openheart Cold hypersensitivity in the lower extremities: an underappreciated symptom in patients with varicose veins

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ABSTRACT

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Background This study aimed to investigate the frequently overlooked symptoms of cold hypersensitivity and heavy leas related to varicose veins in a large sample

of patients. **Methods** Data on 8782 adults aged 30–70 years without a history of cancer were sourced from the Taiwan Biobank between 2008 and 2020. Varicose veins, cold hypersensitivity and heavy leg sensations were assessed using questionnaires and analysed using logistic regression models with various covariates. Statistical analyses were performed, with analysis of variance for continuous variables and χ^2 tests for categorical variables at a significance level of 0.05.

Results Our analysis showed significant associations between varicose veins, cold hypersensitivity, and heavy legs (p<0.0001). Logistic regression models showed that moderate and severe cold hypersensitivity increased the risk of varicose veins with ORs of 1.490 (95% Cl 1.205 to 1.842) and 1.894 (95% Cl 1.546 to 2.320), respectively. Similarly, heavy legs were strongly associated with varicose veins (OR 4.239, 95% Cl 3.381 to 5.315), and the interaction between cold hypersensitivity and heavy legs was significant (p=0.0009). Notably, the greatest risk for varicose veins was observed in individuals with heavy legs and severe cold hypersensitivity (OR 7.135, 95% Cl 4.980 to 10.221).

Conclusions The results of this study highlight the clinical significance of considering cold hypersensitivity and heavy legs as vital symptoms for diagnosing varicose veins, particularly in the absence of arterial disorders, which can improve diagnostic accuracy and patient outcomes.

INTRODUCTION

Varicose veins are characterised by the emergence of elongated, tortuous or contorted veins in the lower extremities. This condition is significantly attributable to compromised functionality of valves within deep or superficial veins, perforator veins, venous tributaries and occasionally venous obstructions. These factors collectively increase venous pressure and impede blood flow. The prevalence of varicose veins in adults ranges from 2% to 30%, with a higher prevalence among women.¹ The symptoms frequently linked

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Varicose veins are significantly attributable to compromised functionality of valves and occasionally venous obstructions. Increased venous pressure impedes blood flow and is frequently linked with a tightness sensation and swelling. However, the relationship between venous leg symptoms—specifically the sensation of heaviness and varying degrees of cold sensitivity—in individuals diagnosed with varicose veins remains unclear.

WHAT THIS STUDY ADDS

⇒ Moderate and severe cold hypersensitivity increased the risk of varicose veins with ORs of 1.490 and 1.894, respectively. Moreover, heavy legs were strongly associated with varicose veins (OR 4.239) and the interaction between cold hypersensitivity and heavy legs was significant (p=0.0009).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The is the largest sample of patients with varicose veins to date, highlighting pivotal markers suggestive of latent varicose veins and empowering healthcare practitioners to make informed decisions in their routine clinical practice. Both leg heaviness and pronounced cold sensation can serve as vital diagnostic clues for varicose veins, ultimately improving the quality of life for affected individuals.

with varicose veins include sensations of heaviness, aching, swelling, throbbing, itching, restlessness in the legs, oedema (fluid retention), muscle cramps, formation of leg ulcers and a sensation of tightness in the affected region.²

Coldness in the extremities refers to a subjective and uncomfortable sensation in the hands, feet or other peripheral body areas, even when the ambient temperature is within the normal range. Studies indicate that this sensation is correlated with various chronic conditions including arthritis, gastritis, gastroduodenal ulcers, reflux oesophagitis and rhinitis,³ implying that these conditions may be crucial in initiating or intensifying

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the perception of coldness in the hands, feet or other peripheral extremities. However, these diseases do not encompass other leg-related symptoms such as heaviness, cramping pain, sensations of tightness or swelling.

