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Appearance-related concerns and their impact on health-related quality of life in patients with peripheral vascular malformations

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Received 4 March 2022; accepted 18 August 2022

KEYWORDS

Vascular malformations;
Venous anomaly;
Port-wine stain;
Aesthetic appearance;
Health-related quality of life;
Patient-reported outcome measures (PROM)

Summary Background: Peripheral vascular malformations (VMs) may lead to disfigurement of the body and face, potentially impairing aesthetic appearance. Yet, data on appearance in this population is limited. This study aimed to examine appearance-related concerns and their impact on health-related quality of life (HR-QoL) in patients with VMs.

Methods: In this cross-sectional study, 384 adults and 194 children with VMs were invited to complete the Outcome Measures for VAScular MALformations (OVAMA) questionnaire to evaluate potential appearance-related concerns on a five-point verbal-rating scale, with higher scores indicating more appearance-related concerns (e.g., colour-difference, facial-distortion, reduced self-esteem, and dissatisfaction with appearance). HR-QoL was evaluated using Patient-Reported Outcome Measurement Information System (PROMIS). Subgroups of patients reporting more appearance-related concerns were identified using univariate analysis. Associations between appearance-related concerns and various HR-QoL domains (e.g., *anxiety* and *social participation*) were assessed.

Results: A total of 184 patients (32%) completed the questionnaires; 121 patients (66%) reported that one or more appearance outcome was severely affected (i.e., 4-5 out of 5). The

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following factors statistically significant associated with more appearance-related concerns: capillary/combined origin, facial localization, subcutaneous tissue involvement, larger size, overgrowth, and diagnosis of a syndrome. In adults, dissatisfaction with appearance and reduced self-esteem due to the appearance of the VM correlated with more *anxiety* and *depression* symptoms. Reduced self-esteem correlated with less *social participation*. In children, bodily distortion and being stared at were correlated with less *peer relationships*.

Conclusion: Severe appearance-related concerns were present in two-thirds of patients with VMs, impairing their mental HR-QoL. Clinicians should acknowledge appearance-related aspects, monitor psychological well-being, and offer intervention aimed at improving satisfaction with appearance.

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Introduction

Peripheral vascular malformations (VMs) are congenital vessel anomalies characterized by dilated and tortuous vessels, which can be of capillary, venous, lymphatic, arteriovenous or combined origin.¹ VMs arise during embryogenesis due to localized defects in vasculogenesis and angiogenesis and may become visible later in life.²

The clinical presentation of VMs is highly variable, with signs and symptoms varying in nature and severity depending on the VM type, anatomical location, tissue involvement and lesion size. Symptoms include pain, swelling, physical impairment, bleeding and thrombosis.^{3–5} It is now well established that patients with VMs experience impaired health-related quality of life (HR-QoL), including worse mental health.^{6,7} Moreover, VMs differ from normal skin regarding colour, swelling and texture, and they may lead to a disfigurement of the body and of highly visible areas such as the head and neck. Therefore, appearance-related concerns may be present in this patient population.

Appearance is of great importance in the development of personality and relationships^{8,9}, and negative psychosocial consequences are known to occur in patients with craniofacial abnormalities.¹⁰ Previous studies found that children with vascular anomalies have a negative perception of how others value them.^{10,11} Furthermore, the presence of facial capillary malformations has a severely negative impact on HR-QoL, in which the emotional domain is affected mostly.¹²

In the development of the core outcome set for VMs, appearance was identified as an important aspect by 300 international experts and patients, and it was selected as a core outcome domain that should be measured when evaluating treatment effect.⁴ In addition, appearance-related concerns can be an indication to initiate treatment. However, to date, no studies have addressed appearance outcomes specifically, and it is unknown which subgroups of patients report clinically relevant appearance-related concerns and which appearance aspects patients find the most cosmetically disturbing. It is relevant to recognize these appearance aspects to treat the appearance-related concerns properly.

Therefore, the aim of this study is to examine appearance-related concerns in patients with VMs by using the condition specific OVAMA (Outcome measures for Vascular Malformations) questionnaire.^{4,13,14} Furthermore, we

assessed how the appearance of VMs affects HR-QoL in these patients.

Methods

Study design

To assess appearance-related concerns and HR-QoL in patients with VMs, a cross-sectional study was performed at the Amsterdam University Medical Centres (i.e., tertiary vascular anomaly expert centre in the Netherlands). The STROBE (Strengthening the Reporting of Observational Studies of Epidemiology) guidelines for cross-sectional studies were followed.¹⁵ The study adhered to the Declaration of Helsinki, and informed consent was obtained digitally from all patients. The study was exempted from full ethical review by the Medical Ethics Committee since patients were not subjected to interventions or rules of conduct.

Study procedure

Patient selection

All patients with VMs who visited the outpatient clinic between June 2012 and May 2021, identified through ICD-codes, treatment codes, and manual screening of patients visiting the outpatient clinics, were included in our local VM database. The VM diagnosis was based on clinical examination and confirmed with imaging or histopathology in case of uncertainty. Patients with VMs of the central nervous system or isolated malformations in visceral organs were excluded. Data were retrospectively extracted from electronic patient files on patient age, gender, VM type according to the ISSVA classification¹, lesion localization, types of tissues involved, lesion size (maximal diameter, obtained from imaging reports or measured on MRI), overgrowth (including leg-length discrepancy) and the diagnosis of a syndrome and received treatments.

