The post-VTE functional status scale for assessment of functional limitations in patients with venous thromboembolism: construct validity and responsiveness in a prospective cohort study

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The post-VTE functional status scale for assessment of functional limitations in patients with venous thromboembolism: Construct validity and responsiveness in a prospective cohort study

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ABSTRACT

Background: A large proportion of patients experience functional limitations after an acute episode of venous thromboembolism (VTE). Recently, the post-VTE functional status (PVFS) scale was proposed to capture these limitations. We performed a prospective cohort study to validate this scale.

Methods: The PVFS scale, PROMIS physical function 10a, EQ-5D-5L, and disease-specific quality of life (VEINES-QOL/Sym, PEmb-QoL) were assessed within three weeks of VTE diagnosis and after a median (IQR) follow-up of 13.4 (12.7–15.9) weeks. To evaluate construct validity of the PVFS scale, we determined correlations of PVFS scale with the other health measurements and investigated differences in patients above/below 70 years. Responsiveness was evaluated with a linear regression model, predicting change in PROMIS with change in PVFS scale.

Results: We included 211 patients (median (IQR) age: 55.1 (44.1–67.6) years, 40 % women). Pulmonary embolism was diagnosed in 105 (49.8 %) patients and 62.6 % of events were unprovoked. The PVFS scale correlated with PROMIS physical function (Spearman's rho (r): −0.67 and −0.63, $p < 0.001$) and EQ-5D-5L index ($r = -0.61$ and −0.61, $p < 0.001$) at baseline and follow-up. Furthermore, PVFS correlated moderately to strongly with disease-specific quality of life. Patients >70 years had significantly higher PVFS grades at follow-up (median (IQR): 2 (0–3) vs. 1 (0–2), $p = 0.010$). Changes in PVFS scale over time were significantly associated with changes in PROMIS physical function.

Conclusions: The PVFS scale showed adequate construct validity and responsiveness in a prospective cohort study of patients with VTE, suggesting that it can be incorporated as additional health measurement and outcome parameter in research and clinical practice.

1. Introduction

Venous thromboembolism (VTE), encompassing pulmonary embolism (PE) and deep vein thrombosis (DVT), is a common disease with an incidence rate of about 1.43 per 1000 persons per year in Europe [1]. Following an acute episode of VTE, a substantial number of patients experiences functional limitations and impaired quality of life [2–5]. Several tools to assess generic quality of life and disease-specific quality of life have been developed for patients with DVT and PE, e.g., the VEnous INsufficiency Epidemiological and Economic Study Quality of Life/Symptom questionnaire (VEINES-QOL/Sym) and the Pulmonary Embolism Quality of Life questionnaire (PEmb-QoL). However, there has been a lack of tools to capture functional outcomes after acute VTE. Such a tool should be easy to apply in clinical practice, ideally patient reported, and able to capture the overall consequences of VTE on the functional status of patients.

Recently, an expert group proposed a new tool to measure functional limitations after VTE, the post-VTE functional status (PVFS) scale [6].

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This tool is intended to capture functional outcomes in clinical trials, cover the entire range of functional outcomes, and assess both limitations in daily activities and lifestyle changes [6]. To refine the scale, a Delphi analysis driven optimization involving 53 VTE experts from all over the world with a broad range of clinical and scientific backgrounds was performed [7]. Furthermore, three focus groups involving 18 VTE patients were conducted, highlighting the relevance and potential of the scale and feasibility of the scale manual [7]. However, clinical studies assessing the PVFS scale (i.e., an external validation), and data on its applicability in clinical routine are needed.

Therefore, we aimed to investigate the construct validity and responsiveness of the PVFS scale in patients with VTE.

