MEDICAL SCIENCES / DAHİLİ TIP BİLİMLERİ

Clinicoepidemiologic Characteristics and Prevalence of Venous Insufficiency in Patients with Pigmented Purpuric Dermatosis

Pigmente Purpurik Dermatoz Hastalarında Klinik-Epidemiyolojik Özellikler ve Venöz Yetmezlik Sıklığının İncelenmesi

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Abstract

Objectives: To describe clinic-epidemiological characteristics of pigmented purpuric dermatosis (PPD) and to assess the potential relationship between venous insufficiency and PPD.

Materials and Methods: We retrospectively reviewed the medical records of all patients diagnosed with PPD at University of Health Sciences Türkiye, İstanbul Training and Research Hospital dermatology clinics between January 2010 and September 2022. Clinical, demographic, and radiological characteristics were examined.

Results: The study included a total of 195 PPD patients, of whom 111 were female (57%). The mean age of the patients was 44.25 ± 19.99 years, and the average disease duration was 15.4 ± 24.1 months. The most common subtype of the disease was Schamberg's disease (66%), followed by Majocchi's disease (16%), lichen aureus (8%), pigmented purpuric lichenoid dermatitis of Gougerot-Blum (7%), and eczematid-like purpura of Doucas and Kapetanakis (2%). Almost all patients (99%) had lesions on their lower extremities, while only 26 (13%) had lesions on the upper body. Lesion distribution was bilateral in 167 (87%) of the cases. Venous Doppler ultrasonography was performed in 101 patients, with venous insufficiency detected in 24 (23.8%) of them. There were no statistically significant differences in terms of age, gender, and disease duration between patients with and without venous insufficiency. There was no correlation between the laterality of venous insufficiency and the laterality of lesion distribution.

Conclusion: Considering venous insufficiency is reported to affect 7% to 30% of the general population, our study implies that its occurrence in PPD patients may not be higher than in the general population, contrary to prior research.

Key Words: Venous insufficiency, pigmented purpuric eruption, doppler ultrasonography, pigmentation disorders

Öz

Amaç: Pigmente purpurik dermatozların (PPD) klinik ve epidemiyolojik özelliklerini tanımlamak ve hastalığın venöz yetmezlik ile olası ilişkisini araştırmaktır.

Gereç ve Yöntem: Ocak 2010 ile Eylül 2022 tarihleri arasında Sağlık Bilimleri Üniversitesi, İstanbul Eğitim ve Araştırma Hastanesi dermatoloji polikliniklerine başvuran, histopatolojik olarak PPD tanısı konmuş tüm hastaların dosyaları retrospektif olarak taranarak; klinik, demografik ve radyolojik özellikleri kaydedildi.

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Bulgular: Çalışmaya 111'i kadın (%57) toplam 195 PPD hastası dahil edilmiş olup, hastaların ortalama yaşı 44,25±19,99 idi. Ortalama hastalık süresi 15,4±24,1 aydı. En sık tespit edilen hastalık subtipi Schamberg hastalığı (%66) iken bunu sırası ile Majocchi hastalığı (%16), liken aureus (%8), Gougerot-Blum'un likenoid pigmente purpurik dermatiti, (%7) ve Doucas ve Kapetanakis'in egzama benzeri purpurası (%2) izledi. Hastaların neredeyse tamamında (%99) alt ekstremitede lezyon bulunurken, yalnızca 26 (%13) hastada bel üstü vücut bölgelerinde lezyon tespit edildi. Lezyonların dağılımı 167 (%87) hastada bilateraldi. Alt ekstremite venöz Doppler ultrasonografi incelemesi 101 hastada yapılmış olup, bunların 24'ünde (%23,8) venöz yetmezlik tespit edildi. Venöz yetmezlik tespit edilen ve edilmeyen hastalar arasında yaş, cinsiyet, hastalık süresi açısından istatistiksel olarak anlamlı fark bulunmadı.

Sonuç: Genel popülasyonda venöz yetmezlik prevalansının %7-30 arasında değişen sıklıkla bildirildiği göz önüne alındığında, bizim çalışmamızda önceki çalışmalardan farklı olarak PPD hastalarında venöz yetmezlik görülme sıklığının topluma göre artmış olmadığı düşünülmüştür.

