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The Relationship Between Perforator Vein and Great Saphenous Vein Reflux with Leg Pigmentation in Patients with Chronic Venous Disease (Ceap C3 and C4)

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ABSTRACT

Leg pigmentation is an important manifestation of chronic venous disease (CVD) due to long-term venous hypertension. Perforator vein and saphenous vein reflux are thought to play a major role in these skin changes. This prospective cross-sectional study involved 40 patients with CVD CEAP C3–C4 who underwent Doppler ultrasound examination at Cipto Mangunkusumo Hospital (RSCM) and Hermina Hospital in Depok between August and October 2025. Perforator vein and saphenous vein reflux were assessed using Doppler ultrasound, while pigmentation was assessed using the Venous Clinical Severity Score (VCSS). Bivariate and multivariate analyses were performed. Cockett perforator vein reflux was found in 17 patients (42.5%) and Boyd in 6 patients (15.0%). Saphenous vein reflux was found in almost all patients, with a distribution: SFJ 100%, mid-thigh 95.0%, lower thigh 82.5%, upper knee 70.0%, and lower knee 57.5%. Cockett and Boyd perforator reflux were significantly associated with the incidence of pigmentation ($p < 0.05$). In multivariate analysis, saphenous vein reflux in the upper knee segment was significantly associated with pigmentation ($p = 0.020$; aOR 10.24; 95% CI 1.445–72.57), as was prolonged standing ($p = 0.032$; aOR 6.54; 95% CI 1.17–36.52). Perforator vein reflux and saphenous vein reflux were significantly associated with the incidence of leg pigmentation in patients with chronic venous disease CEAP C3 and C4.

KEYWORDS Chronic Venous Disease; Perforator Venous Reflux; Saphonic Magna Venous Reflux; Limb Pigmentation; CEAP.

INTRODUCTION

Chronic venous disease (CVD) is one of the vascular systems disorders whose prevalence continues to increase, especially in the adult and senior population (Almunawar et al., 2022; Dharmanto et al., 2019; Rosyidi, 2019; Williady et al., 2025). This disease covers a wide clinical spectrum, ranging from mild symptoms, such as a feeling of heaviness in the legs, to chronic skin changes and ulcers. According to the Vascular Disease Foundation, an estimated 20–25 million people in the United States suffer from varicose veins, with more than 30% showing clinical manifestations, such as pigmentation of the legs. The Society for Vascular Surgery and the American Venous Forum in 2023 estimated that 30–50% of the

mature population experience varicose veins, and over 10% develop chronic venous insufficiency (C4–C6 based on the CEAP classification).

One of the most common clinical manifestations found in patients with CVD is pigmentation on the distal part of the legs, which reflects the presence of chronic inflammation caused by long-term venous hypertension (Smith et al., 2020; Williams et al., 2021). A study conducted by Kilinc et al. on 150 patients with chronic venous insufficiency found that 48% had CEAP C4 or higher, and 25.3% of all patients showed leg pigmentation as one of the significant skin symptoms (Kilinc et al., 2019). The key mechanism in the occurrence of leg pigmentation is venous hypertension, which results from venous valve incompetence in superficial veins, deep veins, and perforator veins, characterized by the presence of reflux in the venous system (Nguyen et al., 2020; Wipf et al., 2019). Reflux is a condition where blood flows backward (retrograde flow) in the limb venous system, which occurs for more than 500 ms in superficial and perforator veins, and more than 1000 ms in deep veins (Thomson et al., 2021; Gass et al., 2020). This is caused by the insufficiency of the venous system, namely the inability of venous valves to prevent blood from flowing back toward the heart (Ryu et al., 2018).