2. Data and methods

2.1. Study design and procedures

This study was performed within the framework of an ongoing study entitled *A prospective observational study to investigate predictors of Bleeding and Assess long-term outComes on Health in patients with Venous ThromboEmbolism – the BACH-VTE study*. The BACH-VTE study was initiated in July 2020 and is a prospective, observational, single center cohort study conducted at the Vienna General Hospital, a tertiary care center in Austria, which offers comprehensive care for patients with VTE from diagnosis to long-term management. Patients older than 18 years of age with an acute, objectively confirmed DVT and/or PE are eligible for inclusion within 21 days after diagnosis. Diagnosis of DVT has to be confirmed by compression ultrasonography, multi-detector computed tomography, or magnetic resonance imaging venography; diagnosis of PE has to be confirmed by multi-detector computed tomography pulmonary angiography or ventilation perfusion scintigraphy. Patients who received therapeutic anticoagulant treatment within 3 months prior to VTE diagnosis are excluded from the study. The primary objective of the BACH-VTE study is to assess incidence and risk factors of bleeding. One prespecified secondary objective is to assess functional limitations in patients with acute VTE. Patients are prospectively followed throughout the duration of anticoagulant treatment up to a maximum of five years. According to the initial protocol, patients with active cancer and pregnant women were not included in the study, therefore we excluded these patients from the present analysis.

Patients in the present analysis were included between July 2020 and June 2022. At baseline, medical history, demographic data, and data on VTE diagnosis were collected in a face-to-face interview and retrieved from medical records. A follow-up visit was performed 3–6 months after diagnosis and incorporated into routine clinical care, encompassing a face-to-face interview and review of medical records. Patients who did not show up to their follow-up visit were contacted with phone calls. At baseline and at follow-up, we assessed the PVFS scale; the Patient Reported Outcome Measurement Information System (PROMIS) physical function short form 10a; the EuroQoL Group 5-Dimension 5-Level (EQ-5D-5L) questionnaire and visual analogue scale; and the VEINES-QOL/Sym and PEmb-QoL questionnaires. The details of the PVFS scale and the other questionnaires are described in the following sections. All patients included in the analysis provided written informed consent. The study was conducted according to the principles of the Declaration of Helsinki and approved by the local Ethics Committee of the Medical University of Vienna (EK 1045/2020). Study data were managed using Research Electronic Data Capture (REDCap) tools [8].

2.2. Post-VTE functional status (PVFS) scale

The PVFS scale aims to assess patient-relevant functional limitations following an episode of VTE [6,7]. It comprises 5 categories of functional limitations: 0, no functional limitations; 1, negligible functional limitations; 2, slight functional limitations; 3, moderate functional limitations; and 4, severe functional limitations [7]. A separate category (D) is reserved for patients who pass away before the scheduled assessment. The PVFS scale can either be assessed through a structured interview or self-assessed by patients. For structured interview and self-reported assessment, a published manual is available [7]. In our study, the PVFS scale was assessed with the structured interview provided in the scale manual by two investigators (DS and SN).

2.3. EQ-5D-5L questionnaire and visual analogue scale

For the assessment of generic quality of life, we chose the EQ-5D-5L questionnaire and visual analogue scale [9]. The EQ-5D-5L questionnaire encompasses five dimensions. Based on a country-specific reference value set, all dimensions are integrated in an overall index, with higher values indicating better health. Since no value set for Austria is available, we used the value set for Germany for calculating the overall index, ranging from −0.661 to 1 [10]. The visual analogue scale ranges from 0 to 100, with 100 indicating 'the best health you can imagine'. The EQ-5D-5L questionnaire and visual analogue scale refer to the day of assessment.

2.4. PROMIS physical function short form 10a

PROMIS provides short form and computerized adaptive testing options for self-reported measures of global, physical, mental, and social health [11]. One of these instruments is the PROMIS physical function short form 10a, which consists of 10 questions on a five point Likert scale. For scoring, an online tool is provided to calculate a standardized T-score and impute missing data [12,13]. The comparison cohort is a cohort from the general population with a mean T-score of 50 and a standard deviation of 10 [14].

2.5. Disease-specific quality of life

To assess disease-specific quality of life, the VEINES-QOL/Sym and the PEmb-QoL questionnaires were used in patients with DVT and PE, respectively. Both questionnaires refer to the time period of the four weeks previous to the assessment.

The VEINES-QOL/Sym is a self-administered, disease-specific questionnaire to evaluate symptoms and quality of life in patients with chronic venous disorders of the leg, which has been shown to be valid and reliable in patients with acute DVT [15,16]. Two summary scores can be computed, i.e., the VEINES-QOL summary score, which measures the overall impact on the patient's quality of life, and the VEINES symptoms score, which measures symptom severity [16]. For scoring, we used an intrinsic standard by scoring every question 1, 2, 3, …, k, where k is the number of categories and recoding each item score i to $(i\text{-}1)/(k\text{-}1)$, thus receiving score between 0 and 1 for each item which could then be averaged over all questions to provide a final score [17]. With this method, higher scores indicate better outcomes.