During the clinical evaluation of patients presenting with varicose veins, the concurrent occurrence of frequent complaints related to cold legs usually remains unrecognised. Additionally, cold hypersensitivity is frequently overlooked, particularly during clinical encounters. Notably, cold hypersensitivity is more prevalent in the East Asian population, with a significantly higher occurrence rate observed in women.^{3 4} The connection between this symptom and varicose veins is partially acknowledged or emphasised in the literature or during routine clinical assessments.^{5–7} Therefore, we aimed to explore the relationship between venous leg symptoms—specifically the sensation of heaviness and varying degrees of cold sensitivity—in individuals diagnosed with varicose veins.

METHODS

The data were obtained from the Taiwan Biobank, the largest genetic and population-based database in Taiwan. Volunteers aged 30–70 years without a history of cancer who were strictly Taiwanese were included. All volunteers signed an informed consent form before enrolment, and physical examinations, bioinformatics analyses and questionnaires were administered during recruitment. The data were collected between January 2008 and December 2020.

Varicose veins were defined in the questionnaire by the question: "Can you see distorted blood vessels on your four limbs (varicose veins)?" The answer choices were none, mild, moderate, severe or extreme. We excluded those with mild varicose veins and classified those who answered 'none' as controls, while those with moderate, severe and extreme varicose veins were classified as cases. For cold hypersensitivity, the option "I feel cold, cold hypersensitivity in hands and feet, or need to put on more clothes" was presented. Cold hypersensitivity was divided into three groups: (1) no cold hypersensitivity; (2) mild cold hypersensitivity; and (3) those with moderate, severe or extreme were classified as severe cold hypersensitivity. To determine if patients had heavy legs, the following question was asked: "Do you feel heavy in your body or lower body?" There were two groups of heavy legs: (1) non-heavy legs, including those answering none or mild; and (2) heavy legs for those with moderate, severe or extreme heaviness. Both evaluations of cold hypersensitivity and heavy legs were based on self-reported symptoms assessed by patients. Other covariates in the logistic regression model included sex (women/men), vegetarian diet (yes/no), age, cigarette smoking (yes/ no), alcohol intake (yes/no), exercise (yes/no), body mass index (BMI) (normal weight/underweight/overweight obese), education level (elementary and below/ junior and senior school/university and above), job type

(non-prolonged standing/prolonged standing), hypertension (yes/no) and diabetes (yes/no).

SAS version 9.4 (SAS Institute, Cary, North Carolina, USA) was used to analyse the associations among individuals with cold hypersensitivity, heavy legs and varicose veins. Odds ratios (OR) with 95% confidence intervals (CI) were determined using logistic regression. Analysis of variance was used to examine the differences between cold hypersensitivity and continuous variables. The results are shown as mean±SE. The χ^2 test was used to examine the differences between the cold hypersensitivity status and categorical variables. The results are presented as numbers and percentages, and the significance level was set at p<0.05.

RESULTS

After excluding participants with incomplete and missing values and those with mild varicose veins, 8782 participants were included in the analysis. The basic characteristics of the participants according to cold hypersensitivity are shown in table 1. Among those with no, moderate and severe cold sensitivity, 5.77%, 9.38% and 14.13% had varicose veins, respectively, while 4.74%, 7.36% and 14.13% had heavy legs (p<0.0001). In those with no cold hypersensitivity (n=5888), 340 (5.77\%) had varicose veins while 5548 (94.23\%) did not. Similarly, significant differences were observed between cold hypersensitivity status and sex, age, cigarette smoking, alcohol intake, exercise, BMI, education level, hypertension and diabetes (p<0.0001). In addition, job type was associated with cold sensitivity (p=0.0384).

