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Depression and anxiety up to two years after acute pulmonary embolism: Prevalence and predictors

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1. Introduction

Pulmonary embolism (PE) is an acute life-threatening event and the most common cardiovascular disease following myocardial infarction and stroke [1]. Patients after PE can suffer from long-term symptoms such as persistent dyspnoea and reduced physical performance or even more severe consequences such as right heart failure and chronic thromboembolic pulmonary hypertension [2]. However, the long-term consequences of PE can go beyond the physical symptoms. Several qualitative studies based on interviews with patients have examined their emotional experience after PE [3–9]. Patients described receiving the diagnosis as traumatic [3] and a feeling of their life being forever changed [9]. Many suffered from being more sensitive and hypervigilant, rumination, sleep disturbance, loss of energy, and feelings such as frustration, uncertainty, stress, anger, and panic. Overall, symptoms of anxiety and depression were commonly reported after venous thromboembolism (VTE) including PE [4–8]. Several experiences may contribute to the development of those psychological symptoms.

Abbreviations: BMI, body mass index; CRQ, Chronic Respiratory Disease Questionnaire; HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; LEA, Lungenembolie Augsburg study; LRT, likelihood ratio test; sPESI, simplified pulmonary embolism severity index; PE, pulmonary embolism; PEmb-QoL, Pulmonary Embolism Quality of Life; VTE, venous thromboembolism.

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Patients often experience dyspnoea, pain, and fear of death during the acute event. In the long-term, patients reported worries about an unknown cause of their PE and a recurrent PE event [3,4,6]. Anticoagulant medication was considered as lifesaving and useful to prevent further events on the one hand. On the other hand, patients were afraid of the bleeding risk, reported fears of missing the regular medication intake [6,8] and stopping anticoagulant therapy after at least three months recommended by medical guidelines [1,3,5].

So far, it has not been comprehensively investigated how many patients suffer from symptoms of anxiety and depression after PE and how long the symptoms persist. Etchegary et al. indicated that psychosocial issues are most important within the first six months after VTE [7]. Other studies suggested that mental problems after VTE may persist over time [10,11]. Also, due to the lack of quantitative data analyses little is known about predictors of anxiety and depression after PE. Liu et al. found in patients one week after PE that depression and anxiety scores were related to PE risk stratification, age and arterial blood oxygen pressure at admission [12]. Feehan et al. reported associations of emotional harms with previous venous thromboembolism events and multimorbidity [13]. Overall, Tzeng et al. found a 1.5-fold and a 1.7-fold increased risk for developing depression or anxiety, respectively, during the first year after PE [14]. Depression and anxiety were associated with below average physical and mental quality of life in patients with VTE [15] and may affect the recovery process after PE. Therefore, it seems important to enhance investigations on the mental consequences after an acute PE. The notable results of previous studies about emotional response of patients with PE using qualitative approaches are in need to be supported by quantitative analyses. Thus, the aim of this study is to examine prevalence, long-term course and predictors of anxiety and depression after PE.

2. Methods

2.1. Sample and data collection

The sample was comprised of participants of the 'Lungenembolie Augsburg' (LEA) study. The LEA study is a long-term observational cohort study including patients 18 years and older with PE who were treated at the University Hospital Augsburg. All patients with incident or recurrent confirmed PE diagnosis based on multidetector CT pulmonary angiography or ventilation–perfusion lung scanning were included. Between July 2017 and April 2022, a total of 729 patients were recruited for the study. Detailed information about the study design can be obtained from the published study protocol [16]. Clinical baseline characteristics were extracted from medical records. Further demographic information was collected through interviews conducted by study nurses during the hospital stay. After discharge, the participants received postal questionnaires after 3, 6, 12, and 24 months including the Hospital Anxiety and Depression Scale (HADS), Pulmonary Embolism Quality of Life (PEmb-QoL) questionnaire and Chronic Respiratory Disease Questionnaire (CRQ). For the present analyses, we selected participants who completed the HADS questionnaire at three months after PE and used their baseline and follow-up data.