The PEmb-QoL is a self-administered, disease-specific questionnaire to measure quality of life after PE which was developed in 2009 and modelled after the VEINES-QOL/Sym [18]. Since then, it has been validated and used in clinical studies [19,20]. The questionnaire covers six dimensions with 40 items in 8 questions [18]. The scores for all dimensions are calculated by summing the scores for each item of the dimension and dividing the sum by the number of items. Of note, for the PEmb-QoL, higher scores indicate worse outcome [20].

2.6. Determination of validity and responsiveness

Measurement properties for health-related patient-reported outcomes include reliability, validity, responsiveness, and interpretability [21]. The three main types of validity testing are criterion validity, content validity, and construct validity. The construct validity assesses to which degree a score is consistent with a priori formulated hypotheses

[21,22]. These hypotheses include relationships to scores of other instruments and differences between relevant groups [21].

We hypothesized that there would be a strong correlation between PVFS scale and PROMIS T-score since they are intended to measure the same construct. The direction of the correlation was hypothesized to be negative because higher values indicate more functional limitations for the PVFS scale, but better physical functioning for the PROMIS T-score. For the disease-specific and generic quality of life questionnaires, we expected moderate correlations. A patient with severe functional limitations due to pre-existing morbidity might not be necessarily highly symptomatic regarding the VTE. Since symptoms make up a great proportion of disease-specific questionnaires, this patient might have a low to average score while still exhibiting severe functional limitations. This holds true for generic quality of life as well. Furthermore, we aimed to assess the differences between known groups. It has been shown that older age is associated with difficulties in physical functioning [23]. Therefore, we hypothesized that older patients (age >70 years) have more functional limitations, i.e., a higher PVFS scale grade. Determinants of the construct validity were assessed at two time points, i.e., baseline and follow-up.

Responsiveness describes the ability of an instrument to detect change over time [21]. To assess responsiveness, we assessed the PVFS scale changes over time in relation to corresponding changes in PROMIS physical function.

2.7. Statistical analysis

Categorical variables are presented as absolute numbers and proportions, continuous variables as median and interquartile range (IQR). Missing values for the PVFS scale grade, the main outcome parameter, and for the EQ-5D-5L visual analogue scale, a single value, were not imputed. For the EQ-5D-5L questionnaire and disease-specific quality of life, missing values were imputed by predictive mean matching in case of a missing rate below 20 %. Spearman correlation coefficients between the PVFS scale and PROMIS physical function, EQ-5D-5L, PEmb-QoL, and VEINES-QOL/Sym were calculated to assess the construct validity of the PVFS scale. A coefficient of (−)0.10 to (−)0.39 was considered weak, (−)0.40 to (−)0.69 moderate, (−)0.70 to (−)0.89 strong, and (−)0.90 to (−)1.00 very strong [24]. We chose this conventional approach of classifying the strength of correlation to facilitate interpretability of results. Subgroup analyses according to type of event, i.e., DVT or PE, for correlations between the PVFS scale and PROMIS physical function as well as EQ-5D-5L were conducted. The differences in the PVFS scale according to provider and between patients ≤70 years and >70 years were assessed with the Wilcoxon rank-sum test. We used a linear regression model to assess responsiveness by predicting change in PROMIS physical function with change in PVFS scale. Model 1 was unadjusted, model 2 was adjusted for age, sex, type of event, smoking status, comorbidities (arterial hypertension, cardiovascular disease, respiratory disease, hypothyroidism, history of cancer, and diabetes mellitus type 2), and baseline PROMIS physical function and PVFS scale values. We evaluated changes in PROMIS T-score for every unit decrease in PVFS scale grade and goodness of fit by means of adjusted R-squared. The level of significance was set at $p < 0.05$ beforehand. All analyses were performed using R Statistical Software (v4.2.0; R Core Team 2022).

3. Results

In total, 211 patients were recruited for this study (median (IQR) time between event and inclusion, 3 (1–7) days). Median (IQR) age at inclusion was 55.1 (44.1–67.6) years and 84 (39.8 %) patients were female. The baseline characteristics of the study cohort are shown in Table 1. Median follow-up time was 13.4 (12.7–15.9) weeks, and follow-up data was available for 164 (77.7 %) patients. Of the missing patients, 24 (11.4 %) were lost to follow-up, 1 (0.5 %) died and 22 (10.4 %) have not had their scheduled follow-up yet. Baseline values of patients with and without follow-up data are shown in Supplementary Table 1.