Logistic regression was used to analyse the associations between cold hypersensitivity, heavy legs and varicose veins (table 2). Moderate and severe cold hypersensitivities were associated with a higher risk of varicose veins, with an OR of 1.490 (95% CI 1.205 to 1.842) and 1.894 (95% CI 1.546 to 2.320), respectively, than no cold hypersensitivity. Similarly, heavy legs were associated with varicose veins (OR 4.239; 95% CI 3.381 to 5.315). Men had a lower risk of varicose veins than women (OR 0.241; p<0.0001). Age and job type were associated with an increased risk of varicose veins, with ORs of 1.013 (95% CI 1.004 to 1.023) and 1.452 (95% CI 1.219 to 1.730), respectively. Furthermore, the association between cold hypersensitivity and heavy legs was significant (p=0.0009).

Table 3 shows the association between heavy legs and varicose veins stratified based on cold hypersensitivity. In the absence of cold hypersensitivity, the OR for heavy legs and varicose veins was 7.141 (95% CI 5.191 to 9.823) compared with that of non-heavy legs. Furthermore, the ORs were 1.905 (95% CI 1.072 to 3.385) for moderate cold hypersensitivity and 3.175 (95% CI 2.140 to 1.710) for severe cold hypersensitivity.

Table 4 shows the association between cold hypersensitivity and varicose veins stratified according to heavy legs. Compared with no cold hypersensitivity in non-heavy legs, moderate and severe cold hypersensitivities were

	No cald Medewite cald Course cald			
	hypersensitivity	hypersensitivity	hypersensitivity	
Variables	(n=5888)	(n=1535)		P value
Varicose veins, n (%)				<0.0001
No	5548 (94.23)	1391 (90.62)	1167 (85.87)	
Yes	340 (5.77)	144 (9.38)	192 (14.13)	
Heavy legs, n (%)				< 0.0001
No	5609 (95.26)	1422 (92.64)	1182 (86.98)	
Yes	279 (4.74)	113 (7.36)	177 (13.02)	
Sex, n (%)				<0.0001
Women	3114 (52.89)	939 (61.17)	994 (73.14)	
Men	2774 (47.11)	596 (38.83)	365 (26.86)	
Vegetarian diet, n (%)				0.6361
No	5285 (89.76)	1374 (89.51)	1208 (88.89)	
Yes	603 (10.24)	161 (10.49)	151 (11.11)	
Age, years (mean±SE)	50.01±0.13 46.81±0.	27 46.14±0.29 <0.0001		
Cigarette smoking, n (%)				< 0.0001
No	4549 (77.26)	1259 (82.02)	1173 (86.31)	
Yes	1339 (22.74)	276 (17.98)	186 (13.69)	
Alcohol intake, n (%)				< 0.0001
No	5312 (90.22)	1414 (92.12)	1274 (93.75)	
Yes	576 (9.78)	121 (7.88)	85 (6.25)	
Exercise, n (%)				< 0.0001
No	3297 (56.00)	938 (61.11)	897 (66.00)	
Yes	2591 (44.00)	597 (38.89)	462 (34.00)	
BMI categories, n (%)				<0.0001
Normal weight (BMI \leq 18.5– $<$ 24 kg/m ²)	2583 (43.87)	862 (56.16)	843 (62.03)	
Underweight (BMI <18.5 kg/m²)	110 (1.87)	52 (3.39)	78 (5.74)	
Overweight (BMI \leq 24– $<$ 27 kg/m ²)	1825 (31.00)	373 (24.30)	299 (22.00)	
Obese (BMI ≥27 kg/m²)	1370 (23.27)	248 (16.16)	139 (10.23)	
Education level, n (%)				<0.0001
Elementary and below	296 (5.03)	64 (4.17)	45 (3.31)	
Junior and senior school	2403 (40.81)	579 (37.72)	476 (35.03)	
University and above	3189 (54.16)	892 (58.11)	838 (61.66)	
Job type, n (%)				0.0384
Non-prolonged standing	2349 (39.89)	578 (37.65)	575 (42.31)	
Prolonged standing	3539 (60.11)	957 (62.35)	784 (57.69)	
Hypertension, n (%)				<0.0001
No	4599 (78.11)	1296 (84.43)	1211 (89.11)	
Yes	1289 (21.89)	239 (15.57)	148 (10.89)	
Diabetes, n (%)				< 0.0001
No	5258 (89.30)	1433 (93.36)	1296 (95.36)	
Yes	630 (10.70)	102 (6.64)	63 (4.64)	
BMI, body mass index; SE, standard error.				