2.2. Hospital Anxiety and Depression Scale

The HADS is a self-administered questionnaire designed to identify symptoms of depression and anxiety. It consists of two scales with seven items on depression and seven items on anxiety. Questions about symptoms during the previous week are answered on a four-point response scale ranging from "not at all" to "most of the time". The sum scores of the two scales can be divided into four categories: 0–7 for no depression or anxiety, 8–10 for mild depression or anxiety, 11–14 for moderate depression or anxiety and 15–21 for severe depression or anxiety. As a binary cut-off threshold, 8 points has been shown as appropriate in several studies [17]. In this study the validated German version HADS-D was used [18]. If participants had missing items in the HADS questionnaire, no score was calculated.

2.3. PEmb-QoL questionnaire

The PEmb-QoL questionnaire is a PE-specific quality of life questionnaire that includes 38 items in six dimensions. All items are answered on two-point to six-point Likert response scales regarding the PE-related experiences during the past 4 weeks. Dimension scores were calculated by taking the mean of all items and transformed into a scale from 0 to 100. Higher scores indicate worse quality of life [19]. For the present study we only used the dimension PE-related limitations in activities of daily living (ADL).

2.4. CRQ

The CRQ comprises 20 items across four domains rated on a 7-point Likert response scale. Higher scores indicate less impairment due to respiratory disease [20]. In the present study, only the dyspnoea dimension of the self-administration version was applied.

2.5. Clinical data

Clinical data at hospital admission, e.g. symptoms of dyspnoea, oxygen saturation, body mass index (BMI), uni- or bivariate localisation of PE, number of previous PE events, history of cancer and the length of hospital stay were used to describe the PE-related health status at baseline. Additionally, we calculated the simplified pulmonary embolism severity index (sPESI) that uses six clinical variables namely age, history of cancer, chronic cardiopulmonary disease, heart rate, systolic blood pressure and arterial oxygen saturation to classify patients into high ($\geq$1) or low (0) PE-related risk of death [21].

2.6. Statistical analyses

Sociodemographic and clinical characteristics were summarized as medians with interquartile range (IQR) or numbers with percentages stratified by depression and anxiety scores three months after PE. Mann-Whitney-*U* Test and Chi^2-test or Fisher's Exact test were conducted to compare baseline characteristics of patients with high or low depression and anxiety levels. Sensitivity analyses of baseline variables were conducted for excluded patients that did not complete the follow up HADS questionnaire. For investigating associations of sociodemographic and clinical baseline variables with depression and anxiety levels after PE we fitted mixed models with random intercepts to account for repeated measurements within the two-year time period. Restricted Maximum Likelihood (REML) was used as estimation method and time-varying effects were explored by including interaction terms. Additionally, we built multiple linear regression models for each of the four follow-up time points 3, 6, 12, and 24 months. Inclusion of variables in the models was based on a theoretical selection process by depicting possible associations in a directed acyclic graph using the free web application DAGitty version 3.0 [22]. Since there are not many quantitative data regarding this topic, the analyses had an exploratory character. We based our variable selection on the results of the few existing studies and on studies investigating mental health problems after other cardiovascular diseases such as stroke and myocardial infarction. Assumptions were checked using residual plots for normal distribution and homoscedasticity, polynomial terms and scatterplots for linearity, Cooks Distance for outliers, Durbin-Watson-test for independence of the residuals and variance inflation factor for multicollinearity. Models were compared based on Akaike Information Criterion, Bayesian Information Criterion and likelihood ratio test (LRT) using maximum likelihood estimation. For all analyses, an alpha level of 0.05 was defined. Analyses were conducted using R version 4.2.1 [23].

3. Results

We used data of 297 participants who completed either HADS depression or HADS anxiety questionnaire or both of them three months after PE. Patients who did not return any follow-up questionnaire or did not complete the HADS questionnaire at the three-months follow-up were excluded from the current analyses (n = 432). The response rate based on all recruited patients at baseline was 41 %. The sample consisted of 294 patients with depression scores and 292 patients with anxiety scores. Socio-demographic and clinical baseline variables stratified by HADS depression and anxiety score three months post PE are shown in Table 1. Overall, median age was 64 years (IQR: 55–74) with 55.6 % male patients. Nine percent of patients had a recurrent PE and 10.8 % had a history of depression. Fifty-three percent were in the high risk (≥1) group for PE-related death stratified by sPESI (Supplementary material: Table S1).