Table 1
Patient characteristics at baseline.

Baseline characteristics (n = 211)	
Median age, years (IQR)	55.1 (44.1–67.6)
Patients above 70 years of age, n (%)	44 (20.9)
Female, n (%)	84 (39.8)
Median body mass index, kg/m^2 (IQR)	27.9 (24.7–31.5)
Type of event, n (%)	
Deep vein thrombosis	106 (50.2)
Pulmonary embolism (with or without deep vein thrombosis)	105 (49.8)
Pulmonary embolism risk stratification[a]	
High risk, n (%)	4 (3.8)
Intermediate-high risk, n (%)	24 (22.9)
Intermediate-low risk, n (%)	36 (34.3)
Low risk, n (%)	38 (36.2)
Admitted to hospital, n (%)	79 (37.4)
Unprovoked event, n (%)	132 (62.6)
Provoked event, n (%)[b]	79 (37.4)
Major persisting risk factor	14 (6.6)
Major transient risk factor	39 (18.5)
Minor transient risk factor	47 (22.3)
History of venous thromboembolism, n (%)	56 (26.5)
Family history of venous thromboembolism, n (%)	66 (31.3)
Comorbidities, n (%)	
Arterial hypertension	81 (38.4)
Cardiovascular disease	31 (14.7)
Respiratory disease	30 (14.2)
Hypothyroidism	16 (7.6)
History of cancer[c]	11 (5.2)
Diabetes mellitus type 2	8 (3.8)
Smoking, n (%)[d]	
Current	55 (26.1)
Former	46 (21.8)
Never	104 (49.3)

[a] Pulmonary embolism risk stratification according to Konstantinides et al. [4] Risk stratification data missing in 3 patients.
[b] Categorization of provoked VTE events based on Kearon et al. [30] Some patients had more than one risk factor.
[c] No patient had active cancer at baseline. Additionally, 3 patients were diagnosed with cancer during follow-up.
[d] No data available for 6 patients.

Median (IQR) PVFS scale grade at baseline and follow-up were 2 (1–3) and 1 (0–2), respectively. The distribution of PVFS scale grades is shown in Supplementary Table 2. Detailed results for all other health measurement tools assessed are shown in Supplementary Table 3. In 3 patients (1.4 %) at baseline and in 3 (1.8 %) at follow-up, PVFS data were missing. Missing values for other health measurement tools ranged between 2.4 % and 26.7 %, with a detailed description given in Supplementary Table 4.

Assignment of PVFS scale grade to patients was similar between the two investigators who recruited and assessed patients ($p = 0.076$). SN assessed 243 patients with a median (IQR) and mean (standard deviation) PVFS scale grade of 2 (1–3) and 1.7 (1.3), respectively. DS assessed 126 patients with corresponding values of 2 (1–3) and 1.9 (1.3).

3.1. Construct validity

The PVFS scale correlated significantly with PROMIS physical function at baseline and at follow-up, with a moderate magnitude of correlation (Spearman's rank correlation rho (r) −0.67 and −0.63, respectively; $p < 0.001$ for both). PROMIS T-scores stratified by PVFS scale at baseline and follow-up are shown in Fig. 1. Similarly, the PVFS scale correlated moderately with EQ-5D-5L index ($r = -0.61$ for