Table 2	Associations between cold hypersensitivity in the
hands an	d feet, heavy legs and varicose veins determined
using log	istic regression

Variable	OR	95% CI	P value				
Cold hypersensitivity (ref: No)							
Moderate	1.490	1.205 to 1.842	0.0002				
Severe	1.894	1.546 to 2.320	<0.0001				
Heavy legs (ref: No)							
Yes	4.239	3.381 to 5.315	<0.0001				
Sex (ref: women)							
Men	0.241	0.186 to 0.313	<0.0001				
Vegetarian diet (ref: No)							
Yes	0.936	0.724 to 1.211	0.6160				
Age	1.013	1.004 to 1.023	0.0062				
Cigarette smoking (ref: No)							
Yes	0.962	0.708 to 1.307	0.8034				
Alcohol intake (ref: No)							
Yes	1.114	0.755 to 1.643	0.5878				
Exercise (ref: No)							
Yes	0.882	0.737 to 1.056	0.1719				
BMI categories (ref: Normal)							
Underweight	0.769	0.469 to 1.259	0.2959				
Overweight	1.072	0.880306	0.4904				
Obese	0.765	0.591 to 0.991	0.0422				
Education level (ref: Elementary and below)							
Junior and senior school	1.068	0.727 to 1.569	0.7367				
University and above	1.060	0.713 to 1.576	0.7718				
Job type (ref: Non-prolonged standing)							
Prolonged standing	1.452	1.219 to 1.730	< 0.0001				
Hypertension (ref: No)							
Yes	0.830	0.643 to 1.072	0.1535				
Diabetes (ref: No)							
Yes	0.699	0.484 to 1.008	0.0555				
Interaction cold hypersensitivity	\times heavy legs		0.0009				

associated with varicose veins, with ORs of 1.802 (95% CI 1.435 to 2.264) and 2.199 (95% CI 1.753 to 2.758), respectively. In those with heavy legs, only moderate cold hypersensitivity was significantly associated with varicose veins (OR 0.519, 95% CI 0.290 to 0.926) and not severe cold hypersensitivity (OR 0.999, 95% CI 0.636 to 1.569).

The relationships between cold hypersensitivity, heavy legs and varicose veins are shown in table 5.

The reference group had non-heavy legs and no cold hypersensitivity; the OR of non-heavy legs and moderate cold hypersensitivity was 1.799 (95% CI 1.434 to 2.258) and that of non-heavy legs and severe cold hypersensitivity was 2.183 (95% CI 1.743 to 2.734). Similarly, heavy legs and no cold hypersensitivity were associated with a higher risk of varicose veins than the reference group (OR 6.879; 95% CI 5.041 to 9.387). A similar association was observed in heavy legs with moderate cold hypersensitivity (OR 2.583; 95% CI 2.121 to 6.053) and severe cold hypersensitivity (OR 7.135; 95% CI 4.980 to 10.221).