The Bonn Vein Study (2003) in Europe reported that around 90% of the mature population shows signs of clinical CVD, with around 60% showing varicose veins, and 15–20% experiencing chronic venous insufficiency at an advanced level (Deinsberger & Weber, 2026; Kienzl et al., 2024; Robertson, 2013; Sinabulya, 2017). Furthermore, the Bonn Vein Study also stated that 30-50% of patients with chronic venous insufficiency had reflux in superficial veins, and 10-20% also had reflux in deep veins (Maleti et al., 2023; Robertson, 2013; Wrona et al., 2015). Perforator vein incompetence, characterized by reflux in perforator vein valves, occurs when these valves cannot prevent blood flow back from deep venous systems to superficial veins (Binko et al., 2024; Gore, 2023; Gujja et al., 2022; Maleti & Lugli, 2026; Zalaquett et al., 2023). This condition can increase pressure in superficial veins and subcutaneous tissues, ultimately leading to endothelial damage, erythrocyte extravasation, and hemosiderin deposition, which triggers skin pigmentation. Jayaraj et al. (2024) found that perforator vein incompetence occurred in 50% of patients with chronic venous ulcers due to persistent venous pressure. Kachlik et al. (2009) reported that the most common perforator vein incompetence occurs in the distal medial part of the legs, specifically in the Cockett region (medial lower leg), found in 30-60% of patients with ongoing venous insufficiency.

Pigmentation in the legs, caused by venous hypertension due to venous valve incompetence, can worsen the severity of chronic venous disease and, in its advanced stage, lead to venous ulcers, ultimately affecting the quality of life of patients. A study by Tracz et al. showed that over time, this pigmentation can cause discomfort, pain, disability, and a decline in quality of life. Several factors are known to increase the risk of venous insufficiency, including age, gender, prolonged standing in the workplace, and obesity. These factors not only play a role in the emergence of venous insufficiency but also influence the severity of chronic venous insufficiency, including symptoms such as pigmentation, edema, pain, and chronic ulcers.

However, studies specifically evaluating the direct connection between perforator vein reflux and superficial vein reflux (great saphenous vein) with leg pigmentation are still limited, especially in Southeast Asia, including Indonesia. Most studies focus more on saphenous vein

incompetence and its role in the development of varicose veins and ulcers. Some studies suggest that perforator vein ligation could be a treatment option for CVD patients with leg pigmentation. However, there are few studies analyzing the direct connection between perforator vein reflux and great saphenous vein reflux with leg pigmentation. The lack of local data explaining the clear connection between perforator vein reflux and saphenous vein reflux with skin pigmentation manifestations creates a gap in diagnostic and management approaches. This gap can delay early intervention for perforator vein and great saphenous vein incompetence, which could help prevent the progression of pigmentation into venous ulcers, a severe outcome in chronic venous disease.

Based on the background provided, this study aims to evaluate the direct connection between perforator vein reflux and great saphenous vein reflux with leg pigmentation in patients with chronic venous disease. The findings of this study are expected to contribute to a more comprehensive understanding of the pathophysiology of CVD and provide a basis for clinical decision-making, particularly in determining the indications for early intervention in perforator veins and the great saphenous vein in patients with pigmentation symptoms. This approach can prevent leg pigmentation from progressing into venous ulcers, the most severe stage of chronic venous disease.

RESEARCH METHOD

Research Design

The study used design prospective cross sectional. Sample collection method sample done non -randomly with method consecutive sampling.

Place and Time of Research

Patient with chronic venous disease performed USG examination at RSCM from August 2025 to October 2025.