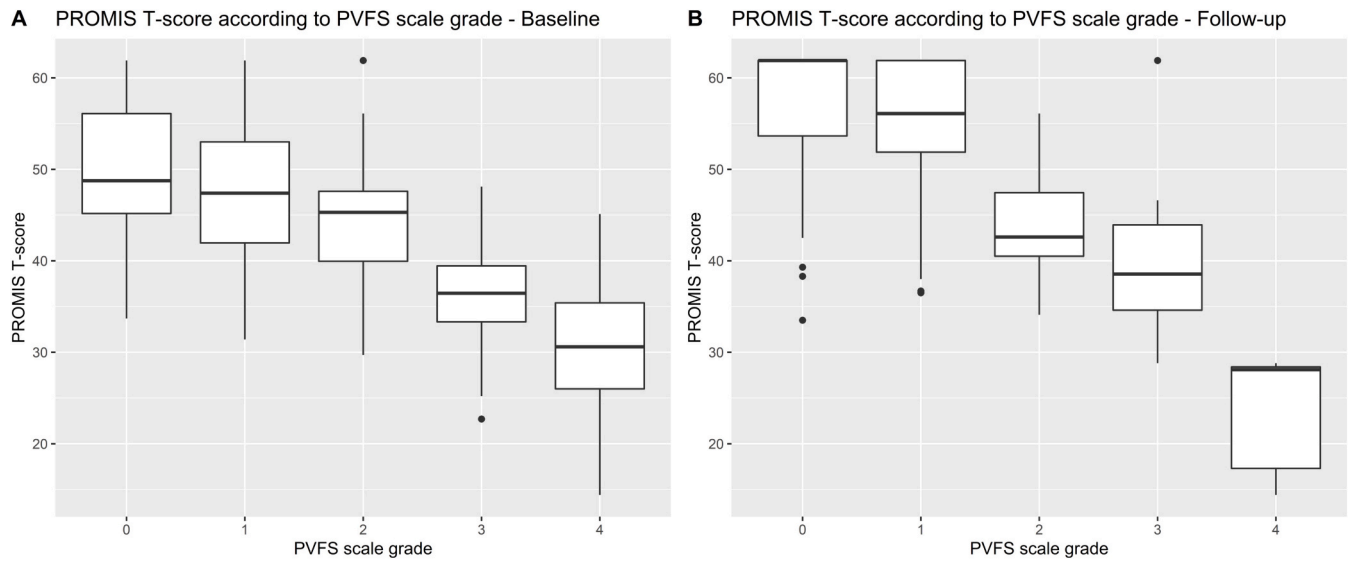

Fig. 1. PROMIS T-score according to PVFS scale grade at baseline and follow-up.
Grid A depicts baseline values, grid B follow-up values. Higher PVFS scale grades indicate more functional limitations, lower PROMIS T-scores indicate worse physical function. Bold line represents median, upper and lower hinge represent third and first quartile, respectively, and outliers (distance to hinge >1.5× interquartile range) are plotted individually. PROMIS, Patient Reported Outcome Measurement Information System; PVFS, post-VTE functional status.

baseline and −0.61 for follow-up; $p < 0.001$ for both) and EQ-5D-5L visual analogue scale ($r = -0.51$ and −0.52, respectively; $p < 0.001$ for both). When stratifying patients according to their type of event, correlation coefficients for the PVFS scale with PROMIS T-score and EQ-5D-5L index and visual analogue scale were in a similar range for both DVT and PE patients, without an obvious influence of the type of event on the strength of correlation (Supplementary Table 5).

Regarding disease-specific quality of life, the PVFS scale correlated weakly with PEmb-QoL summary score at baseline ($r = 0.32$, $p = 0.003$) and moderately at follow-up ($r = 0.53$, $p < 0.001$). Correlations with all PEmb-QoL domains are shown in Table 2. For patients with DVT, the PVFS scale correlated moderately with VEINES-QOL summary score ($r = -0.53$, $p < 0.001$) and weakly with VEINES symptoms score ($r = -0.31$, $p = 0.002$) at baseline. At follow-up, the correlations with the summary score and symptoms was moderate to strong ($r = -0.71$ and −0.69, $p < 0.001$).

At baseline, 43 patients above an age of 70 years had a median (IQR) PVFS scale grade of 3 (1.5–3), as compared to 2 (1–3) in 165 patients in the younger age group ($p = 0.067$). Corresponding values in 25 and 136 patients at follow-up were 2 (0–3) and 1 (0–2), respectively ($p = 0.010$).

Table 2
Correlations of the post-VTE functional status scale (PVFS) with domains of the Pulmonary Embolism Quality of Life questionnaire (PEmb-QoL).