Sensitivity analyses of baseline characteristic of excluded patients revealed that they were significantly older. A higher proportion suffered from high-risk PE and low oxygen saturation (<90 %) at admission and they had a longer average length of hospital stay, but less bilateral PE. More of the excluded patients had a history of cancer or depression. Furthermore, less of the excluded patients were married or lived with their partner and less had a school education > 9 years. Excluded patients had higher baseline HADS depression and anxiety scores (Supplementary material: Table S2).

In the bivariate analyses age (p = 0.012), sPESI (p = 0.026), school education (p = 0.030), history of depression (p < 0.001), oxygen saturation < 90 % at admission (p = 0.006) and the length of hospital stay (p = 0.012) showed significant differences between the two groups of high or low depression score three months after PE. Regarding high and low anxiety scores, only the length of hospital stays (p = 0.031) showed a significant difference (Table 1).

Table 2 presents HADS medians with IQR and the absolute and relative frequencies of the HADS severity categories for all time points from baseline to two years after PE.

Mixed models with random intercepts were built to account for within subject correlation due to repeated measurements. According to the mixed model, HADS depression score was independently associated with age, previous depression diagnosis and sPESI (Table 3). In a further step, we investigated time-varying effects by adding time interaction terms for each variable (LRT: p = 0.003). The risk stratification variable sPESI showed a decreasing association with depression over the two-year time period (Supplementary material: Fig. S1). For age and previous depression, the effect remained constantly positive over time. Furthermore, being married and higher education level were inversely related to the HADS depression score over time. These two effects became significantly stronger over the two-year time period. For HADS anxiety we only found an association with the presence of dyspnoea at

Table 2
Distributions of HADS scores at baseline and 3, 6, 12, and 24 months after PE.

	Time after PE				
	Baseline	3 months	6 months	12 months	24 months
HADS Depression score	n = 218[a]	n = 294	n = 239	n = 179	n = 92
Min-max	0–21	0–19	0–17	0–17	0–20
Median (IQR)	4 (2–7)	3 (1–7)	3 (1–6)	3 (1–6)	3 (1–6)
No depression	166 (76.15 %)	226 (76.87 %)	194 (81.17 %)	147 (82.12 %)	74 (80.43 %)
Mild depression	24 (11.01 %)	32 (10.88 %)	23 (9.62 %)	15 (8.38 %)	13 (14.13 %)
Moderate depression	18 (8.26 %)	29 (9.86 %)	15 (6.28 %)	10 (5.59 %)	3 (3.26 %)
Severe depression	10 (4.59 %)	7 (2.38 %)	7 (2.93 %)	7 (3.91 %)	2 (2.17 %)
HADS Anxiety score	n = 213[a]	n = 292	n = 239	n = 183	n = 92
Min-max	0–20	0–16	0–19	0–16	0–16
Median (IQR)	5 (2–8)	4 (1–7)	3 (1–7)	3 (1–6)	4 (1–7)
No anxiety	151 (70.89 %)	229 (78.42 %)	191 (79.92 %)	150 (81.97 %)	70 (76.09 %)
Mild anxiety	40 (18.78 %)	39 (13.36 %)	31 (12.97 %)	16 (8.74 %)	14 (15.22 %)
Moderate anxiety	20 (9.39 %)	22 (7.53 %)	13 (5.44 %)	14 (7.65 %)	6 (6.52 %)
Severe anxiety	2 (0.94 %)	2 (0.68 %)	4 (1.67 %)	3 (1.64 %)	2 (2.17 %)

[a] Available data based on selected patients that completed the HADS questionnaire at the 3 months follow-up.

Table 1
Socio-demographic and clinical variables stratified for depression and anxiety 3 months post PE.