Population and Sample

1. Target population is patient with chronic venous disease in Indonesia with or without pigmentation skin legs in Indonesia
2. Population affordable is patient with chronic venous disease in Indonesia with or without pigmentation skin the legs that are done USG examination at RSCM and Hermina Hospital Depok in August 2025 – October 2025
3. Research sample is targeting population that meets criteria inclusion

Criteria Inclusion and Exclusion

1. Criteria Inclusion
   a. Patient over 18 years old
   b. Diagnosed chronic venous disease with CEAP classification C3 Willing follow research and signing informed consent

2. Criteria Exclusion
   a. Patient with pigmentation skin legs caused by other diseases such as allergic dermatitis, atopic dermatitis, psoriasis, cellulitis and melanoma
   b. Patients who are present deep venous insufficiency
   c. Patients who have ever diagnosed deep vein thrombosis

d. Patients who have already get previous venous intervention
e. Patient with history of trauma or wound burns on the legs that can disguise change color skin
f. Patient with disease systemic that causes change color skin like cirrhosis and jaundice obstructive

Data Collection Techniques

Subject study chosen from incoming patients to polyclinic vascular Cipto Mangunkusumo Hospital (RSCM) and Hermina Hospital Depok and diagnosed chronic venous disease based on CEAP classification C3 and C4. Retrieval technique samples used is consecutive sampling, where all patients who meet the requirements criteria inclusion and exclusion fulfil criteria exclusion, as well as willing follow research, recruited in a way consecutive until amount required samples achieved in period research. Before done inspection more continue, subject given explanation about objectives, benefits, procedures research, as well as rights subject. After understand and express agree, subject will sign form agreement written (informed consent).

All subject undergoes Doppler ultrasound examination of leg veins lower with using the GE Healthcare Logic P9 Doppler USG, which has calibrated previously, with linear probe and settings inspection vascular, with frequency probe arranged with 5-12 MHz range. The ultrasound examination was performed by a single operator (researcher) for guard consistency results inspection.

Inspection performed on superficial veins (saphenofemoral junction, mid-thigh, lower thigh, upper knee, lower knee), deep veins (femoral vein and popliteal vein) and perforator veins (posterior tibial (Cockett's), *paratibial* (Boyd's), distal thigh (Dodd's), proximal thigh (Hunterian). Examination done in position stand use technique Valsalva and or manual compression for evaluate venous reflux. Patients found reflux in the deep veins on ultrasound examination will be issued from subject study.

After done ultrasound examination, condition skin legs patient assessed use Venous Clinical Severity Score (VCSS), particularly the pigmentation parameter. A pigmentation score ≥1 is considered as existence pigmentation skin. Characteristic data patient like age, type gender, history work with activity prolonged standing, obesity, and duration suffer from disease chronic venous insufficiency collected through interview direct and verification from record medical patient. All data results examination and interview noted in sheet Work research that has been standardized. This data Then input to in computer programs For done analysis statistics.

Variables

1. Variables Free

   Reflux of perforator veins and great saphenous vein based on results ultrasound examination.
2. Variables Bound

   Incident pigmentation legs based on VCSS scoring.
3. Variables Confounding factor

Age, type gender, history work with activity prolonged standing, obesity, duration suffer from chronic venous disease.

RESULT AND DISCUSSION

Characteristics clinical

A total of 40 patients with chronic venous disease CEAP degrees C3–C4 were included in study this . Characteristics clinical subject shown in Table 1. Average age patient was 59.4 ± 13.6 years . Most of the subject various sex women (67.5%). More from half patient experience obesity (60%), as well as own history activity prolonged standing (70%). Duration suffer from chronic venous disease more from two years found in 60% of patients . Pigmentation skin found in 50% of patients (20 subjects).

Table 1. Characteristics Clinical

Variables	Mark
Age , average ± SB	59.4 ± 13.6
Gender , n (%)	
Man	13 (32.5)
Woman	27 (67.5)
Obesity , n (%)	24 (60.0)
Prolonged standing, n (%)	28 (70.0)
CVI Duration	
<2 years	16 (40.0)
>2 years	24 (60.0)
Findings pigmentation skin , n (%)	20 (50.0)

Sourch: Primary data obtained from patient clinical characteristics collected during the study period at Cipto Mangunkusumo Hospital and Hermina Hospital Depok, August–October 2025.