Between June 2020 and May 2021, all adults and children with peripheral VMs from our database, of whom an e-mail address was available (80%), were sent a digital invitation for this study. Using an online patient-reported outcome measure (PROM) portal called Kwaliteit van Leven In Kaart (KLIK) (which translates to Mapping QoL in Clinical Practice)

patients were asked to complete the questionnaires. KLIK enables patients to create an account and complete questionnaires.¹⁶ Parents of children aged 0-13 years were instructed to help their child fill in the questionnaires. Children aged 14-17 years were asked to complete the questionnaires independently. The cut-off points for age were determined during the concept interviews in the OVAMA-project and were based on the comprehensibility of the questions by different age groups.¹⁴

Questionnaires

OVAMA

The OVAMA-questionnaire is a condition-specific PROM for patients with VMs, which focuses on VM symptoms and appearance (supplement 1).^{4,13,14} The OVAMA questionnaire addresses appearance of the VM with the following items: patient-reported size, swelling, colour difference, texture difference, facial distortion, bodily distortion, being stared at, reduced self-esteem due to the appearance of the VM, and dissatisfaction with appearance. All questions refer to issues that occurred within the last four weeks. The items 'colour difference' and 'texture difference' imply a difference compared to the normal skin. All appearance questions referred to the patient's perspective on the VM and are answered on a five-point verbal rating scale. Higher scores indicate more appearance-related concerns, scores four or five out of five are regarded as severely affected. Additionally, a comprehensive appearance score was generated by $((\text{the sum of all 9 appearance outcomes}) / 9) * 20$.

PROMIS

HR-QoL was measured using PROMIS (Patient-Reported Outcome Measurement Information System¹⁷), which is a set of person-centred measures that evaluate physical, mental and social health in adult and children. PROMIS was used because other quality of life measures seemed not responsive to changes in HR-QoL in adults and children with peripheral VMs.^{18,19} HR-QoL domains that should be measured in patients with VMs were determined in the core domain set.^{4,13} To fully capture these HR-QoL domains, the following PROMIS scales were identified: *pain interference*, *physical functioning*, *anxiety*, *depression* and *social participation*. For each PROMIS scale, a T-score can be calculated and plotted against the reference population, where the mean T-score for the general population is 50 and the standard deviation is 10. Subsequently, the measured T-score represents the deviation from the general population. For PROMIS scales, T-scores higher than 50 indicate more of the concept being measured in comparison to the general population (e.g., more *anxiety*, more *social participation*), and T-scores lower than 50 equal less of the concept being measured.

Data analyses

Baseline characteristics are presented as frequencies and percentages for categorical variables and median and interquartile range (IQR) for nonparametric continuous data.

Baseline characteristics were compared between responders and non-responders of the questionnaires in order to detect response bias using chi-square tests for categorical variables and the Mann-Whitney U test for nonparametric continuous variables. Responders were defined as patients who completed at least one questionnaire.

Univariate analysis was performed to compare the appearance outcomes between different subgroups of patients with VMs (e.g., gender, lesion localization). The variable age was grouped as 0-20, 21-40, 41-60 and 61-80, thereby children and adolescents were combined, and these groups reflect major developmental stages. Mann-Whitney U tests were used for dichotomous variables, and the Kruskal-Wallis test was used for categorical nominal variables.

To investigate correlations between the various appearance outcomes and PROMIS HR-QoL scales, Spearman's rank correlations were computed. Additionally, the appearance outcomes were correlated with each other using a Spearman's rank correlation. For the correlations of the appearance outcome facial distortion, only patients with head and neck VMs were included (n=57). For all statistical analyses, $p < 0.05$ was considered statistically significant. Statistical analyses were performed with SPSS Statistics, Version 26.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 384 adults and 194 children with peripheral VMs and valid contact information were invited by e-mail to complete the questionnaires. Of the invited patients, 32% (n=184) completed the OVAMA questionnaire; 36% (n=137) of invited adults and 24% (n=47) of invited children completed at least one PROMIS questionnaire. Patient baseline characteristics are listed in [Table 1](#). Several statistically significant differences in baseline characteristics were found between non-responders and responders of the questionnaires. Responders were older of age ($p=0.001$), more frequently had intraosseous VMs (18% vs 10%, $p=0.006$), and fewer patients had capillary malformations (8% vs 16%, $p=0.020$) (Supplemental Table 1).

Appearance outcomes

Of the included patients, 66% (n=121) reported that one or more appearance-related outcomes were severely affected (i.e., scoring four or five out of five); medical photographs of three of these patients are shown in [Figure 1](#). Thirty-six percent (n=66) of the patients reported the size as large or very large, and 23% (n=41) indicated a large or very large swelling. Furthermore, 34% (n=63) found the colour of the VM very or extremely different than their normal skin, and 26% (n=48) reported that the texture of the VM was very or extremely different. Thirteen percent (n=25) described their facial features as very or extremely distorted, and 21% (n=39) expressed their bodily features as very or extremely distorted. Eighteen percent (n=33) indicated that they were being stared at a lot or all the time, and 11% (n=20) described that their self-confidence as a lot or extremely reduced. Lastly, 31% (n=56) of the patients



Figure 1 Medical photographs of 3 patients with peripheral VMs who expressed severe appearance-related concerns. A, B & C: A 26-year-old female with a combined capillary-venous malformation of the left leg and a capillary malformation of the right leg. Additionally, a leg-length discrepancy and overgrowth of the left leg and foot were present, and she has been diagnosed with Klippel-Trenaunay Syndrome. A: displays the side view of the left leg. B: shows the rear view of both legs. C: rear view of both lower legs with evident overgrowth of the left lower leg. D: A 19-year-old male with a small venous malformation at the inside of the upper lip. Although the VM was small, he expressed severe appearance-related concerns. E & F: A 22-year-old female with a large venous malformation of the right back, flank and chest. D: her back, with a venous malformation on the right side. E: displays the venous malformation from a lateral view.

indicated that they were dissatisfied or very dissatisfied with the appearance of the VM.