Variable	N	No depression N = 226	Depression[a] N = 68	p-value[b]	N	No anxiety N = 229	Anxiety[b] N = 63	p-value[c]
Median (Q_{25}, Q_{75})								
Age	294	64.0 (53.0, 71.8)	67.0 (57.0, 78.0)	**0.012**	292	64.0 (54.0, 72.0)	64.0 (55.0, 75.5)	0.352
BMI (kg/m^2)	292	28.1 (24.9, 31.8)	27.7 (24.9, 31.5)	0.772	291	27.8 (24.6, 31.8)	28.3 (25.1, 32.9)	0.285
Length of hospital stay	292	8.5 (6.0, 13.0)	9.0 (7.0, 17.0)	**0.012**	290	9.0 (6.0, 13.0)	9.0 (7.0, 17.5)	**0.031**
n (%)								
Sex (male)	294	125.0 (55.3)	40.0 (58.8)	0.609	292	129.0 (56.3)	35.0 (55.6)	0.912
History of PE	292	22.0 (9.8)	5.0 (7.4)	0.538	290	22.0 (9.7)	3.0 (4.8)	0.217
PE localisation (bilateral)	285	163.0 (74.8)	54.0 (80.6)	0.328	283	164.0 (74.2)	51.0 (82.3)	0.190
sPESI[d] (≥1)	263	98.0 (49.0)	41.0 (65.1)	**0.026**	261	103.0 (51.0)	34.0 (57.6)	0.369
Cancer	291	35.0 (15.7)	13.0 (19.1)	0.506	289	36.0 (15.9)	13.0 (20.6)	0.379
School education (>9 years)	282	132.0 (60.6)	29.0 (45.3)	**0.030**	281	133.0 (59.4)	28.0 (49.1)	0.162
History of depression	283	16.0 (7.4)	15.0 (22.4)	**<0.001**	281	19.0 (8.7)	10.0 (16.1)	0.089
Living with partner	286	151.0 (68.0)	42.0 (65.6)	0.719	285	155.0 (68.9)	38.0 (63.3)	0.413
Married	288	143.0 (64.1)	42.0 (64.6)	0.942	287	148.0 (65.2)	37.0 (61.7)	0.611
Dyspnoea (admission)	279	166.0 (76.9)	51.0 (81.0)	0.491	278	163.0 (75.1)	52.0 (85.2)	0.095
Oxygen saturation < 90 % (admission)	274	33.0 (15.7)	20.0 (31.2)	**0.006**	272	35.0 (16.5)	14.0 (23.3)	0.225

Bold font indicates statistical significance with alpha = 0.05.

[a] HADS Depression score ≥ 8.

[b] HADS Anxiety score ≥ 8.

[c] Mann-Whitney-*U* test, Pearson's Chi-squared test, or Fisher's exact test as appropriate.

[d] Simplified Pulmonary Embolism Severity Index that uses six clinical variables (age, history of cancer, chronic cardiopulmonary disease, heart rate, systolic blood pressure and arterial oxygen saturation) to classify patients into high (≥1) or low PE-related risk of death [21].

Table 3
Linear mixed models with random intercepts with HADS depression score as outcome variable.

	Model 1	Model 2	Model 3
(Intercept)	−0.34	−0.42	**7.13*****
	[−4.11; 3.44][e]	[−4.38; 3.53]	**[3.46; 10.79]**
Age	**0.05****	**0.04***	0.01
	[0.01; 0.09]	**[0.00; 0.08]**	[−0.02; 0.04]
Sex (male)	0.33	0.56	0.67
	[−0.69; 1.35]	[−0.51; 1.62]	[−0.15; 1.49]
BMI (kg/m^2)	0.04	0.04	−0.06
	[−0.03; 0.12]	[−0.05; 0.12]	[−0.12; 0.01]
History of PE	0.58	0.46	0.21
	[−1.03; 2.20]	[−1.22; 2.15]	[−1.07; 1.49]
History of depression	**2.12***	**2.07***	0.60
	[0.44; 3.80]	**[0.32; 3.82]**	[−0.77; 1.97]
School education (>9 years)	−0.94	−0.62	−0.65
	[−1.98; 0.10]	[−1.70; 0.47]	[−1.50; 0.20]
sPESI[a]	**0.64***	**0.82***	**0.51***
	[0.04; 1.23]	**[0.20; 1.44]**	**[0.01; 1.01]**
Length of hospital stay	0.02	0.01	−0.02
	[−0.04; 0.07]	[−0.05; 0.07]	[−0.06; 0.03]
PE localisation (bilateral)	0.30	0.50	0.57
	[−0.91; 1.51]	[−0.76; 1.77]	[−0.41; 1.56]
Dyspnoea (admission)	0.66	0.73	−0.48
	[−0.56; 1.88]	[−0.54; 2.00]	[−1.47; 0.50]
Married	−0.73	−0.30	−0.10
	[−1.76; 0.30]	[−1.38; 0.77]	[−0.94; 0.74]
Follow-up time[b]	**−0.03***	−0.02	0.00
	[−0.05; −0.01]	[−0.21; 0.16]	[−0.02; 0.03]
PEmb-QoL (ADL limitations)[c]			**0.06*****
			[0.04; 0.07]
CRQ dysnpoea[d]			**−0.66*****
			[−0.94; −0.38]
Age × time		0.00	
		[−0.00; 0.00]	
Sex × time		−0.04	
		[−0.09; 0.02]	
BMI × time		0.00	
		[−0.00; 0.00]	
History of LE × time		0.01	
		[−0.07; 0.10]	
History of depression × time		0.03	
		[−0.06; 0.12]	
School education (>9 years) × time		**−0.06***	
		[−0.11; −0.01]	
sPESI × time		**−0.03***	
		[−0.06; −0.00]	
Length of hospital stay × time		0.00	
		[−0.00; 0.00]	
PE localisation (bilateral) × time		−0.04	
		[−0.10; 0.02]	
Dyspnoea (admission) × time		−0.01	
		[−0.07; 0.05]	
Married × time		**−0.07****	
		[−0.12; −0.02]	
N (observations)	806	806	571
N (subjects)	232	232	222