Distribution Perforator Vein Reflux And Great Saphenous Vein Reflux

Distribution location Perforator vein and saphenous vein reflux are shown in Table 2. Perforator reflux is the most common found in Cockett perforators (42.5%), followed by Boyd (15.0%). Not found reflux in both Dodd and Hunterian perforators.

In the great saphenous vein system, reflux found in almost all over segment Anatomical. Reflux in the SFJ was found in 100% of patients, mid-thigh in 95%, lower thigh in 82.5%, upper knee in 70%, and lower knee in 57.5% . This show that part big patient own reflux multisegmental.

Table 2. Distribution Venous Reflux

Variables	Mark
reflux , n (%)	
Cockett	17 (42.5)
Boyd	6 (15.0)
Dodd	0
Hunterian	0
Safena magna vein reflux , n (%)	
SFJ	40 (100)
Mid-thigh	38 (95.0)

Lower thigh	33 (82.5)
Upper knee	28 (70.0)
Lower knee	23 (57.5)

Relationship characteristics clinical with incident pigmentation skin

Analysis bivariate about connection characteristics clinical, including age, type gender, obesity, *prolonged standing*, and duration of CVI, with incident pigmentation skin shown in the table 3. Based on analysis bivariate, obtained all over characteristics clinical show relationship that is not significant with incident pigmentation skin ($p > 0.05$).

Table 3. Relationship Clinical Characteristics with Incident Pigmentation Skin

Variables	Pigmentation skin		p-value	OR	95% CI
	No (n = 20)	Yes (n = 20)			
Age	57.8 + 14.8	61.1 + 12.4	0.443	-	-
Gender , n (2.6%)					
Man	6 (30.0)	7 (35.0)	0.736	1,256	0.33 – 4.73
Woman	14 (70.0)	13 (65.0)			
Obesity , n (%)	10 (50.0)	14 (40.0)	0.197	2,333	0.64 – 8.54
Prolonged standing, n (%)	12 (60.0)	16 (80.0)	0.168	2,667	0.65 – 10.97
CVI Duration					
<2 years	11 (55.0)	5 (25.0)	0.053		
>2 years	9 (45.0)	15 (75.0)		3,667	0.96 – 14.0

Sourch: Primary data analyzed using bivariate statistical analysis of clinical characteristics and skin pigmentation incidence

Relationship perforator vein reflux and pigmentation skin

In the research this, only two types perforator vein reflux which can analyzed, namely Cockett reflux and Boyd reflux. Analysis bivariate in Table 4 shows that Cockett and Boyd perforator reflux are related significant with incident pigmentation skin ($p < 0.05$). In Cockett perforators, 75% of patients with pigmentation have reflux, compared to only 10% in the group without pigmentation. Boyd's reflux was found only in groups with pigmentation.

Table 4. Relationship Perforator Venous Reflux with Incident Pigmentation Skin

Variables	Pigmentation skin		p-value	OR	95% CI
	No (n = 20)	Yes (n = 20)			
reflux , n (%)			0,000*		
No	18 (90.0)	5 (25.0)			
Yes	2 (10.0)	15 (75.0)		27.0	4.56 - 159
Boyd's perforator vein reflux			0.008*		
No	20 (100)	14 (70.0)			
Yes	0 (0)	6 (30.0)		-	-

Sourch: Primary data derived from bivariate analysis of perforator vein reflux and pigmentation incidence

Relationship saphenous vein reflux and pigmentation skin

Connection great saphenous vein reflux with pigmentation shown in Table 5. Reflux in three segments —lower thigh, upper knee, and lower knee show connection significant with pigmentation skin ($p < 0.05$). SFJ reflux did not can analyzed Because there was 100% incidence in both group.