Univariate analyses of factors associated with higher appearance scores, indicating more appearance-related concerns, are displayed in [Table 2](#). Overall, the characteristics that were associated with more appearance-related concerns included the following: lesions of capillary of combined origin, facial localization, subcutaneous and intrasosseous tissue involvement, larger lesion size, overgrowth and lesions part of an associated syndrome. Older age showed a statistically significant association with more

facial distortion and dissatisfaction with appearance, meaning that with the increase of age, their facial distortion worsens and patients are more dissatisfied with the appearance of the VM.

Dissatisfaction with appearance

Correlations between the various appearance outcomes are displayed in Supplemental Table 2. All appearance outcomes had a statistically significant correlation with dissatisfaction

Table 1 Baseline characteristics of the included patients (n=184).

Patient Characteristics	n (%)
Male	64 (35%)
Age in years (median, IQR)	29 (18-50)
Children (<18 years)	47 (26%)
Lesion characteristics	
Syndrome (%)	25 (14%)
Overgrowth	21 (11%)
Vascular malformation type	
Venous malformation	90 (49%)
	18 (10%)
Lymphatic malformation	
Capillary malformation	14 (8%)
Arteriovenous malformation	23 (13%)
Combined malformation	38 (21%)
Unclear	1 (0.5%)
Localization	
Head and neck	70 (38%)
Upper extremity	43 (23%)
Lower extremity	63 (34%)
Trunk	46 (26%)
Tissue extension	
(sub)cutaneous	155 (84%)
Intramuscular	85 (46%)
Intraosseous	33 (18%)
Maximal diameter in cm (median, IQR)	7.3 (4-15)
Size groups	
<5 cm	61 (33%)
5-10 cm	33 (24%)
10-30 cm	33 (24%)
>30 cm	31 (17%)
Unclear	4 (2%)
Previous therapies	
None	38 (26%)
Laser therapy	28 (15%)
Compression stockings	48 (26%)
Sclerotherapy	66 (36%)
Surgery	71 (39%)

IQR = Interquartile range.

with appearance ($p < 0.001$), meaning that if an appearance outcome was more severely affected (e.g., reporting more bodily distortion) patients were more dissatisfied with the appearance of the VM. Dissatisfaction with appearance was moderately correlated with bodily distortion ($r = 0.316$), texture difference ($r = 0.352$), patient-reported size ($r = 0.370$), colour difference ($r = 0.442$), swelling ($r = 0.483$) and being stared at ($r = 0.492$). A high correlation existed between dissatisfaction with appearance and reduced self-esteem ($r = 0.525$) and facial distortion ($r = 0.569$).

Health-related quality of life

Correlations between the appearance outcomes and PROMIS scales are shown in Table 3. In adults, moderate to high correlations were found between the appearance outcome reduced self-esteem and PROMIS scales *anxiety* and *de-*

pression, meaning that patients with reduced self-esteem because of the appearance of the VM reported more *anxiety* and *depression*. Additionally, a correlation was found between dissatisfaction with appearance and *depression*. Furthermore, a moderate to high negative correlation was found between patient-reported size and the PROMIS scale *physical functioning*, meaning that a greater patient-reported size is associated with reduced *physical functioning*.

In children, a moderate to high correlation was found between bodily distortion and *pain interference*, meaning that more bodily distortion was associated with more *pain interference*. Moderate to high negative correlations were found between bodily distortion and the PROMIS scales *mobility* and *peer relationships*, meaning that more bodily distortion will lead to less *mobility* and less *peer relationships*. Further, being stared at was negatively correlated with *peer relationships*.

Discussion

In this study, approximately two-thirds (66%) of patients with peripheral VMs indicated that one or more appearance-related outcomes were severely affected, and one-third (31%) were dissatisfied or very dissatisfied with the appearance of their VM. The following factors associated with more appearance-related concerns: facial localization, capillary/combined origin, subcutaneous and intraosseous tissue involvement, larger lesion size, overgrowth and the lesion being part of a syndrome. Appearance-related concerns that led to the most 'dissatisfaction with appearance' included swelling, being stared at, reduced self-esteem and facial distortion. Another clinically relevant finding was the impact of appearance-related concerns on the HR-QoL, as dissatisfaction with appearance, a higher appearance composite score (indicating more problems with aesthetic appearance), and reduced self-esteem were associated with more *anxiety* and *depression* in adults. Furthermore, aesthetic concerns caused by the VM seemed to lead to psychosocial difficulties, i.e., reduced self-esteem seemed to worsen *social participation* in adults, and in children bodily distortion and being stared negatively affected their *peer relationships*.