	Baseline Spearman correlation coefficient r (*p*-value)	Follow-up Spearman correlation coefficient r (*p*-value)
PVFS scale – PEmb-QoL frequency domain	0.23 ($p = 0.036$)	0.50 ($p < 0.001$)
PVFS scale – PEmb-QoL ADL domain	0.45 ($p < 0.001$)	0.53 ($p < 0.001$)
PVFS scale – PEmb-QoL work domain	0.21 ($p = 0.055$)	0.45 ($p < 0.001$)
PVFS scale – PEmb-QoL social domain	0.14 ($p = 0.200$)	0.42 ($p < 0.001$)
PVFS scale – PEmb-QoL intensity domain	0.17 ($p = 0.123$)	0.60 ($p < 0.001$)
PVFS scale – PEmb-QoL emotional domain	0.14 ($p = 0.221$)	0.14 ($p = 0.284$)

PVFS, post-VTE functional status; PEmb-QoL, Pulmonary Embolism Quality of Life questionnaire.

3.2. Responsiveness

Over time, median (IQR) change in PVFS scale grade was −1 (−2–0) and median (IQR) change in PROMIS T-score was 8.1 (1.2–15.8). Change in PVFS scale grade was significantly associated with change in PROMIS T-score. For every unit decrease in PFVS scale grade, the PROMIS T-score increased by about 4.8 units in the unadjusted model, corresponding to a change of approximately half a standard deviation (95 % CI 3.7–5.9, $p < 0.001$, adjusted R-squared 0.33). This association remained significant after adjusting for age, sex, type of event, smoking status, comorbidities, and baseline PROMIS physical function and PVFS scale values (increase in PROMIS T-score for one unit decrease in PVFS scale grade: 5.3, 95 % CI 4.2–6.4, $p < 0.001$, adjusted R-squared 0.61).

4. Discussion

In this prospective cohort study, we showed that the PVFS scale correlated with PROMIS physical function and EQ-5D-5L index at baseline and follow-up. Similarly, it correlated moderately to strongly with disease-specific quality of life measurements at follow-up. Furthermore, the scale captured expected group differences between patients above and below 70 years of age. These results suggest an adequate construct validity of the PVFS scale. Additionally, the change in PVFS scale grade over time was associated with a corresponding change in PROMIS physical function in a linear regression model, indicating its responsiveness.

In this study, two investigators applied and evaluated the PVFS scale grade through a structured interview in patients at inclusion and follow-up, without relevant inter-observer differences. Since the original language of the manual is English but the interviews were conducted in German, the investigators translated the scale manual while conducting the interview. The authors of the PVFS scale argue that due the simplicity of the scale, differences in scale performance and interobserver agreement might be negligible when translated into other languages [7]. We noted only a low degree of numerical interobserver differences in mean PVFS and it is unclear whether this observed difference was due to a different translation, due to differences between providers, or due to chance alone. Further cross-cultural validation studies and interobserver assessments are needed to clarify this.

To our knowledge, the construct validity and responsiveness of the

PVFS scale have not been assessed previously. We hypothesized that the PVFS scale and PROMIS physical function would show a strong negative correlation since they are intended to measure the same construct. Although our results indicated a moderate correlation, the correlation coefficient approached the threshold for a strong correlation at baseline ($r = -0.67$). Furthermore, the cut-off points to determine the strength of a correlation are arbitrary and the specific coefficient should be interpreted in the context of the research question [24]. In analogy to the PVFS scale, the Post-COVID-19 Functional Status (PCFS) scale was proposed in 2020 for the assessment of functional outcomes in patients following COVID-19 [25]. There are no studies relating this scale to PROMIS physical function, but its association with EQ-5D-5L measurements has been evaluated. One study of 1939 subjects about 3 months after the onset of infection-related symptoms showed weak-to-strong associations between the PCFS scale and EQ-5D-5L dimensions, with the strongest for usual activities ($r = 0.661$) and the weakest for anxiety ($r = 0.233$) [26]. However, the association for the overall index and the EQ-5D-5L visual analogue scale were not investigated. In our study, the PVFS scale correlated moderately with EQ-5D-5L index and visual analogue scale, with coefficients of about −0.6 and −0.5, respectively. When stratifying between type of event, there were only minor differences between patients with DVT and PE and we did not see an obvious influence of the type of event on the strength of correlation.