Bold font indicates statistical significance with alpha = 0.05.
Italics represent the interaction terms.
*** $p < 0.001$.
** $p < 0.01$.
* $p < 0.05$.
[a] Simplified Pulmonary Embolism Severity Index.
[b] Follow-up time consists of the five time points: 0, 3, 6, 12 and 24 months after PE.
[c] Higher scores of PEmb-Qol indicate worse disease-specific quality of life in the limitations in ADL dimension.
[d] Higher scores in CRQ dyspnoea dimension indicate less impairment.
[e] Estimates with 95 % confidence intervals.

time of hospital admission and an inverse association with time since PE (Table 4). History of depression showed a positive trend towards higher levels of anxiety after PE, but failed to reach statistical significance. For anxiety, no significant interactions of baseline variables with time were found. Multiple linear regression models for each follow up time point supported the results and showed i.e. significant associations for sPESI and depression scores at 3 and 6 months, but not at 12 and 24 months. Similarly, only dyspnoea at admission showed a significant association with anxiety score 12 months after PE (Supplementary material: Table S3 and Table S4).

Further models were built by adding the PEmb-Qol scale about PE-related limitations in ADL and the CRQ dyspnoea scale as independent

Table 4
Linear mixed models with random intercepts with HADS anxiety score as outcome variable.

	Model 1	Model 2
(Intercept)	**4.68***	**13.13*****
	[1.14; 8.22][e]	**[9.45; 16.80]**
Age	0.00	**−0.04***
	[−0.03; 0.04]	**[−0.07; −0.01]**
Sex (male)	−0.10	0.19
	[−1.05; 0.85]	[−0.62; 1.00]
BMI (kg/m^2)	−0.03	**−0.12*****
	[−0.10; 0.04]	**[−0.18; −0.05]**
History of PE	−0.88	−1.01
	[−2.41; 0.65]	[−2.29; 0.27]
History of depression	1.49	−0.10
	[−0.09; 3.07]	[−1.45; 1.24]
School education (>9 years)	−0.61	−0.30
	[−1.58; 0.35]	[−1.14; 0.53]
sPESI[a]	0.21	0.25
	[−0.36; 0.77]	[−0.25; 0.75]
Length of hospital stay	0.03	−0.01
	[−0.02; 0.08]	[−0.05; 0.04]
PE localisation (bilateral)	0.28	0.36
	[−0.84; 1.41]	[−0.61; 1.33]
Dyspnoea (admission)	**1.21***	0.04
	[0.09; 2.32]	[−0.92; 1.00]
Married	−0.51	−0.00
	[−1.47; 0.45]	[−0.83; 0.83]
Follow-up time[b]	**−0.04*****	−0.01
	[−0.07; −0.02]	[−0.04; 0.02]
PEmb-QoL (ADL limitations)[c]		**0.04*****
		[0.03; 0.06]
CRQ dysnpoea[d]		**−0.81*****
		[−1.09; −0.52]
N (observations)	808	575
N (subjects)	231	222