DISCUSSION

We examined the frequently overlooked symptoms of cold hypersensitivity and heavy legs related to varicose veins in a large sample and found that patients with varicose veins exhibit notable sensations of extremity heaviness and coldness compared with those without this condition. In clinical practice, the sensation of coldness is usually relegated to a secondary position among the many varicose vein symptoms. This relegation is attributed to its subjectivity and the consequent ease with which it can be overlooked. However, our study showed the presence of a moderate-to-severe degree of hypersensitivity to cold in the lower extremities, which has hitherto been underestimated as a subjective symptom associated with varicose veins. Of note is the significance of the concurrent symptoms of heaviness and cold feet. When these symptoms coexist, the likelihood of confirming the presence of varicose veins is notably amplified compared with individuals without such symptoms. To date, no direct empirical evidence or animal studies have been conducted to elucidate these specific relationships of symptom and disease, so our study could provide novel findings. It may be that the extracellular matrix remodelling in varicose veins contributes to subsequent venous hypertension.⁸ Under physiological circumstances, the presence of venous dilation while under a dependent position instigates the venous-arterial reflex, inducing a subsequent contraction response within the arteries. This reflex mechanism counteracts precapillary resistance and venous hypertension, reducing blood flow through the microvessels. Through these concerted actions, a harmonious equilibrium of venous blood flow is maintained.⁹¹⁰ As a consequence of this physiological reaction, the body experiences the sensation of cold feet owing to the sequential response of arterial vasoconstriction. Over time, this phenomenon can be exacerbated, resulting in the progressive intensification of the cold sensation. Furthermore, Asians have notably narrower diameters of the great saphenous vein than their Caucasian counterparts. Venous distal reflux frequently extending down to the ankle level was observed in one study among many in an Asian patient cohort.¹¹ The presence of an increased frequency of venous blood reflux may cause heightened activity of the venoarterial reflex. Finally, blood stasis and local hypoxia resulting from varicose veins may stimulate unmyelinated C-fibres in the vicinity of the saphenous veins. This phenomenon may contribute to the local disruption of cold sensation regulation.¹²¹³

A recent questionnaire-based study of 1120 patients found that coldness was significantly higher than other symptoms in patients with varicose veins.⁷ Moreover, there was a significant correlation between the varicose vein diagnosis and coldness (r=0.47, p<0.001).⁷ Among

Table 3 Association between heavy legs and varicose veins stratified based on cold hypersensitivity of the hands and feet									
	No col	d hypersensitiv	ity	Moderate cold hypersensitivity			Severe cold hypersensitivity		
Variable	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Heavy legs (ref: No)			·					
Yes	7.141	5.191 to 9.823	< 0.0001	1.905	1.072 to 3.385	0.0279	3.175	2.140 to 1.710	< 0.0001
Sex (ref: women)									
Men	0.283	0.202 to 0.396	< 0.0001	0.128	0.068 to 0.243	< 0.0001	0.278	0.154 to 0.501	<0.0001
Vegetarian diet (re	f: No)								
Yes	0.891	0.617 to 1.286	0.5367	0.897	0.510 to 1.576	0.7047	1.102	0.677 to 1.794	0.6951
Age	1.011	0.997 to 1.024	0.1245	1.032	1.011 to 1.054	0.0025	1.009	0.990 to 1.028	0.3654
Cigarette smoking	(ref: No)								
Yes	0.952	0.637 to 1.424	0.8120	1.813	0.957 to 3.436	0.0682	0.450	0.210 to 0.961	0.0391
Alcohol intake (ref:	No)								
Yes	1.339	0.837 to 2.144	0.2237	0.702	0.262 to 1.881	0.4816	0.799	0.267 to 2.386	0.6873
Exercise (ref: No)									
Yes	0.901	0.706 to 1.151	0.4049	0.698	0.467 to 1.043	0.0793	1.030	0.717 to 1.480	0.8736
BMI categories (ret	f: Normal)								
Underweight	0.395	0.123 to 1.262	0.1170	1.873	0.862 to 4.068	0.1129	0.610	0.270 to 1.379	0.2348
Overweight	0.993	0.761 to 1.296	0.9580	1.074	0.685 to 1.683	0.7564	1.383	0.926 to 2.067	0.1135
Obese	0.655	0.469 to 0.916	0.0133	0.955	0.532 to 1.715	0.8785	0.956	0.521 to 1.754	0.8841
Education level (re	f: Elementa	ary and below)							
Junior and senior school	0.972	0.598 to 1.579	0.9083	1.009	0.438 to 2.325	0.9823	1.684	0.620 to 4.574	0.3065
University and above	0.829	0.500 to 1.376	0.4684	1.496	0.634 to 3.529	0.3581	1.624	0.589 to 4.479	0.3484
Job type (ref: Non-	prolonged	standing)							
Prolonged standing	1.399	1.095 to 1.788	0.0072	1.855	1.248 to 2.757	0.0023	1.312	0.941 to 1.830	0.1094
Hypertension (ref:	No)								
Yes	0.828	0.599 to 1.144	0.2519	0.724	0.397 to 1.320	0.2920	0.955	0.523 to 1.743	0.8799
Diabetes (ref: No)									
Yes	0.802	0.524 to 1.228	0.3109	0.668	0.269 to 1.660	0.3854	0.248	0.058 to 1.066	0.0609
BMI. body mass	index.								