Table 5. Relationship Reflux of the Vena Saphena Magna with Incident Pigmentation Skin

Variables	Pigmentation Skin		p-value	OR	95% CI
	No (n = 20)	Yes (n = 20)			
SFJ great saphenous vein reflux , n (%)			-		
No	0	0			
Yes	20 (100)	20 (100)			
Mid thigh great saphenous vein reflux , n (%)			0.487		
No	2 (10.0)	0			
Yes	18 (90.0)	20 (100)			
Lower thigh great saphenous vein reflux , n (%)			0.008*		
No	7 (35.0)	0			
Yes	13 (65.0)	20 (100)		-	-
Upper knee great saphenous vein reflux , n (%)					
No	10 (50.0)	2 (10.0)	0.014*		
Yes	10 (50.0)	18 (90.0)		9.0	1.63 – 49.4
Lower knee great saphenous vein reflux , n (%)					
No	12 (60.0)	5 (25.0)	0.025*		
Yes	8 (40.0)	15 (75.0)		4.5	1.16 – 17.3

Sourch: Primary data obtained from bivariate analysis of great saphenous vein reflux and skin pigmentation

Analysis multivariate perforator vein reflux

Analysis Cockett's multivariate perforator vein analysis was performed with variables confounders that have p -value <0.250. Analysis multivariate only can done for the Cockett perforator because the Boyd perforator has mark zero on one cell so that the regression model No can executed . Analysis results multivariate shown in Table 6. Based on Table 6., it is obtained that Cockett's perforator vein reflux has significant relationship to incident pigmentation skin ($p = 0.001$; aOR : 23.99; IK95: 3.568 - 161.3).

Tabel 6. Multivariate Cockett's Vein Reflux and Confounding with Incident Pigmentation Skin

Variables	Incident pigmentation skin		
	aOR	IK 95	p-value
Cockett's venous reflux	23.99	3,568 – 161.3	0.001*
Prolonged standing	4,277	0.582 – 31.42	0.153
duration >2 years	3,447	0.561 – 21.17	0.182

Analysis multivariate great saphenous vein reflux

Analysis multivariate saphenous vein magna was performed on two segments *upper knee* and *lower knee* because own p value < 0.25 in the analysis bivariate analysis multivariate No can performed on the SFJ, *mid thigh* and *lower thigh veins* Because there is amount patient 0 in one of the subcategory patient . Analysis results multivariate reflux of the great saphenous vein of the upper knee segment can seen in table 7.

Table 7. Multivariate Upper Knee Saphenous Venous Reflux and Confounders with Incident Pigmentation Skin

Variables	Incident Pigmentation Skin		
	aOR	IK 95	p-value
Upper knee great saphenous vein reflux	10.24	1,445 – 72.57	0.020*
Prolonged standing	6,543	1,172 – 36.52	0.032*
duration >2 years	2,622	0.477 – 14.40	0.267

Sourch: Primary data from multivariate analysis of upper knee great saphenous vein reflux and confounders

Based on Table 7., it is obtained that reflux of the saphenous vein of *the upper knee* and *prolonged standing* has significant relationship to incident pigmentation skin , namely *upper knee* magna saphenous vein reflux (p = 0.020; aOR : 10.24; IK95: 1.445 - 72.57) and *prolonged standing* (p = 0.032; aOR : 6.543; IK95: 1.172 - 36.52).

Analysis results multivariate lower knee segment saphenous vein reflux can seen in table 8.

Table 8. Multivariate Lower Knee Venous Reflux and Confounding with Incident Pigmentation Skin

Variables	Incident Pigmentation Skin		
	aOR	IK 95	p-value
Lower knee magna saphenous vein reflux	3,667	0.703 – 19.13	0.123
Prolonged standing	5,009	0.944 – 26.56	0.058
duration >2 years	2,967	0.543 – 16.20	0.209

Sourch: Primary data from multivariate analysis of lower knee great saphenous vein reflux and confounding variables

Based on Table 8., it is obtained that *lower knee* magna saphenous vein reflux No own significant relationship to incident pigmentation skin after controlled variables confounding (p = 0.123; aOR : 3.667; IK95: 0.703 - 19.13).