Bold font indicates statistical significance with alpha = 0.05.
*** $p < 0.001$.
* $p < 0.05$.
[a] Simplified Pulmonary Embolism Severity Index.
[b] Follow-up time consists of the five time points: 0, 3, 6, 12 and 24 months after PE.
[c] Higher scores of PEmb-Qol indicate worse disease-specific quality of life in the limitations in ADL dimension.
[d] Higher scores in CRQ dyspnoea dimension indicate less impairment.
[e] Estimates with 95 % confidence intervals.

variables. The results showed statistically significant associations of limitations in ADL (0.06; 95 % CI: [0.04; 0.07]; $p < 0.001$) and CRQ dyspnoea (−0.66; 95 % CI: [0.94; −0.38]; $p < 0.001$) with HADS depression score. For HADS Anxiety score we also found significant associations with limitations in ADL (0.04; 95 % CI: [0.03; 0.06]; $p < 0.001$) and CRQ dyspnoea (−0.81; 95 % CI: [−1.09; −0.52]; $p < 0.001$). Additionally, age and BMI showed a significantly inverse relation with anxiety in this model.

4. Discussion

Our findings highlight the presence of mental problems after PE. In our sample, 23.1 % showed depressive and 21.6 % anxiety symptoms according to the HADS three months after PE. Two years after PE 19 % and 24 % of the remaining participants in our study still showed mild to severe HADS depression and anxiety scores, respectively. Our results are comparable to Feehan et al. who reported 24.7 % of patients with high HADS anxiety scores in VTE patients, but they also reported only 11.5 % with high depression scores after the acute event [13]. Other studies reported about 35 % [24] to about 50 % [25] of patients that reported depressive or anxiety symptoms three months post PE. Since according to our sensitivity analyses older and more severely affected patients tended to drop out of our study, the prevalence of depressiveness and anxiety might be even higher in reality.

Psychological disorders are also known to occur after other cardiovascular events such as myocardial infarction and stroke. Studies about post-stroke-depression revealed predictors such as disease severity, level of disability, history of depression, social support, female sex, marital status, length of hospital stay, socioeconomic status, comorbidity, smoking, diabetes and level of education [26–29]. For cardiac events similar and also additional predictors including financial strain, obesity, younger age and poor self-rated health were found [30,31]. We used these findings to investigate predictors for emotional harm after PE.

Our analyses revealed associations of age, history of depression and risk stratification (sPESI) with HADS depression score. Since time interaction showed that the association of sPESI decreases over the two-year time period, risk stratification may play a role in evaluating possible short-term mental consequences only. However, a long-term deterioration of mental health after PE may occur regardless of acute risk stratification, as it was already stated by Valerio et al. [24]. Our results are partly in line with Liu et al. who also showed significant associations between PE risk stratification and occurrence of depressiveness after the acute event [12]. Age was inversely associated in their study and also in the study by Feehan et al. [11] indicating younger age was related with increased emotional harm. In contrast, our study revealed higher age to be associated with higher level of depression scores, but with lower level of anxiety scores. According to Liu et al. younger patients may worry more about their health status and coping strategies [12].

Patients experience PE as a life-threating event and therefore report anxiety and even fear of death in the acute phase [6]. However, considering our results, clinical baseline variables were not associated with anxiety scores in the long-term except for dyspnoea. Our finding that dyspnoea at hospital admission was related to HADS anxiety score afterwards is comparable to the result of Liu et al. who found that arterial blood oxygen pressure in the acute phase was related to depression and anxiety after PE [12]. Like in our anxiety models, Feehan et al. also found that time since VTE was negatively related to emotional harm [13]. VTE recurrence, female sex and length of hospital stay were associated with emotional distress after PE in other studies, but could not be confirmed in our longitudinal analyses [13,32]. The duration of hospital stay was only significantly associated with HADS anxiety score in our bivariate analyses for the three months follow-up.