For disease-specific quality of life, we expected moderate correlations of the PVFS scale with PEmb-QoL and VEINES-QoL/Sym. At baseline, the activities of daily living domain of the PEmb-QoL were moderately associated with the PVFS scale ($r = 0.45$), while all the other domains showed considerably lower coefficients (0.14 to 0.21). Notably, the recall period for PEmb-QoL is four weeks, calling into question the usefulness of administering this measurement within three weeks of VTE index date. Interestingly, we found a moderate correlation for all domains at follow-up, except for the emotional domain. In contrast, correlation of VEINES-QOL summary score with the PVFS scale was moderate at baseline and moderate to strong at follow-up. It is unclear why the strength of correlation of the PVFS scale was higher with the DVT-specific quality of life assessment than with the PE-specific quality of life assessment. Since the scale is intended to assess VTE patients in general, these differences need to be evaluated thoroughly. Importantly, the disease-specific questionnaires had substantially higher rates of missing values compared to PROMIS physical function, generic quality of life, and PVFS scale.

In our study, patients above 70 years of age had numerically higher PVFS scale grades, with more pronounced differences at follow-up. The less pronounced difference at baseline might be due to the fact that younger patients are also affected severely at the time of the initial event but recover better and faster, unmasking the difference at follow-up. As it has been shown that higher age is associated with impairment in physical functioning [23,27], these results indicate that the PVFS scale is able to capture known differences and further add to its construct validity. However, the number of patients in the higher age group was relatively small and therefore the results need to be interpreted with caution until confirmed independently.

To assess the responsiveness of the PVFS scale, we used a linear regression model [28]. Changes in the PVFS scale were associated with changes in PROMIS physical function. These results suggest that the PVFS scale is responsive. We chose to use the PROMIS physical function short form as an external criterion in assessing responsiveness due to the lack of a gold standard in assessing functional limitations after VTE. Further studies might relate the change in PVFS scale to other measurement tools. Notably, a considerable proportion of patients were lost to follow-up. The unadjusted model showed poor goodness of fit, whereas the multivariable model had a considerably higher adjusted R-squared. This is most probably due to the fact that the second model incorporated baseline PROMIS physical function and PVFS values, and patients with lower and higher baseline values, respectively, are more likely to have a larger change in follow-up. The remaining unexplained variance might be due to other factors which have not been considered to influence the change in PROMIS physical function.

We believe that our study has clinical implications. As already outlined, more research is definitely necessary to evaluate all aspects of the PVFS scale and confirm the observations of this study, notably also for self-reported functional limitations when the scale is used as a patient-reported outcome measure. Nevertheless, this study confirms the potential usefulness of the scale and supports its application in research and clinical practice. Also, this study provides ground for the decision of an international working group of experts and VTE patients to select the PVFS scale as one of the core instruments of the international standard set of outcome measures for VTE patients [29].

However, our study has also several limitations. Firstly, the study is prone to selection bias due to the observational, single center design and the conduction at a tertiary care center. Additionally, patients with active cancer, pregnant women, and patients on therapeutic anticoagulation at diagnosis were not included. Therefore, our results are not generalizable to these subgroups and further studies in other settings and specific patient populations are needed. Furthermore, the sample size is relatively small, especially for subgroup analyses, e.g., patients above 70 years of age, and further attenuated by missing values. A strength of our study is the assessment at two different time points, allowing us to evaluate changes in the PVFS scale over time.

5. Conclusions

In a prospective cohort study of patients with VTE, we demonstrated that the PVFS scale is an instrument with adequate construct validity by means of relationships to other health outcome measures and scale grade differences between age groups which could be easily applied in clinical routine. Furthermore, it showed adequate responsiveness, i.e., the ability to capture changes over time. Our results support that the PVFS scale can be incorporated as additional health measurement and outcome parameter in research and clinical practice.

CRediT authorship contribution statement

DS participated in data curation, formal analysis, methodology, visualization, and writing - original draft. SN participated in conceptualization, data curation, formal analysis, and supervision. BW and OS participated in data curation. OK participated in conceptualization and supervision. FAK participated in resources. IP participated in data curation, conceptualization, and supervision. CA participated in data curation, conceptualization, project administration, and supervision. All authors participated in writing - review and editing.

Role of the funding source

The current work was not funded.

Ethics committee approval

The study was approved by the local Ethics Committee of the Medical University of Vienna (EK 1045/2020).

Data sharing statement

Data cannot be shared because Austrian law forbids the sharing of primary patient data.

Declaration of competing interest

DS, SN, and BW have no potential conflicts of interest do declare. OS received personal fees from Abbott, BARD/BD, Bayer, Biotronik, and Optimed, outside the submitted work. OK received personal fees for lectures and/or participation in advisory boards from BMS. FAK

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.thromres.2022.11.006.

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