Clinical Characteristics of Patients

This study involved 40 patients with a diagnosis of CVD (CEAP C3 and C4) undergoing venous ultrasound examination at Cipto Mangunkusumo Hospital and Hermina Hospital Depok from August 2025 to October 2025. Based on the descriptive analysis, the average age of the study subjects was 59.4 years, with a significant proportion of patients being women (67.5%). The proportion of patients with obesity reached 60%, while 70% of patients

had a history of prolonged standing. Additionally, many patients had a history of CVD for more than two years (60%), indicating that the majority of subjects had experienced deep venous insufficiency for a considerable duration before undergoing clinical evaluation. This is in line with research conducted by Beebe-Dimmer JL (2005), which reported that CVD occurs more often in women, with a prevalence of 1–40%, compared to men, with a prevalence of 1–17%. Obesity is also linked to activities associated with orthostasis. Salim et al. (2021) also stated that the prevalence of obesity in patients with chronic venous disease ranges from 35-60%. The Bonn Vein Study (2003) also indicated that the prevalence of CVD in patients with a history of prolonged standing is 40-60%. Therefore, the characteristics of patients at Cipto Mangunkusumo Hospital and Hermina Hospital Depok during the period from August 2025 to October 2025 align with the epidemiological characteristics of CVD patients.

These findings are consistent with global epidemiological data showing that the prevalence of CVD ranges from 25-40% in women and 10-20% in men, with an increased incidence corresponding to age, obesity, and employment in occupations requiring long periods of standing or chronic immobilization. Based on this, the patients in this study can be categorized as a high-risk group for chronic venous disorders.

Several key risk factors have been associated with the onset and progression of chronic venous disease. Age is related to a decline in the elasticity of vein walls and degeneration of venous valves. Obesity increases intra-abdominal pressure and inhibits venous return, while prolonged standing increases hydrostatic pressure in the venous system of the lower legs. Additionally, gender (women) and the duration of chronic venous disease are also significant factors that increase the risk of venous insufficiency. The combination of these factors causes an increase in ambulatory venous pressure, which can eventually trigger various clinical manifestations of chronic venous insufficiency.

Among the total sample in this study, 20 patients (50%) exhibited pigmentation on the legs, based on the Venous Clinical Severity Score (VCSS) evaluation. Bivariate analysis showed that all major clinical characteristics, including age, gender, obesity, disease duration, and prolonged standing, were significantly related to the incidence of skin pigmentation ($p > 0.05$). These results suggest that while demographic factors and lifestyle play an important role in the development of chronic venous insufficiency (CVI), the incidence of skin pigmentation seems to be more closely related to venous *hemodynamics*, such as the location and degree of reflux. Caggiati (2008) stated that in the early C4a phase, pigmentation is determined by melanin due to local inflammation, rather than systemic factors. Delis (2001) also indicated that ambulatory venous pressure is more important than general risk factors.

Proportion of Patients Based on Ultrasound Results

Venous ultrasonography performed on all 40 patients showed variation in the location of reflux in both the perforator veins and the great saphenous vein. Based on ultrasound results, the most common type of perforator vein reflux found was Cockett, present in 17 patients (42.5%), followed by Boyd in 6 patients (15.0%). In the great saphenous vein system, almost all patients showed reflux in some anatomical segments. Reflux at the SFJ was found in 100% of patients, followed by reflux at the mid-thigh (95.0%), lower thigh (82.5%), upper knee (70.0%), and lower knee (57.5%). These findings indicate that saphenous vein reflux is

generally multisegmented in nature and frequently involves several anatomical levels simultaneously.

Relationship Between Perforator Venous Reflux and Leg Pigmentation

The analysis of the relationship between perforator vein reflux and skin pigmentation revealed that the Cockett and Boyd types of perforator veins had a significant relationship with the incidence of skin pigmentation ($p < 0.05$). This indicates that perforator vein reflux, especially in the lower leg area, plays an important role in increasing local venous pressure, which then triggers skin changes such as pigmentation.