Patients with capillary or combined, facial, subcutaneous and larger VMs reported more appearance-related concerns as these lesions are generally more visible. Additionally, patients with overgrowth or associated syndromes reported more appearance-related problems. This may be because overgrowth looks distinctly different from normal skin, and larger proportions of the body are affected in these patients, which can be more noticeable. This finding is also in line with previous research, which found that patients with overgrowth reported more impaired HR-QoL than patients without overgrowth.²⁰ Surprisingly, we found that intraosseous VMs were also associated with appearance-related concerns, which is probably because the included intraosseous VMs were larger in size.

Our study found that with the increase of age, their facial distortion worsens, and older patients were more dissatisfied with the appearance of their VM. This may be explained by the fact that VMs may evolve, as capillary malformations

Table 2 Univariate analysis of risk factors for appearance-related concerns.

	Appearance composite score		Patient-reported size		Swelling		Colour difference		Texture difference		Facial distortion		Bodily Distortion		Being stared at		Reduced self-esteem		Dissatisfaction with appearance	
	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P	Mdn, IQR	P
<i>Patient Characteristics</i>																				
Gender																				
Male	47 (33-58)	0.10	3 (2.25-4)	0.27	3 (1-3)	0.75	2 (1-4)	0.05	2 (1-4)	0.65	1 (1-2)	0.65	2 (1-2.75)	0.40	2 (1-3)	0.35	1 (1-2)	0.003	3 (2-4)	0.57
Female	51 (38-62)		3 (2.25-4)		3 (2-3)		3 (1-5)		2 (1-4)		1 (1-2)		2 (1-3)		2 (1-3)		2 (1-3)		3 (2-4)	
Age																				
0-20 years (n=57)	49 (34-57)		3 (2-4)		3 (2-4)		3 (1-4)		2 (1-4)		1 (1-2)		1 (1-3)		2 (1-3)		2 (1-2)		3 (2-4)	
21-40 years (n=69)	47 (36-59)		3 (2-4)		3 (2-3)		2 (1-4)		2 (1-3.5)		1 (1-2)		2 (1-3.5)		2 (1-3)		2 (1-3)		3 (2-4)	
41-60 years (n=38)	48 (33-62)	0.31	3 (3-3.25)	0.55	3 (2-3)	0.83	3 (1-4.25)	0.23	2.5 (1-3)	0.20	1.5 (1-3)	0.003	2 (1-3.25)	0.58	2 (1-3)	0.59	1 (1-2.25)	0.20	3 (2-3)	0.05
61-80 years (n=20)	59 (43-76)		4 (2-4)		3 (2-4)		4 (1.25-5)		3 (2-4)		1.5 (1-3.75)		1.5 (1-4)		3 (1.25-3)		2 (1-3)		4 (3-4.75)	
<i>Lesion Characteristics</i>																				
Syndrome																				
No	47 (33-58)	0.003	3 (2-4)	<0.001	2 (2-3)	0.05	2 (1-4)	<0.001	2 (1-3)	0.18	1 (1-2)	0.54	1 (1-3)	<0.001	2 (1-3)	0.012	2 (1-3)	0.65	3 (2-4)	0.33
Yes	62 (42-74)		4 (3-5)		3 (2-4)		5 (3-5)		3 (1-4.5)		1 (1.5)		3 (2-4.5)		3 (1.5-4)		1 (1-3)		3 (2-4)	
Overgrowth																				
No	47 (33-60)	0.007	3 (2-3)	0.001	3 (2-3)	0.083	2 (1-4)	<0.001	2 (1-3)	0.45	1 (1-2)	0.47	1 (1-3)	<0.001	2 (1-3)	0.014	2 (1-3)	0.75	3 (2-4)	0.26
Yes	58 (44-68)		4 (3-5)		3 (2-4)		5 (3-5)		2 (1-4)		1 (1-1.5)		4 (2-5)		3 (2-4)		2 (1-2.5)		3 (3-4)	
Vascular Malformation type																				
Venous	46 (31-53)		3 (2-4)		3 (2-4)		1.5 (1-3)		2 (1-3)		1 (1-2)		1 (1-3)		2 (1-3)		2 (1-2)		3 (2-4)	
Lymphatic	44 (37-56)		3 (2-3.25)		2 (2-3)		2 (1-3.25)		2.5 (1-4)		1 (1-1.25)		2 (1-3)		2 (1-3)		2 (1-3)		3 (2-3.25)	
Arteriovenous	47 (36-62)	<0.001	3 (2-4)	<0.001	3 (2-4)	0.089	3 (2-3)	<0.001	3 (1-4)	0.045	1 (1-2)	0.005	1 (1-3)	0.034	2 (1-3)	<0.001	2 (1-3)	0.56	3 (2-4)	0.12
Capillary	60 (42-71)		4 (3-5)		1 (1-3.25)		5 (3-5)		1 (1-4)		3 (1-4.25)		1 (1-3.25)		3.5 (2-5)		1.5 (1-4.25)		3 (3-4.25)	
Combined	62 (49-69)		4 (3-4)		3 (2-4)		4 (3-5)		3 (2-4)		1 (1-3.25)		2.5 (1-4)		3 (2-4)		2 (1-3)		3 (2-4)	
Localization																				
Head and neck																				
No	47 (33-62)	0.43	3 (3-4)	0.23	3 (2-4)	0.001	2 (1-4)	0.09	2 (1-4)	0.30	1 (1-1)	<0.001	2 (1-4)	<0.001	2 (1-3)	0.001	2 (1-3)	0.33	3 (2-4)	0.82
Yes	49 (38-61)		3 (2-4)		2 (1.75-3)		3 (2-4)		2 (1-3)		2 (1-4)		1 (1-2)		3 (2-4)		2 (1-3)		3 (2-4)	