the 495 patients complaining of coldness, 70% had heavy legs.¹⁴ Additionally, a feeling of heaviness was positively associated with varicose veins primarily in females patients (OR 2.6, 95% CI 2.1 to 3.3). Moreover, as the severity of varicose veins progressed, the feeling of heaviness showed a stronger association with the varicose veins diagnosis, with OR of 1.4 (95% CI 0.9 to 2.2) in C1 patients and OR 4.8 (95% CI 1.6 to 14.6) in C5-C6 patients.¹⁴ However, there is a lack of advanced investigations into the association between cold hypersensitivity, heavy legs and varicose veins in the existing literature. The present study provides more information about this issue (table 5), indicating that the diagnosis of varicose veins is more accurate as long as there is a higher proportion of the coexistence of heavy legs and moderate cold hypersensitivity (OR 3.583; 95% CI 2.121 to 6.053) and severe cold hypersensitivity (OR 7.135).

Varicose veins frequently cause various symptoms in the lower limbs, including sensations such as heaviness, swelling, aching, restlessness, cramps, itching and tingling.^{14 15} These abnormal vessels represent a chronic and advanced condition that exerts a substantial and discernible influence on the patient's overall quality of life. These varices can lead to subsequent complications including superficial vein thrombosis, deep venous insufficiency, arthrogenic congestive syndrome and a propensity for bleeding arising from variceal sources. According to the findings from the Edinburgh Vein Study conducted over 13.4 years, a substantial proportion of individuals (57.8%) who presented with varicose saphenous veins or chronic venous incompetence showed a progressive deterioration in their varicose vein condition throughout their lifetime.¹⁶ Close to one-third of individuals with varicose veins experience skin changes associated with

Table 4 Association between cold hypersensitivity in the hands and feet and varicose veins based on leg heaviness						
	No hea	ivy legs		Heavy legs		
Variable	OR	95% CI	P value	OR	95% CI	P value
Cold hypersensitivity in the hands and feet (ref: No)						
Moderate	1.802	1.435 to 2.264	< 0.0001	0.519	0.290 to 0.926	0.0265
Severe	2.199	1.753 to 2.758	< 0.0001	0.999	0.636 to 1.569	0.9973
Sex (ref: women)						
Men	0.243	0.183 to 0.323	< 0.0001	0.224	0.110 to 0.457	<0.0001
Vegetarian diet (ref: No)						
Yes	0.824	0.611 to 1.111	0.2032	1.563	0.887 to 2.752	0.1220
Age	1.012	1.001 to 1.023	0.0258	1.025	1.001 to 1.049	0.0385
Cigarette smoking (ref: No)						
Yes	0.961	0.681 to 1.357	0.8218	1.007	0.512 to 1.983	0.9831
Alcohol intake (ref: No)						
Yes	1.156	0.753 to 1.775	0.5067	0.993	0.387 to 2.545	0.9876
Exercise (ref: No)						
Yes	0.882	0.725 to 1.073	0.2105	0.915	0.576 to 1.454	0.7068
BMI categories (ref: Normal)						
Underweight	0.753	0.444 to 1.276	0.2915	1.062	0.242 to 4.662	0.9369
Overweight	1.139	0.917 to 1.415	0.2388	0.797	0.490 to 1.295	0.3592
Obese	0.796	0.589 to 1.076	0.1385	0.660	0.392 to 1.112	0.1186
Education level (ref: Elementary and below)						
Junior and senior school	1.005	0.676 to 1.494	0.9802	2.191	0.428 to 11.213	0.3464
University and above	0.964	0.639 to 1.455	0.8619	2.648	0.513 to 13.674	0.2449
Job type (ref: Non-prolonged standing)						
Prolonged standing	1.441	1.187 to 1.750	0.0002	1.593	1.050 to 2.416	0.0286
Hypertension (ref: No)						
Yes	0.795	0.600 to 1.055	0.1120	1.084	0.575 to 2.043	0.8038
Diabetes (ref: No)						
Yes	0.739	0.495 to 1.103	0.1388	0.487	0.190 to 1.249	0.1343
BMI, body mass index.						