Multivariate analysis was conducted on Cockett's perforator vein, entering confounder variables that had a p-value < 0.250 in the bivariate analysis. The results showed that Cockett's perforator vein reflux remained significantly related to the incidence of skin pigmentation after controlling for confounding factors. However, for Boyd's perforator vein, the multivariate analysis could not be performed because there were zero instances in the data distribution, meaning there were no patients with pigmentation who had reflux in Boyd's perforator vein. This could be due to the limited sample size or because the reflux distribution was more typical of patients with advanced skin changes (CEAP C4).

This study shows that reflux in the distal medial perforator veins (including the Cockett perforator group) is significantly related to the emergence of leg pigmentation in patients with chronic venous disease (C3–C4). These findings are consistent with research conducted by Kachlik (2009) and Jayaraj (2024), which found that the most common location of perforator vein incompetence in patients with leg pigmentation is the Cockett perforator vein. Huang et al. (2022) also stated that patients with leg pigmentation have a higher incidence of distal perforator vein incompetence compared to those without leg pigmentation. The underlying pathophysiology of these findings is that perforator incompetence increases blood flow and retrograde pressure from the deep venous system to the superficial system, causing local capillary hypertension, erythrocyte extravasation into dermal tissue, and subsequent hemosiderin deposition, which triggers skin pigmentation and trophic changes.

This phenomenon is reinforced by the fact that the distal medial perforator is located in the gait zone (ankle-calf and lower leg), which is anatomically the most vulnerable to decreased muscle venous pump function and elevated hydrostatic pressure during prolonged standing.

Relationship Between Reflux of the Great Saphenous Vein and Leg Pigmentation

Further evaluation of the relationship between the location of reflux in the great saphenous vein and skin pigmentation showed that three main segments lower thigh, upper knee, and lower knee showed a significant relationship with the incidence of skin pigmentation ($p < 0.05$). Reflux at the SFJ level was found in all patients, but multivariate analysis could not be performed on several segments, such as SFJ, mid-thigh, and lower thigh, because there were zero instances in some subgroup analyses.

In the multivariate analysis that could be performed, reflux in the upper knee saphenous vein and prolonged standing showed a significant relationship with the incidence of skin pigmentation. Reflux in the upper knee segment showed a p-value = 0.020 with an aOR of 10.24 (95% CI: 1.445–72.57), while prolonged standing showed a p-value = 0.032 with an aOR of 6.543 (95% CI: 1.172–36.52). These findings suggest that more distal reflux in the great

saphenous vein contributes significantly to the emergence of leg pigmentation in patients with chronic venous insufficiency (CVI). These results align with research conducted by Chastanet & Pittaluga (2013), which stated that axial reflux in the distal segment, especially when it reaches the mid-knee or upper-knee segment, exerts the highest pressure.

Huang et al. (2022) also stated that reflux in the distal segment of the great saphenous vein has a greater influence on leg pigmentation. In contrast, reflux in the lower knee segment of the great saphenous vein did not show a significant relationship with skin pigmentation after controlling for confounder variables ($p = 0.123$; aOR: 3.667; 95% CI: 0.703–19.13). These results suggest that while there is a trend toward increased risk of pigmentation in patients with reflux in the distal segment, the strength of the association may be influenced by the limited sample size and individual variation in the degree of venous hypertension and disease duration.

The findings of this study suggest that reflux in the lower knee segment of the great saphenous vein does not have a significant relationship with skin pigmentation. This is consistent with the theory that the more distal the location of reflux in the great saphenous vein, the greater its contribution to skin changes, including pigmentation. Several mechanisms could explain this discrepancy. Physiologically, the lower knee segment is an area of high hydrostatic pressure accumulation. Skin changes in chronic venous disease typically occur in the gaiter area (ankle–lower calf), which has the highest venous pressure and is also an area with critical perforators, such as Cockett's perforator group, which has been shown to have the strongest relationship with skin changes.