(continued on next page)

Table 2 (continued)

	Appearance composite score		Patient-reported size	Swelling	Colour difference	Texture difference	Facial distortion	Bodily Distortion	Being stared at	Reduced self-esteem	Dissatisfaction with appearance									
Face																				
No	47 (33-60)	0.018	3 (2-4)	0.33	3 (2-4)	0.032	2 (1-4)	0.003	2 (1-4)	0.40	1 (1-1)	<0.001	2 (1-3)	<0.001	2 (1-3)	0.001	2 (1-2,25)	0.14	3 (2-4)	0.23
Yes	54 (42-64)		3 (2-4)		2 (1-3)		3 (2.75-4.25)		2 (1-3)		3 (2-4)		3 (2-4)		3 (2-4)		2 (1-3)		3 (2-4)	
Upper extremity																				
No	47 (33-60)	0.25	3 (2-4)	0.05	2 (2-3)	0.04	3 (1-4)	0.53	2 (1-3)	0.20	1 (1-2)	0.011	1 (1-3)	0.002	2 (1-3)	0.72	2 (1-3)	0.13	3 (2-4)	0.53
Yes	51 (36-64)		3 (3-4)		3 (3-4)		3 (1-4)		3 (1-4)		1 (1-1)		2 (2-4)		2 (1-3)		1 (1-2)		3 (2-4)	
Trunk																				
No	47 (36-58)	0.29	3 (2-4)	0.06	3 (2-3)	0.28	3 (1-4)	0.15	2 (1-3)	0.22	1 (1-2.5)	0.003	1 (1-3)	<0.001	2 (1-3)	0.79	2 (1-3)	0.20	3 (2-4)	0.82
Yes	55 (33-64)		3 (3-4)		3 (2-4)		3 (1-5)		2 (1-4)		1 (1-1)		3 (2-4)		2 (1-3)		1 (1-2)		3 (2-4)	
Lower extremity																				
No	47 (36-59)	0.57	3 (2-4)	0.03	3 (2-3)	0.09	3 (1-4)	0.90	2 (1-3)	0.68	1 (1-3)	<0.001	1 (1-3)	0.008	2 (1-3)	0.64	2 (1-3)	0.76	3 (2-4)	0.96
Yes	51 (33-64)		3 (3-4)		3 (2-4)		2 (1-5)		2 (1-4)		1 (1-1)		2 (1-4)		2 (1-3)		2 (1-3)		3 (2-4)	
Tissue involvement																				
Subcutaneous																				
No	33 (29-50)	0.001	3 (2-3.5)	0.18	2 (1-3)	0.13	1 (1-2)	<0.001	2 (1-3)	0.19	1 (1-1)	0.024	1 (1-3.5)	0.58	1 (1-2.5)	0.005	1 (1-2)	0.046	2 (1-3)	0.002
Yes	51 (38-62)		3 (3-4)		3 (2-4)		3 (1-4)		2 (1-4)		1 (1-2)		2 (1-3)		2 (1-3)		2 (1-3)		3 (2-4)	
Intramuscular																				
No	49 (38-62)	0.62	3 (2-4)	0.63	2 (2-3)	0.19	3 (1-4)	0.21	2 (1-3)	0.71	1 (1-3)	0.019	2 (1-3)	0.43	2 (1-3)	0.38	2 (1-3)	0.53	3 (2-4)	0.25
Yes	47 (33-62)		3 (3-4)		3 (2-3.5)		2 (1-4)		2 (1-4)		1 (1-1)		2 (1-4)		2 (1-3)		2 (1-3)		3 (2-4)	
Intraosseous																				
No	47 (33-58)	0.001	3 (2-4)	0.053	2 (2-3)	0.001	3 (1-4)	0.15	2 (1-3)	0.002	1 (1-2)	0.18	2 (1-3)	0.31	2 (1-3)	<0.001	2 (1-2)	0.009	3 (2-4)	0.058
Yes	58 (49-69)		3 (3-4)		3 (2.5-4)		3 (2-4.5)		3 (2-4)		1 (1-3)		2 (1-4)		3 (2-4)		3 (1-3)		3 (3-4)	
Lesion size																				
<5 cm	42 (31-52)	<0.001	3 (2-3)	<0.001	2 (2-3)	<0.001	2 (1-3)	<0.001	2 (1-3)	<0.001	1 (1-2)	0.32	1 (1-2)	<0.001	1 (1-3)	<0.001	2 (1-2)	0.20	3 (2-3)	0.023
5-10 cm	41 (32-53)		3 (2-4)		2 (1-3)		2 (1-4)		1 (1-3)		1 (1-2)		1 (1-3)		2 (1-3)		1 (1-2)		3 (2-4)	
10-30 cm	53 (38-68)		3.5 (3-4)		3 (2-4)		3 (1-4)		3 (1-4)		1 (1-3)		1.5 (1-3)		3 (1-3.75)		2 (1-3)		3 (2-4)	
>30 cm	62 (51-67)		4 (4-5)		3 (3-4)		5 (3-5)		3 (1-4)		1 (1-1)		3 (2-4)		3 (2-4)		2 (1-3)		3 (3-4)	

