8 / 4)	0.003*
		Vein 3	2.3 (2.2 / 2.4)	2.3 (2.1 / 2.5)	2.4 (2.1 / 2.5)	2.5 (2.2 / 2.5)	3 (2.5 / 3.5)	0.001*

Kruskal-Wallis H Test (Monte Carlo); Post Hoc Test: Dun's Test, Med.: Median, Q1: Percentile 25%, Q3: Percentile 75%

For the analysis of the correlation between vein diameters and BMI, age and gender, the explanation factor (r^2) of Kendall's tau-b test was applied and a very weak correlation between these values was observed. Thus, it did not represent any statistical relevance (Table 4).

Table 4. Correlations statistics of vein diameters and demographic data

n:298		Supine position							
		Age		Height		Weight		BMI	
		r	p	r	p	r	p	r	p
Right	Femoral								
	Vein 1	0.113	0.006	-0.052	0.212	0.125	0.002	0.131	0.001
	Vein 2	0.146	<0.001	-0.076	0.068	0.142	0.001	0.158	<0.001
	Vein 3	0.131	0.002	-0.088	0.035	0.109	0.008	0.133	0.001
	Great Saphenous								
	Vein 1	0.087	0.032	0.089	0.028	0.165	<0.001	0.097	0.015
	Vein 2	0.096	0.019	0.11	0.007	0.121	0.003	0.055	0.172
	Vein 3	0.062	0.127	0.154	0	0.061	0.13	-0.012	0.761
	Vein 4	0.03	0.465	0.254	<0.001	-0.001	0.973	-0.106	0.009
	Vein 5	0.017	0.682	0.266	<0.001	0.001	0.977	-0.109	0.007
Left	Femoral								
	Vein 1	0.074	0.07	-0.017	0.676	0.182	<0.001	0.179	<0.001
	Vein 2	0.081	0.046	-0.053	0.193	0.176	<0.001	0.203	<0.001
	Vein 3	0.051	0.208	-0.102	0.012	0.135	0.001	0.185	<0.001
	Great Saphenous								
	Vein 1	0.055	0.174	0.048	0.239	0.033	0.417	0.017	0.679
	Vein 2	0.078	0.054	-0.004	0.919	0.033	0.415	0.043	0.286
	Vein 3	0.052	0.196	0.005	0.909	-0.007	0.854	-0.003	0.944
	Vein 4	0.032	0.432	0.055	0.174	-0.005	0.897	-0.023	0.568
	Vein 5	0.049	0.224	0.073	0.075	0.01	0.797	-0.023	0.567

Kendall's tau-b Test, r: Correlation Coefficient

DISCUSSION

In this study, no relationship was found between BMI, age, and gender in terms of the diameters of the lower extremity venous system. Both lower limbs' vein diameters were significantly larger in upright position either superficial, or deep veins. We found higher diameters in class II obese patients.

Although much research has been conducted on subjects with venous disease, little is known about the hemodynamics of normal limbs (10). Several epidemiologic studies evaluated strong evidence to the hypothesis that obesity is a risk factor for chronic venous insufficiency and venous thrombo-embolism (11-13).

Data about the association between obesity and CVD, as well as between obesity and severity of CVD are inconsistent (1, 2). Kügler et al. showed that increased body weight significantly correlates with higher venous pressure in lower extremities. Elevated venous pressure in obese subjects without any known venous pathology can be explained by several possible mechanisms. One is increased intra-abdominal pressure caused by the abdominal fat (14). The study conducted by Amélia et al revealed non-significant changes of great saphenous vein diameters in obese patients compared to lean subjects. The authors also emphasized that age is not necessarily associated directly with an increase in venous diameter of the deep and superficial venous system. The age-related increase in BMI was the most important determinant for an increase in diameter of veins in the standing position (15).

In this study we attempted to pierce out that there were significantly higher diameters (mm) of great saphenous and femoral veins at upright position in both lower limbs compared to corresponding levels in the supine position. In line with our results, Kröger et al observed that the cross-sectional area (CSA) of the femoral vein and great saphenous vein as well as the volume increase in the standing position compared to the supine position (6). Orthostatic stress promotes translocation of thoracic blood volume into the compliant venous system of the legs, buttock, and pelvis (16, 17). This rapid fluid shift reduces central blood volume and represents a substantial cardiovascular stress, as reflected in reflex increases in heart rate and sympathetic nerve activity (18).

A previous study reported that venous diameter in the upright position is significantly higher in obese subjects compared with non-obese subjects (17). In healthy people, there is usually no difference in vein diameter between the right and left leg whereas varicose veins are frequently more extended on one limb (19).

In our study, we found higher diameters in right femoral vein, proximal part and distal two levels of the right great saphenous vein and left proximal small saphenous vein diameters in class II obese patients. Wallenberg et al. found femoral vein diameter was significantly greater in obese compared with non-obese participants (20). This could be interpreted as a result of elevated intraabdominal pressure transmitted to the femoral veins and leading to vein wall distension. Increased stasis and reduced forward flow velocity might be a consequence.

The possible effect of obesity on the initiation of varicose veins and the effect that obesity has on the severity of venous reflux and the complications of venous insufficiency must be viewed differently. According to Bonn study, obesity was not a risk factor for varicose veins but was a risk factor for oedema and skin changes of chronic venous insufficiency (21). Therefore, in our study, we questioned symptoms with the hypothesis that there might be a relationship between BMI and symptoms like oedema or skin changes however we found no relationship between BMI and clinical symptoms.

Our study sample is too limited to stratify venous flow impairment for categories of BMI. Furthermore, an

inference is not possible about venous velocities in patients with moderate overweight (BMI, 25-30 kg/m²) subjects. Our data only indicate that an impairment of lower limb venous outflow is observed in class II obese individuals, but not whether this translates into an increased risk for venous thromboembolism or chronic venous insufficiency. This link has recently been reported by larger, event-driven cohort studies (22-27). However, other factors such as ambulatory activity, ankle-joint function, and gait pattern might be involved as well.

The non-blinded manner of data assessment by doppler ultrasound must be considered a shortcoming in our study protocol. Blinding the observer in our study setting was impossible, and measurements were strictly standardized to overcome this. This standardization and the applied exclusion criteria were also needed to minimize the effect of other factors that might affect venous flow, such as movement, posture or respiration pattern. We found no differences between the right and the left leg regarding doppler ultrasound hemodynamic parameters. Nevertheless, our data indicate that a simple, non-invasive assessment by DU imaging is sufficient to detect differences in flow patterns with respect to obesity, although there was no matching for age between obese and non-obese individuals. While it seems unlikely we cannot rule out this as a possible confounder.

In conclusion we found both lower limbs' vein diameters were significantly larger in the upright position either superficial and deep systems and impairment of lower limb venous outflow is observed in class II obese individuals however the age and BMI relations were not significant. In our opinion, the measurement of the lower extremity venous diameters from different levels and evaluation of the obese individuals according to categorized BMI distinguishes our study from others.

Further longitudinal studies are needed to clarify the influence of anatomic variances in subjects with healthy populations.

Declarations

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

The study protocol was approved by the Acıbadem University, Ethics Committee (Date: 26.07.2018, No: 2018-11/9). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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