chronic venous insufficiency, rendering them susceptible to skin ulcers in the lower extremities. The advancement of chronic venous disease should not be underestimated, underscoring the need for timely interventions to impede disease progression. These interventions are advantageous for the patient's well-being and could reduce the overarching expenses associated with medical services.

The sensation of cold hypersensitivity in the hands and feet is associated with factors such as hypertensive vasoconstriction, stress,¹⁷ inadequate physical activity and a specific bodily constitution (called the cold pattern of the Sasang constitution).¹⁸ Moreover, this particular trait displays an evident hereditary component.⁴ Depending on the underlying cause of cold hypersensitivity, distinct treatment approaches should be considered. These range from conservative strategies involving physical therapy and using insulated clothing to more invasive options including lumbar interventions.^{19 20} In individuals with varicose veins accompanied by sensations of coldness, many supplementary leg-related symptoms usually coexist. These encompass sensations of heaviness, pain, the subjective perception of swelling and cramps. These manifestations can collectively exert considerable influence on an individual's day-to-day activities and social engagement, causing physical and psychological fatigue and substantial inconvenience.

The introduction of efficacious treatment protocols targeting varicose veins can mitigate the symptoms associated with cold hypersensitivity and its accompanying manifestations, possibly enhancing overall clinical outcomes.

Healthcare providers frequently underestimate the gravity and implications of varicose veins, leading to their neglect, and there is usually a gap in understanding the comprehensive spectrum of linked symptoms. Therefore, emphasising the significance of varicose veins, particularly

Table 5	Association between cold hypersensitivity, heavy
egs and	varicose veins

Variable	OR	95% CI	P value
No heavy legs, moderate cold hypersensitivity (ref: No heavy legs, no cold hypersensitivity)	1.799	1.434 to 2.258	<0.0001
No heavy legs, severe cold hypersensitivity	2.183	1.743 to 2.734	<0.0001
Heavy legs, no cold hypersensitivity	6.879	5.041 to 9.387	<0.0001
Heavy legs, moderate cold hypersensitivity	3.583	2.121 to 6.053	<0.0001
Heavy legs, severe cold hypersensitivity	7.135	4.980 to 10.221	<0.0001
Sex (ref: women)			
Men	0.243	0.187 to 0.316	< 0.0001
Vegetarian diet (ref: No)			
Yes	0.935	0.722 to 1.210	0.6081
Age	1.014	1.004 to 1.024	0.0047
Cigarette smoking (ref: No)			
Yes	0.961	0.707 to 1.305	0.7992
Alcohol intake (ref: No)			
Yes	1.113	0.753 to 1.645	0.5905
Exercise (ref: No)			
Yes	0.887	0.741 to 1.062	0.1931
BMI categories (ref: Normal)			
Underweight	0.777	0.475 to 1.271	0.3158
Overweight	1.087	0.892 to 1.325	0.4105
Obese	0.770	0.594 to 0.999	0.0488
Education level (ref: Elementar	y and below	N)	
Junior and senior school	1.061	0.722 to 1.559	0.7639
University and above	1.051	0.706 to 1.563	0.8075
Job type (ref: Non-prolonged s	tanding)		
Prolonged standing	1.453	1.220 to 1.732	< 0.0001
Hypertension (ref: No)			
Yes	0.832	0.644 to 1.075	0.1586
Diabetes (ref: No)			
Yes	0.693	0.479 to 1.003	0.0518
BMI, body mass index.			