All appearance outcomes are on a five-point verbal rating scale, with higher score indicates more appearance-related concerns. P<0.05 are considered statistically significant and are displayed in bold. Mdn = median, IQR = Interquartile range

Table 3 Spearman's rank correlation coefficients between the PROMIS scales and the different appearance outcomes

	n	Appearance composite score	Patient-reported size	Swelling	Colour difference	Texture difference	Facial distortion	Bodily Distortion	Being stared at	Reduced self-esteem	Dissatisfaction with appearance
Adults											
Anxiety	128	0.239**	0.054	0.108	0.173	0.038	0.069	0.171	0.132	0.444**	0.257**
Depression	125	0.222*	0.038	0.103	0.135	-0.036	0.080	0.148	0.103	0.432**	0.345**
Participation	124	-0.072	0.050	-0.022	-0.046	-0.104	0.053	-0.086	-0.032	-0.230*	-0.078
Pain interference	126	0.098	0.240**	0.252**	-0.015	0.117	-0.142	0.131	-0.055	0.126	0.076
Physical Functioning	135	-0.158	-0.307**	-0.270**	-0.085	-0.109	0.037	-0.054	-0.056	-0.048	-0.124
Children											
Anxiety	26	0.223	-0.066	0.078	0.068	0.160	0.115	0.361	0.265	0.041	0.175
Depression	24	-0.053	-0.172	0.105	-0.298	-0.143	-0.227	0.331	0.040	0.042	-0.044
Pain interference	25	0.038	-0.169	0.067	0.051	0.048	-0.107	0.430*	0.046	-0.098	-0.002
Mobility	29	-0.060	0.001	-0.135	-0.033	-0.029	0.114	-0.490*	0.059	-0.066	-0.016
Upper extremity function	25	0.121	0.195	0.053	0.084	-0.072	-0.072	-0.356	0.082	0.178	0.046
Peer relationship	24	-0.400	-0.346	-0.345	-0.318	-0.253	-0.116	-0.517**	-0.505*	-0.213	-0.221

A positive or negative score of 0-0.3 is interpreted as low correlation, 0.3-0.5 as moderate and >0.5 as high. Correlation coefficients in bold are statistically significant (* = $p \leq 0.05$, ** = $p \leq 0.01$).

n = the number of patients who completed the questionnaire.

become darker, thicker, and more nodular over time, and arteriovenous malformations enlarge due to increased blood flow.²¹⁻²³ Patients were also more dissatisfied with their appearance when they felt they were being stared at in public. This indicates that the behaviour of others negatively affects a patient's perception of their VM.

Several studies have demonstrated that patients with VMs may have impaired mental HR-QoL.^{6,7} Our study shows that the appearance of VMs may be partly responsible for this impaired mental HR-QoL, as *anxiety* and *depression* were more likely in adults reporting appearance-related concerns (dissatisfaction with appearance, a higher appearance composite score and reduced self-esteem). This finding shows that the appearance of VMs profoundly affects HR-QoL. In children with VMs, *anxiety* and *depression* were less likely to occur alongside appearance-related concerns. A possible explanation could be that children are less self-conscious of their appearance in comparison to adults. Patients may become more aware of the appearance of the VM as they become more aware of their appearance in general and how they are perceived by others. *Peer relationships* in children were unfavourably affected by the appearance of VMs, in particular perceived bodily distortion and being stared at seemed to affect *peer relationships*. Children may encounter stigmatization and teasing because of the appearance of the VM and may feel less accepted by their peers. Discrimination and teasing early in life can impair psychological development, leading to negative self-perceptions and emotional problems that can persist through adulthood and manifest as difficulties in social situations.²⁴ This seems to be consistent with our findings, as reduced self-esteem due to the appearance of the VM seemed to negatively affect *social participation* in adults.

VMs are a benign condition with a lifelong disease course. In the management of VMs, clinical symptoms, such as bleeding, compression of vital structures and pain may be more in the foreground, and appearance aspects of the VM might, therefore, be forgotten sometimes. Additionally, it can be difficult for clinicians to foresee to what extent a condition can have an aesthetic burden on a patient. However, the impact of the appearance of the VM on HR-QoL suggests that the clinician should not overlook the aesthetic appearance of the VM and the patient's perception of their VM. In a clinical setting, appearance-related concerns should be actively assessed, and patients should be asked whether their self-image is affected, particularly in patients with the identified risk factors (i.e., malformations of capillary/combined origin, facial localization, large size and associated syndromes). Subsequently, it is important to identify the specific appearance-related concerns that may be targeted with distinct interventions. For example, laser therapy can be effective for superficial colour fading and sclerotherapy for volume decrease.^{25,26} Less conventional treatment methods purely focused on aesthetic improvement, such as cosmetic camouflage and medical tattooing, can therefore be deployed additionally.^{27,28} Our results suggest that appearance-related concerns worsen with age and that dissatisfaction with appearance in adulthood leads to more *depression* and *anxiety*. Therefore, one could suggest that a more aggressive therapeutic approach or psychological support could be attempted at a younger age in order to prevent difficulties with appearance and impaired HR-QoL

later in life. However, currently, there is no evidence available to support this hypothesis.