Anahtar Kelimeler: Venöz yetmezlik, pigmente purpurik dermatoz, doppler ultrasonografi, pigmentasyon bozuklukları

Introduction

Pigmented purpuric dermatosis (PPD) encompasses a group of chronic skin conditions characterized by non-palpable petechiae, purpuric patches, and pigmented macules (1). These lesions are primarily localized to the lower limbs, although a more widespread distribution can occasionally be observed (1,2). PPD occurs primarily in adults but can affect individuals of all ages, including children (2,3). Despite its benign nature, this disorder can impact patients' quality of life due to their relapsing-remitting chronic course and rarely accompanying pruritus.

Based on their clinical and histopathological features, the classification of PPD is divided into five main categories: (I) Progressive pigmentary dermatosis (Schamberg disease), (II) purpura annularis telangiectodes (Majocchi disease), (III) lichen aureus, (IV) pigmented purpuric lichenoid dermatosis of Gourgerot and Blum, (V) eczematid-like purpura of Doucas and Kapetanakis. Additionally, there are several non-classified rare variants, including granulomatous PPD, itching purpura, linear PPD, transitory PPD, and familial PPD (4,5). Histopathologically, PPD is characterized by superficial perivascular lymphocytic infiltrates, extravasated erythrocytes, and hemosiderin deposition (6,7).

Several underlying diseases and drugs have been suggested to be associated with PPD, such as diabetes mellitus, dyslipidemia, rheumatoid arthritis, systemic lupus erythematosus, thyroid dysfunction, solid and hematological malignancies, nonsteroidal anti-inflammatory drugs and oral antidiabetics (1,4,6,8). While the precise cause is not fully elucidated, a multifactorial etiopathogenesis is implicated. Vascular fragility, microcirculatory abnormalities, and immunologic dysregulation play a central role in pathogenesis (7,9-11). Very few recent clinical studies investigated chronic venous insufficiency (CVI) incidence among PPD patients and have postulated that CVI might be a potential contributor to PPD (12-14). Still, the relationship between these two conditions is uncertain.

This study aimed to investigate the characteristics and clinical manifestations of PPD and to assess the incidence of chronic CVI in a large cohort of PPD patients.

Materials and Methods

Study Population and Design

A retrospective review of all patients with histopathologically proven PPD managed in the University of Health Sciences Türkiye, İstanbul Training and Research Hospital, Clinic of Dermatology between January 2010 and September 2022 was performed. The study protocol was approved by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital Institutional Review Board (IRB no: 2011-KAEK-50-369). Patients without a skin biopsy were excluded from the study.

Information regarding the epidemiological variables, possible triggers, duration of illness, clinical subtype, and clinical distribution were extracted from the electronic medical reports and the archive of clinical photographs. Similar to the previous studies, subtypes of PPD were classified mainly according to the clinical findings: (I) Schamberg disease, reddish-brown, cayenne pepper-like purpuric patches; (II) Majocchi disease, concentric rings of purpuric patches with telangiectasia; (III) lichen aureus, golden-brown patches with lichenoid appearance; (IV) pigmented purpuric lichenoid dermatosis of Gourgerot and Blum, polygonal to round lichenoid purpuric papules and plaques; (V) eczematid-like purpura of Doucas and Kapetanakis, eczematous purpuric patches. When the characteristics of the rash were not compatible with a specific subtype of the disease, it was called "unclassified".

The lower extremity venous Doppler ultrasound features were retrieved from the ultrasound examination reports, which were performed and reported by radiology specialists of the institution. The venous insufficiency diagnosis was established by detecting venous reflux in one of the superficial veins of the lower extremities. Venous dilatation without signs of venous reflux was not accepted as CVI. Great saphenous vein (GSV) and short saphenous vein (SSV) were primarily assessed.

We have followed the STROBE guidelines for conducting and reporting this observational study.

Statistical Analysis

Statistical analyses were performed with IBM SPSS Statistics version 24.0 (SPSS Inc., Chicago, IL, USA). Data for qualitative variables were presented as a number (percentage), and data for quantitative variables as mean ± standard deviation or median (minimum-maximum) as appropriate. Quantitative variables were compared using the Student's t-test or Mann-Whitney U test as appropriate. For the comparison of quantitative variables for more than two groups, One-way ANOVA or the Kruskal-Wallis test was utilized. The Pearson's chi-squared test or Fisher's exact test was used to compare the qualitative variables. Spearman's correlation analysis was performed to determine the relationship between two continuous variables. P-value <0.05 was considered statistically significant.