considering the substantial population affected by this condition, is crucial. For patients developing varicose veins and other cardiovascular diseases, history-taking and physical assessment are important factors to identify the pathophysiological process.²¹ Common symptoms such as oedema, leg pain and skin changes can easily be reported from self-check-up by patients.²¹ The assessment of a self-reported approach has been validated by a large study including 10423 adult participants, with their severities of varicose veins defined by using self-reported venous

symptoms.²² Self-reported symptom assessment focusing on the leg is a simple and practical method which can be applied to a real-world setting.²³ The pronounced socioeconomic burden stemming from advanced forms of varicose veins further underscores the need for heightened awareness and proactive management.

Study limitations

Our study has some inherent limitations. First, the methodology focused on questionnaires to diagnose peripheral varicose veins, omitting a comprehensive clinical evaluation involving dual ultrasound. This approach carries the potential risk of overlooking latent manifestations of superficial or deep venous reflux. Second, the assessment of cold sensitivity is contingent on the patient's subjective report, as opposed to a quantifiable metric derived from objective criteria. The intensity of cold hypersensitivity may manifest at varying frequencies within East Asian populations. In addition, medical treatment such as venoactive drugs, Ruscus extracts, micronised purified flavonoid fraction, calcium dobesilate, horse chestnut extract, hydroxyethylrutosides, red vine leaf extract and sulodexide are beneficial to patients with varicose veins.²¹ Unfortunately, the data in the present study was obtained from a questionnaire database with self-reported symptoms assessed by patients' subjective observations, which was lacking in details of medical treatment. Further empirical evidence encompassing diverse racial groups is required to confirm the universality of these symptoms.

CONCLUSION

This study presents findings based on the largest sample of patients with varicose veins to date, indicating that these patients show notable sensations of extremity heaviness and coldness, ranging from moderate to severe, compared with individuals without this condition. When assessing patients clinically, complaints pertaining to moderate to severe degrees of coldness should be regarded as a potential symptom of varicose veins, particularly in the absence of arterial disorders. The identification of supplementary leg symptoms linked to varicose veins has significant clinical value, given the relatively limited diagnostic efficacy of venous leg symptoms reported in the existing literature. The legs can be a clue to the heart, and symptoms related to varicose veins could be confused or be coexistent with undetected heart failure.²⁴ There are many communal pathophysiology mechanisms between varicose veins and other cardiovascular diseases, such as inflammation, endothelial dysfunction and thrombosis.²⁴ Furthermore, the genetic correlation between varicose veins and heart failure has been reported in a recent article,²⁵ indicating a higher risk of heart failure in patients with varicose veins.²⁵ Either cold hypersensitivity or heavy legs is a subjective description. Patients with varicose veins have a double risk of congestive heart failure, deep vein thrombosis and pulmonary

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embolism.²⁵ However, early surveillance is difficult for currently limited medical competence and resources. As a result, self-reported symptom assessment focusing on the leg can be a simple and practical method to approach the progress of varicose veins.²³ Awareness of patient-oriented common complaints including cold hypersensitivity and heavy legs can provide more details for early detection and differential diagnosis, which can mitigate the drawbacks of current clinical settings and identify more cases at the early stage of varicose veins. The concurrent manifestations of leg heaviness and pronounced cold sensation can serve as pivotal markers suggestive of latent varicose veins, empowering healthcare practitioners to make informed decisions in their routine clinical practice. These symptoms provide vital diagnostic clues and contribute to enhanced varicose vein diagnosis and management protocols, leading to an improved quality of life for these patients.

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