Lastly, clinicians may support their patients by acknowledging that appearance-related concerns exist in patients with VMs, explaining that these are also common feelings among other patients with VMs, and making patients aware of peer support groups.²⁹ Furthermore, clinicians should anticipate and monitor for signs of psychosocial impairment in their patients, possibly with HR-QoL measurement tools, and provide resources to those who might benefit from psychological intervention.

This study has several strengths and limitations. The study revealed appearance-related concerns in patients with VMs by using a validated condition-specific PROM.

The sub-analysis on clinical characteristics between responders and non-responders showed several statistically significant differences; responders more frequently had intraosseous lesions, fewer had capillary malformations, and were older of age. The older age of responders may have been caused by the lower response rate of children, as parents possibly did not want to burden their children with filling in the questionnaires. Furthermore, the study had a fairly low response rate of 32%, which might have been caused by patients who did not visit the outpatient clinic in recent years and did not feel urged to complete the questionnaires. Parents of children 0-13 years old were instructed to help their children fill in the questionnaires. Therefore, it might be that the parent's opinion unintentionally influenced the provided answers. Yet, this is unavoidable as young children may not be able to read and understand the questions independently.

Conclusion

This study showed that two-thirds of patients (66%) with VMs reported severe appearance-related concerns, and these concerns are associated with a negative impact on perceived HR-QoL. *Anxiety* and *depression* and difficulties with *social participation* and *peer relationships* occurred more often when patients had a negative perception of their appearance. The results of this study highlight the importance of paying attention to patients' perception of their aesthetic appearance. By assessing appearance-related concerns, physicians can offer interventions to potentially improve satisfaction with appearance (targeted at the specific appearance-related concern) and monitor for signs of psychosocial impairment. If necessary, they should refer patients to peer support groups or professional psychological support.

Declaration of Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding source

No funding was received for this article.

Ethical approval

Not required.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.bjps.2022.08.042](https://doi.org/10.1016/j.bjps.2022.08.042).