The characteristics of the study population are presented as proportions, means, or medians as appropriate. The Shapiro-Wilk test was used to determine the normality of the distribution of numeric variables.

Results

Clinical and Demographic Data

A total of 195 histologically proven PPD patients were involved in this study. Among them, 111 patients (57%) were female, and the mean age at the diagnosis was 44.3 ± 20.0 . The demographics and clinical characteristics of the patients are summarized in Table 1. The median duration of the eruption before the initial visit was 15.4 ± 24.1 months. Notably, 107 patients (57%) presented with PPD for less than one year, while 23 patients (12%) had a more chronic course with a disease duration exceeding 3 years.

Schamberg disease was the predominant subtype of PPD, observed in 128 patients (66%), followed by Majocchi's disease in 32 patients (16%), lichen aureus in 16 patients (8%), pigmented purpuric lichenoid dermatitis of Gougerot-Blum in 14 patients (7%), and eczematid-like purpura of Doukas and Kapetanakis in 3 patients (2%). Representative clinical photographs of five patients from our cohort, one for each clinical subtype, are provided in Figure 1.

All 195 patients, except for one, had lower limb involvement. In 169 (87%) patients, PPD only involved lower limbs. In 26 (13%) of the patients, upper extremity involvement and in 18 (9%) patients trunk involvement was seen.

Comparison of the Demographics and Clinical Characteristics Among PPD Subtypes

Table 2 displays a comprehensive comparison of the demographics and clinical features between the PPD subtypes. There was evidence of an overall difference between subtypes regarding the gender distribution (p<0.05). Specifically, an overwhelming majority (87.5%) of patients diagnosed with

Majocchi's disease were female, in stark contrast to the prominent male predominance observed in lichen aureus (68.8%) and pigmented purpuric lichenoid dermatitis of Gougerot-Blum (64.3%). Notably, lichen aureus had a tendency for a longer disease duration, with a duration of 31.4 months; however, this difference was not statistically significant (p=0.088).

Regarding the distribution of the disease across various body parts and the rate of involvement, our analysis revealed overall similarity among the different PPD subtypes. Nevertheless, a statistically significant difference emerged in terms of disease laterality, with lichen aureus presenting the highest rate of unilateral lesions, affecting 46.2% of patients within this subtype (p<0.05).

Table 1: Demographics and clinical characterist	ics of the				
pigmented purpuric dermatosis patients					

	n=195 total n (%)				
Age					
Mean ± SD	44.25±19.99				
Sex					
Female	111 (57%)				
Female/male ratio	1.32				
Disease duration					
Mean disease duration \pm SD (mo)	15.40±24.05				
<1 year	107 (55%)				
1-3 year	44 (23%)				
4-5 year	13 (7%)				
>5 years	10 (5%)				
Missing data	21 (11%)				
PPD subtype					
Schamberg	128 (66%)				
Majocchi's disease	32 (16%)				
Lichen aureus	16 (8%)				
Eczematid-like purpura of Doucas and Kapetanakis	3 (2%)				
Pigmented purpuric lichenoid dermatosis of Gougerot and Blum	14 (7%)				
Unclassified	2 (1%)				
Distribution					
Lower extremity	194 (100%)				
Trunk	18 (9%)				
Upper extremity	26 (13%)				
Lesion above the waist	26 (13%)				
Lower extremity only	169 (87%)				
Laterality of the lesions					
Unilateral	26 (13%)				
Bilateral	169 (87%)				
PPD: Pigmented purpuric dermatosis, SD: Standard deviation					



Figure 1a-e: a. Schamberg disease, b. Purpura annularis telangioctodes of Majocchi, c. Lichen aureus, d. Pigmented purpuric lichenoid dermatitis Gougerot and Blum, e. Eczematid-like purpura of Doucas and Kapetakanis