Reflux in the lower knee segment is often part of a multisegmented reflux pattern from proximal to distal, so it does not always become the main source of local venous hypertension, and its consequences may not contribute independently to pigmentation formation. In the multivariate model, the effect of reflux in this segment can be covered by other, more dominant variables, such as distal perforator incompetence, which has a greater influence on capillary venous hypertension and erythrocyte extravasation, resulting in hemosiderin deposition and pigmentation.

Additionally, methodological factors such as low data variation in the lower knee segment, imbalance in group distributions, and potential collinearity with other reflux segments may cause the disappearance of statistical significance when analyzed together.

In summary, the results of this study show that venous reflux, both in the perforator system and the great saphenous vein, plays an important role in the occurrence of skin pigmentation in patients with chronic venous disease. More distal sites of reflux, such as in the Cockett perforator veins and the upper knee segment of the great saphenous vein, appear to contribute the most to skin changes. This supports the hypothesis that increased chronic venous pressure in the lower leg area is the main trigger of the pathological processes that lead to pigmentation through mechanisms such as erythrocyte extravasation, hemosiderin formation, and activation of melanogenesis in the distal skin of the legs.

The main pathophysiology of chronic venous insufficiency is the existence of reflux or blood flow reversal due to valve incompetence in the superficial, perforator, and deep venous systems. This reflux causes an increase in chronic venous pressure and disrupts normal venous drainage. The two most common locations involved are the great saphenous vein and the perforator veins. Insufficiency in the great saphenous vein causes retrograde flow from the saphenofemoral junction to the distal segment of the leg. Meanwhile, incompetent perforator

veins, which connect the superficial and deep venous systems, cause blood flow reversal from the deep system to the superficial, increasing local venous pressure and accelerating skin changes. Reflux in the perforator veins, especially the Cockett and Boyd types, is known to be associated with increased ambulatory pressure in the lower ankle and leg areas, which are the most frequent sites showing pigmentation.

Advantages study

Study These research specific, rare topics researched, and have mark clinical high, namely about connection perforator vein reflux and pigmentation legs.

1. Ultrasound examination in study This carried out by a single operator who has get training vascular ultrasound examination so that low bias potential.
2. Study This use analysis multivariate so that the result more strong
3. Retrieval sample conducted at Cipto General Hospital Mangunkusumo which is House Sick centre references national so that the result expected can presenting CVI conditions in Indonesia.

Limitations study

1. Inspection venous reflux with using Doppler ultrasound only can done at home Sick with complete facilities, which have Doppler ultrasound with good specifications so that can count reflux time in a way precision.
2. Use one operator at a time is researchers potential cause observer bias, especially due to the assessment process Venous anatomy and hemodynamic are highly dependent on technique, experience, and interpretation. individual. In addition, no existence verification results by independent operators can reduce objectivity findings and lowering reliability measurement. For reduce potential bias in research Next, it is recommended that the ultrasound examination be carried out by more than from one independent operator, with reliability testing interobserver variability for ensure consistency research result next also can involving the examiner who does not knowing clinical status or degrees pigmentation patient (blinded assessor) to improve objectivity evaluation.

CONCLUSION

In conclusion, there is a meaningful connection between the reflux of perforator veins and the great saphenous vein with the occurrence of skin pigmentation in patients with chronic venous disease. More distal reflux sites, such as in Cockett's perforator veins and the upper knee segment of the great saphenous vein, contribute significantly to the development of skin pigmentation, reflecting the higher venous pressure in the lower leg area. The mechanism behind this pigmentation is believed to be related to the increased chronic venous pressure, which leads to erythrocyte extravasation, hemosiderin formation, and the activation of melanogenesis in the distal skin of the legs.

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