References

- Wassef M, Blei F, Adams D, et al. Vascular Anomalies Classification: Recommendations From the International Society for the Study of Vascular Anomalies. *Pediatrics* Jul 2015; **136**(1):e203-14. doi:[10.1542/peds.2014-3673](https://doi.org/10.1542/peds.2014-3673).
- Brouillard P, Vikkula M. Vascular malformations: localized defects in vascular morphogenesis. *Clin Genet* May 2003; **63**(5):340-51. doi:[10.1034/j.1399-0004.2003.00092.x](https://doi.org/10.1034/j.1399-0004.2003.00092.x).
- Carqueja IM, Sousa J, Mansilha A. Vascular malformations: classification, diagnosis and treatment. *Int Angiol* Apr 2018; **37**(2):127-42. doi:[10.23736/s0392-9590.18.03961-5](https://doi.org/10.23736/s0392-9590.18.03961-5).
- Horbach SER, van der Horst C, Blei F, et al. Development of an international core outcome set for peripheral vascular malformations: the OVAMA project. *Br J Dermatol* Feb 2018; **178**(2):473-81. doi:[10.1111/bjd.16029](https://doi.org/10.1111/bjd.16029).
- Stor MLE, Lokhorst MM, Horbach SER, et al. Clinical characteristics associated with pain in patients with peripheral vascular malformations. *Journal of vascular surgery* Oct 1 2021. doi:[10.1016/j.jvs.2021.08.101](https://doi.org/10.1016/j.jvs.2021.08.101).
- Nguyen HL, Bonadurer GF 3rd, Tollefson MM. Vascular Malformations and Health-Related Quality of Life: A Systematic Review and Meta-analysis. *JAMA Dermatol* Jun 1 2018; **154**(6):661-9. doi:[10.1001/jamadermatol.2018.0002](https://doi.org/10.1001/jamadermatol.2018.0002).
- Berger S, Andersen R, Dorenberg E, et al. Quality of life in patients with vascular malformations outside the central nervous system: Comparison with the general Norwegian population. *J Plast Reconstr Aesthet Surg* Dec 2019; **72**(12):1880-6. doi:[10.1016/j.bjps.2019.09.024](https://doi.org/10.1016/j.bjps.2019.09.024).
- Berscheid E, Gangestad S. The social psychological implications of facial physical attractiveness. *Clin Plast Surg* Jul 1982; **9**(3):289-96.
- Kvalem IL, von Soest T, Roald HE, Skolleborg KC. The interplay of personality and negative comments about appearance in predicting body image. *Body Image* Sep 2006; **3**(3):263-73. doi:[10.1016/j.bodyim.2006.04.002](https://doi.org/10.1016/j.bodyim.2006.04.002).
- Snyder H, Pope AW. Psychosocial adjustment in children and adolescents with a craniofacial anomaly: diagnosis-specific patterns. *Cleft Palate Craniofac J* May 2010; **47**(3):264-72. doi:[10.1597/08-227.1](https://doi.org/10.1597/08-227.1).
- Dieterich-Miller CA, Cohen BA, Liggett J. Behavioral adjustment and self-concept of young children with hemangiomas. *Pediatr Dermatol* Sep 1992; **9**(3):241-5. doi:[10.1111/j.1525-1470.1992.tb00339.x](https://doi.org/10.1111/j.1525-1470.1992.tb00339.x).
- Hagen SL, Grey KR, Korta DZ, Kelly KM. Quality of life in adults with facial port-wine stains. *J Am Acad Dermatol* Apr 2017; **76**(4):695-702. doi:[10.1016/j.jaad.2016.10.039](https://doi.org/10.1016/j.jaad.2016.10.039).
- Lokhorst MM, Horbach SER, van der Horst C, Spuls PI, Group OS. Finalizing the international core domain set for peripheral vascular malformations: the OVAMA project. *Br J Dermatol* Nov 2019; **181**(5):1076-8. doi:[10.1111/bjd.18043](https://doi.org/10.1111/bjd.18043).
- Lokhorst MM, Horbach SER, Young-Afat DA, et al. Development of a condition-specific patient-reported outcome measure for measuring symptoms and appearance in vascular malformations: the OVAMA questionnaire. *Br J Dermatol* Oct 2021; **185**(4):797-803. doi:[10.1111/bjd.20429](https://doi.org/10.1111/bjd.20429).
- von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* Dec 2014; **12**(12):1495-9. doi:[10.1016/j.ijsu.2014.07.013](https://doi.org/10.1016/j.ijsu.2014.07.013).
- Haverman L, Engelen V, van Rossum MA, Heymans HS, Grootenhuis MA. Monitoring health-related quality of life in paediatric practice: development of an innovative web-based application. *BMC Pediatr* Jan 12 2011; **11**:3. doi:[10.1186/1471-2431-11-3](https://doi.org/10.1186/1471-2431-11-3).
- Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol* Nov 2010; **63**(11):1179-94. doi:[10.1016/j.jclinepi.2010.04.011](https://doi.org/10.1016/j.jclinepi.2010.04.011).
- Lokhorst MM, Horbach SER, Waner M, et al. Responsiveness of quality-of-life measures in patients with peripheral vascular malformations: the OVAMA project. *Br J Dermatol* Jun 2020; **182**(6):1395-403. doi:[10.1111/bjd.18619](https://doi.org/10.1111/bjd.18619).
- Lokhorst MM, Horbach SER, Waner M, et al. Responsiveness of quality of life measures in children with peripheral vascular malformations: The OVAMA project. *JPRAS Open* Mar 2021; **27**:70-9. doi:[10.1016/j.jpra.2020.11.013](https://doi.org/10.1016/j.jpra.2020.11.013).
- Oduber CE, Khemlani K, Sillevs Smitt JH, Hennekam RC, van der Horst CM. Baseline Quality of Life in patients with Klippel-Trenaunay syndrome. *J Plast Reconstr Aesthet Surg* Apr 2010; **63**(4):603-9. doi:[10.1016/j.bjps.2009.01.055](https://doi.org/10.1016/j.bjps.2009.01.055).
- Lee JW, Chung HY. Capillary Malformations (Portwine Stains) of the Head and Neck: Natural History, Investigations, Laser, and Surgical Management. *Otolaryngol Clin North Am* Feb 2018; **51**(1):197-211. doi:[10.1016/j.otc.2017.09.004](https://doi.org/10.1016/j.otc.2017.09.004).
- Kohout MP, Hansen M, Pribaz JJ, Mulliken JB. Arteriovenous malformations of the head and neck: natural history and management. *Plast Reconstr Surg* Sep 1998; **102**(3):643-54. doi:[10.1097/00006534-199809030-00006](https://doi.org/10.1097/00006534-199809030-00006).
- Greene AK, Orbach DB. Management of arteriovenous malformations. *Clin Plast Surg* Jan 2011; **38**(1):95-106. doi:[10.1016/j.cps.2010.08.005](https://doi.org/10.1016/j.cps.2010.08.005).
- Weinstein JM, Chamlin SL. Quality of life in vascular anomalies. *Lymphat Res Biol* 2005; **3**(4):256-9. doi:[10.1089/lrb.2005.3.256](https://doi.org/10.1089/lrb.2005.3.256).
- Brightman LA, Geronemus RG, Reddy KK. Laser treatment of port-wine stains. *Clin Cosmet Investig Dermatol* 2015; **8**:27-33. doi:[10.2147/ccid.S53118](https://doi.org/10.2147/ccid.S53118).
- Horbach SE, Lokhorst MM, Saeed P, de Gouyon Matignon de Pontouraud CM, Rothova A, van der Horst CM. Sclerotherapy for low-flow vascular malformations of the head and neck: A systematic review of sclerosing agents. *J Plast Reconstr Aesthet Surg* Mar 2016; **69**(3):295-304. doi:[10.1016/j.bjps.2015.10.045](https://doi.org/10.1016/j.bjps.2015.10.045).
- Kornhaber R, Visentin D, Thapa DK, et al. Cosmetic camouflage improves quality of life among patients with skin disfigurement: A systematic review. *Body Image* Dec 2018; **27**:98-108. doi:[10.1016/j.bodyim.2018.08.004](https://doi.org/10.1016/j.bodyim.2018.08.004).
- van der Velden EM, de Jong BD, van der Walle HB, Stolz E, Naafs B. Cosmetic tattooing as a treatment of port-wine stains. *Int J Dermatol* May 1993; **32**(5):372-5. doi:[10.1111/j.1365-4362.1993.tb01478.x](https://doi.org/10.1111/j.1365-4362.1993.tb01478.x).
- Iliffe LL, Thompson AR. Investigating the beneficial experiences of online peer support for those affected by alopecia: an interpretative phenomenological analysis using online interviews. *Br J Dermatol* Nov 2019; **181**(5):992-8. doi:[10.1111/bjd.17998](https://doi.org/10.1111/bjd.17998).