Of interest, Højen et al. stated that perceived health threat seemed actually more important than VTE severity for long-term mental well-being [11]. In general, according to our analyses, not many baseline variables were associated with depression and anxiety scores in the long-term and the significant estimates showed wide confidence intervals indicating a high amount of uncertainty. We assume that the course of the disease including persistent symptoms may contribute to the development of subsequent mental problems. Our models including the additional variables dyspnoea and limitations in ADL that were measured in the follow-up questionnaires, confirmed this hypothesis by showing independent significant associations with both, HADS depression and anxiety scores. These results are supported by Bennett et al. who also reported associations of continuing symptoms and health-related anxiety [10]. Hunter et al. described a cycle of post-thrombotic panic in which fear leads to hypervigilance towards physical symptoms like breathlessness or pain, which in turn trigger emotional distress [33]. However, more variables that were not investigated in our study may influence the development of depression and anxiety after PE. For instance, health literacy, care access barriers and history of medical errors has been reported as correlates of emotional harm after VTE by Feehan et al. [13].

As demonstrated by the present study, long-term mental consequences are not solely predictable by risk stratification and screenings in the acute phase. Consequently, careful long-term monitoring of patients with PE for psychiatric conditions is crucial. The finding that few patients with PE currently seek support for mental health problems [3], stresses the need to implement such strategies of post-acute care.

Keddington et al. have already developed a short tool for the screening of patients for VTE-related emotional distress [34]. Such disease-specific instruments can be useful to conduct a quick screening in clinical settings and should be further investigated in the future.

Notably, patients have reported that emotional distress as a consequence of PE was not mentioned by their attending physician and this kept the patients from addressing this issue [3]. Hence, medical education and access to comprehensive health information about acute PE and its short and long-term consequences might facilitate the prevention of and coping with emotional distress after PE. Currently, even the guidelines of the European Society of Cardiology for diagnosis and management of acute PE [1] do not include recommendations regarding mental health problems among patients with PE. It would be an important objective to address this topic in the future.

The strength of our study is that it comprises data from patients over a two-year time period after PE. In addition, this study included merely patients with PE, instead of VTE in general, e.g. PE and deep vein thrombosis. However, our study has several limitations. The sample is relatively small for longitudinal analyses with various time points and comprises a cohort from a single university hospital in southern Germany. No causal effects can be derived from our results. Since some studies revealed associations of psychiatric disorders with VTE risk [35], reversed causality cannot be excluded. In longitudinal surveys, it has to be considered that patients with severe disease and already existing psychiatric disorders tend to drop out of the study. Since participants who were lost to follow-up were more severely ill according to our sensitivity analysis, we cannot exclude a drop-out bias in our study resulting in an underestimation of mental health problems. A possible bias due to a higher response rate of patients with more severe mental problems seems unlikely since 30 % to 35 % of those who initially had high HADS depression or anxiety scores at 3 months completed the 2-year follow-up. It should be mentioned that the HADS is a screening tool and does not replace a clinical diagnosis of a depression or anxiety disorder. We also did not consider antidepressant medication intake in the present analysis. Results can be seen as supportive information and should be confirmed in other samples.

5. Conclusions

The present long-term study analysed quantitative data on emotional consequences of PE in a time period of two years after the acute event. Overall, our results support the observations from qualitative studies and provide evidence that depressiveness and anxiety occur in about one-in-five patients with PE. Besides age and history of depression, a high-risk PE and dyspnoea at hospital admission seem to be indicators for developing symptoms of depression and anxiety after PE. Baseline characteristics are only related to emotional harm to a limited extent whereas persisting symptoms and limitations in the ongoing course seem to play a major role. Our results underline the importance of screening for depressive and anxiety symptoms among patients with PE. Early detection and appropriate interventions may reduce emotional harm. Moreover, possible negative influence on health care use and recovery after PE may be improved. Therefore, more research including longitudinal data is necessary to confirm our results, to identify further predictors and to investigate possible intervention strategies.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics approval

The study protocol was approved by the Ethics Committee of the Ludwig-Maximilians-Universität München (Date of approval: 1 August 2017. Reference number: 17–378). The study is performed according to the Declaration of Helsinki.

Consent to participate

Written informed consent is obtained from each study participant.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.thromres.2022.12.013.

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