Table 2: Comparison of the demographics and clinical characteristics among PPD subtypes								
	Schamberg disease n=128	Majocchi's disease n=32	Lichen aureus n=16	Pigmented purpuric lichenoid dermatitis of Gougerot and Blum n=14	Eczematid- like purpura of Doucas and Kapetanakis n=3	Unclassified n=2	p-value	
Age, mean ± SD	45.34 <u>+</u> 20.43	36.00 <u>+</u> 19.88	47.81 <u>+</u> 14.02	46.86±20.96	42.33±12.34	62.00 <u>+</u> 4.24	0.167	
Age								
≤40	55 (42.97%)	19 (59.38%)	5 (31.25%)	4 (28.57%)	2 (66.67%)	0 (0%)	0 172	
>40	73 (57.03%)	13 (40.63%)	11 (68.75%)	10 (71.43%)	1 (33.33%)	2 (100%)	0.172	
Gender								
Female	70 (54.69%)	28 (87.5%)	5 (31.25%)	5 (35.71%)	2 (66.67%)	1 (50%)	-0.05	
Male	58 (45.31%)	4 (12.5%)	11 (68.75%)	9 (64.29%)	1 (33.33%)	1 (50%)	<0.05	
Disease duration	14.52 <u>+</u> 24.47	11.86 <u>+</u> 16.01	31.93 <u>+</u> 35.10	12.16±16.04	5.39±5.96	39.42±39.42	0.088	
<1 yr	72 (64.86%)	19 (63.33%)	6 (42.86%)	8 (57.14%)	2 (66.67%)	0 (0%)	0.250	
1-3 yr	26 (23.42%)	8 (26.67%)	3 (21.43%)	5 (35.71%)	1 (33.33%)	1 (50%)		
4-5 yr	8 (7.21%)	2 (6.67%)	3 (21.43%)	0 (0%)	0 (0%)	0 (0%)		
>5 yr	5 (4.5%)	1 (3.33%)	2 (14.29%)	1 (7.14%)	0 (0%)	1 (50%)		
Disease distribution								
Lower extremity	128 (100%)	31 (96.88%)	16 (100%)	14 (100%)	3 (100%)	2 (100%)	0.401	
Upper extremity	17 (13.28%)	5 (15.63%)	1 (6.25%)	3 (21.43%)	0 (0%)	0 (0%)	0.791	
Trunk	14 (10.94%)	2 (6.25%)	1 (6.25%)	1 (7.14%)	0 (0%)	0 (0%)	0.909	
Lesion above the waist	18 (14.06%)	5 (15.63%)	2 (12.5%)	3 (21.43%)	0 (0%)	0 (0%)	0.770	
Disease laterality								
Unilateral	12 (9.45%)	6 (18.75%)	6 (46.15%)	0 (0%)	0 (0%)	0 (0%)	0.05	
Bilateral	115 (90.55%)	26 (81.25%)	7 (53.85%)	14 (100%)	3 (100%)	2 (100%)	<0.05	
Bold values denote statistical significance at the p<0.05 level. PPD: Pigmented purpuric dermatosis, SD: Standard deviation								

Lower Extremity Doppler Ultrasonography Findings

Of the 195 PPD patients, 101 underwent Doppler ultrasonography examinations for the lower extremities. CVI was detected in only 24 (23.8%) patients, with bilateral CVI in 8 patients (8%), right only CVI in 9 patients (8.9%), and left only CVI in 7 patients (6,9%) (Table 3). The GSV was involved in 22 (21.8%) patients and SSV in 13 (12%). In our comprehensive analysis, no statistically significant differences were detected in the prevalence of CVI among distinct subtypes of PPD. Specific CVI prevalence rates observed for each PPD subtype were as follows: Schamberg disease at 20.63%, Majocchi's disease at 31.58%, Lichen aureus at 30.0%, pigmented purpuric lichenoid dermatitis of Gougerot-Blum at 12.5% and Eczematic-like purpura of Doukas-Kapetanakis at 0% (data not shown). The correlation between PPD lesions' and CVI laterality was not statistically significant (Table 4).

Comparison of Demographics and Clinical Characteristics Between the PPD with CVI and PPD Without CVI

The comparison of demographics and clinical characteristics between the PPD with and without CVI is summarized in Table 5. The mean age, gender distribution, and disease subtypes were similar in both groups. The mean disease duration was longer in the group of PPD with CVI compared to PPD without CVI (28.44±33.93 vs. 16.86±26.15 months), but this difference didn't reach statistical significance. PPD with CVI showed a more widespread disease distribution with the presentation of the lesions above the waist in 16.7% of patients, compared to 5.2% in the group of PPD without CVI (p=0.05).

Table 3: Lower extremity Doppler ultrasound findings			
	Total number n=101 n (%)		
CVI absent	77 (76.2%)		
CVI present	24 (23.8%)		
Unilateral CVI	16 (15.8%)		
Bilateral CVI	8 (8.0%)		
CVI: Chronic venous insufficiency			

Discussion

In this retrospective study, we aimed to investigate the clinicoepidemiological characteristics and prevalence of CVI in patients diagnosed with PPD in the largest cohort of patients to our knowledge. PPD encompasses a group of rare skin disorders characterized by distinctive skin lesions, and the findings herein contribute to our understanding of PPD, addressing questions surrounding demographics, clinical presentation, and possible association with chronic venous disease.

Consistent with previous reports, our cohort displayed a wide age distribution, ranging from 8 to 85, and it predominantly affected adult patients with a mean age at diagnosis of 44.3 years. While PPDs have traditionally been reported as more common in men, the patients in this study showed a subtle female predominance (57%) (2). Notably, this observation aligns with findings from two previous Korean studies, emphasizing potential ethnic variations in PPD epidemiology (1,15). The duration of the disease was <1 year in the majority of our patients (55%), similar to the studies by Sharma and Gupta (5) (52%) and Gupta et al. (16) (52%). In the vast majority of the cases (88%), the disease was confined to the lower extremities, which is consistent with the current literature where a widespread distribution has been reported in only 2-21% of patients (1,12,16).

In our study, Schamberg disease emerged as the predominant subtype of PPDs, accounting for 66% of the cases, which aligns with the general trend in the literature where Schamberg disease consistently reported as the most common subtype with prevalence ranging from 41% to 90% (1,12,17). Majocchi's disease was the second most common type (16%), while lichen aureus, pigmented purpuric lichenoid dermatitis of Gougerot-Blum, and eczematid-like purpura of Doukas and Kapetanakis constituted the remaining subtypes in our cohort, with the proportions in line with literature reports (1,4,17). Majocchi's disease exhibited a distinct female predominance (87.5%) and was more prevalent among young adults under <40, a finding that aligns with recent literature suggesting a shift towards a

Table 4: Correspondence ratios between CVI and PPD lateralities						
Variable	CVI laterality n (%)			Correlation between CVI and PPD n (%)		
	Left side only	Right side only	Both side	Group with positive correlation	Group with negative correlation	p-value
PPD disease laterality						
Left side only	0 (0)	1 (11.11)	0 (0)			
Right side only	1 (14.29)	2 (22.22)	0 (0)			
Both side	6 (85.71)	6 (66.67)	8 (100)			
CVI laterality				10 (41.67)	14 (58.33)	0.551
CVI: Chronia vanaus insufficiency DDD: Diamontod nursuvia dermatoria						

CVI: Chronic venous insufficiency, PPD: Pigmented purpuric dermatosis

Table 5: Comparison of demographics and clinical characteristics between PPD with CVI and PPD without CVI					
PPD with CVI n=24	PPD without CVI n=77	p-value			
50±16.35	47.58±17.81	0.361			
Gender n (%)					
16 (66.7%)	46 (59.7%)	0.543			
8 (33.3%)	31 (40.3%)				
28.4 <u>+</u> 33.9	16.8±26.1	0.163			
24 (100%)	77 (100%)	-			
1(4.16%)	4 (5.19%)	0.839			
4 (16.67%)	3 (3.89%)	<0.05			
4 (16.67%)	4 (5.19%)	0.05			
Laterality of PPD n (%)					
4	9 (12%)	0.572			
20	65 (88%)				
Disease subtype n (%)					
13 (54%)	50 (65%)				
6 (25%)	13 (17%)				
3 (13%)	7 (9%)	0.291			
1 (4%)	7 (9%)				
0 (0%)	0 (0%)				
1 (4%)	0 (%)				
	Veen PPD with CVI and F PPD with CVI n=24 50±16.35 16 (66.7%) 8 (33.3%) 28.4±33.9 24 (100%) 1(4.16%) 4 (16.67%) 4 (16.67%) 6 (25%) 3 (13%) 1 (4%) 0 (0%) 1 (4%)	vecen PPD with CVI and PPD without CVI n=24PPD with CVI n=24PPD without CVI n=77 50 ± 16.35 47.58 ± 17.81 16 (66.7%)46 (59.7%)8 (33.3%)31 (40.3%)28.4 \pm 33.916.8 \pm 26.124 (100%)77 (100%)1(4.16%)4 (5.19%)4 (16.67%)3 (3.89%)4 (16.67%)4 (5.19%)2065 (88%)13 (54%)50 (65%)6 (25%)13 (17%)3 (13%)7 (9%)1 (4%)0 (%)			

CVI: Chronic venous insufficiency, PPD: Pigmented purpuric dermatosis, SD: Standard deviation

younger age group affected by this subtype (1,18). Additionally, lichen aureus demonstrated the most prolonged disease duration and exhibited a statistically significant preference for unilateral lesions among other types, emphasizing its distinct clinical profile.

The etiopathogenesis of PPD remains incompletely understood, but several factors, including venous hypertension, gravitational influence, strenuous physical activity, orthostatic pressure, capillary fragility, infections, exposure to certain medications, and contact allergens, have been proposed as potential triggers of the disease (1,4,6). Various theories have been proposed to elucidate the underlying mechanism, with vascular pathology and immune mechanisms being widely acknowledged as the predominant ones. These theories posit that increased capillary dilatation and vascular fragility result in the rupture of end capillaries in the papillary dermis. Endothelial cell dysfunction triggered by oxidative stress or immune-mediated mechanisms, venous hypertension, and gravitational dependency are potential contributors of capillary dilatation and fragility. It has been proposed that increased intravenous pressure due to CVI could be another contributing factor to PPD. The first study suggesting a possible link between CVI and PPD was reported by Gönül et al. (14) where the authors examined the prevalence of CVI in PPD patients and

found that 75% exhibited CVI as detected by venous doppler ultrasonography. However, due to the limited sample size (n=20), no clear correlation and causal relationship between these two entities could be established. Two subsequent more extensive studies corroborated Gönül et al.'s (14) findings, reporting CVI in 62.5% and 76.2% of PPD patients, respectively (12,13). Parsi et al. (12) also demonstrated that treatment of underlying CVI resulted in complete or partial resolution of the lesions in 95% of the patients. Nonetheless, in our cohort, a much lower proportion of the PPD patients (23.8%) exhibited CVI detectable with Doppler, compared to the previous studies. Interestingly, in the study of Gupta et al. (16) Doppler ultrasonography of the lower limbs did not reveal CVI in any of the 60 PPD patients. It is important to note that neither the previous studies nor our study incorporated a control group for comparative assessment of CVI prevalence. Some large epidemiological studies reported that CVI affects 7 to 30% of the general population, and prevalence can vary depending on the population studied and the definition used for CVI (19-21). In Türkiye, 20-25% of women and 10-15% of men are reported to be affected by CVI (22). Considering that the reported prevalence of CVI in the general Turkish population was comparable to the CVI prevalence observed in our PPD cohort, our study suggests that a substantial association between PPD and CVI is not evident. However, further prospective studies with control groups are

needed to draw a definitive conclusion. The comparatively lower prevalence of CVI in our cohort, in contrast to prior studies' findings, could be attributed to the cohort's younger mean age and the more stringent inclusion criteria applied in our study. We exclusively incorporated pathologically confirmed cases of PPD, thereby mitigating the potential for clinical diagnostic ambiguity between PPD and cutaneous manifestations of CVI, such as stasis dermatitis, pigmentary alterations, and skin rashes.

Study Limitations

Our study has a few limitations that warrant consideration. First, its single-centre, retrospective design poses some inherent limitations including selection bias and unknown confounding factors. Second, the operator-dependent nature of Doppler ultrasound investigations, conducted by different operators, may have introduced variability in the result. However, these limitations may be outweighed by the strength of our study's large sample size, which enhances the statistical power and robustness of our findings.

Conclusion

In conclusion, our study expands our understanding of PPD and its epidemiological and clinical characteristics, and offers a valuable contribution to the field, emphasizing the complexity and diversity of PPD presentations. Furthermore, considering the relatively low prevalence of CVI among PPD patients in our cohort, our findings suggest that routine Doppler US investigations in all PPD patients may not be warranted in the absence of other risk factors or relevant symptoms. However, this conclusion should be applied cautiously due to conflicting results in the literature. Further prospective studies with the control groups are needed to establish the relationship between PPD and CVI.

Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital Institutional Review Board (IRB no: 2011-KAEK-50-369).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: A.V.E., A.E.K.A., Concept: S.S.E., A.V.E., A.E.K.A., Design: S.S.E., A.V.E., A.E.K.A., Data Collection and Processing: S.S.E., E.B.A., A.Ö., Analysis or Interpretation: S.S.E., M.S.G., Literature Search: S.S.E., E.B.A., M.S.G., Writing: S.S.E., A.Ö.

Conflict of Interest: The authors declared that there was no conflict of interest during the preparation and publication of this article.

Financial Disclosure: The authors declared that they did not receive any financial support during the research and authoring of this article.

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