Adjustments in the diagnostic work-up, treatment and prognosis of pulmonary embolism
van Es, Josien

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Quality of life after pulmonary embolism as assessed with SF-36 and PEmb-QoL

J. van Es*
P.L. den Exter*
A.A. Kaptein
P.G.M. Erkens
F.A. Klok
R.A. Douma
I.C.M. Mos
D.M. Cohn
P.W. Kamphuisen
M.V. Huisman
S. Middeldorp

*Contributed equally

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ABSTRACT

Introduction: Although quality of life (QoL) is increasingly recognized as an important indicator of the course of a disease, it has rarely been addressed in studies evaluating the outcome of patients with pulmonary embolism (PE). The main objective of this study was to evaluate QoL in the long-term clinical course of patients with acute PE, using the Short Form-36 (SF-36) and the Pulmonary Embolism Quality of Life (PEmb-QoL) questionnaires, in comparison to general population norms, and to patients with other cardiopulmonary diseases.

Methods: SF-36 and PEmb-QoL were distributed among 150 consecutive out-patients with a history of objectively confirmed acute PE. SF-36 scores were compared to those of patients with chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), a history of acute myocardial infarction (AMI) the previous year and a reference group of healthy Dutch individuals. PEmb-QoL, SF-36, and correlations between the PEmb-QoL and clinical patient characteristics were examined.

Results: A total of 109 patients with PE, of whom 9 had recurrent PE, completed the questionnaires, after a median of 25 months, range 5-46 months from time of diagnosis. QoL as assessed with SF-36 was superior in patients with PE compared to patients with COPD and CHF, comparable with patients with AMI the previous year, and worse compared to the general Dutch population. Age, obesity, cardiopulmonary comorbidity, centrally located PE did not correlate with QoL in patients with PE.

Conclusion: Our study demonstrates that this cohort of long-term survivors of acute PE had an impaired QoL compared to population norms. The QoL of PE patients appeared, however, to be comparable with patients with a history of AMI the previous year, and better than patients with COPD and CHF.
Quality of life after pulmonary embolism as assessed with SF-36 and PEmb-QoL

INTRODUCTION

Studies have demonstrated that quality of life (QoL), defined as patients' reported impact of disease and treatment on his/her physical, psychological and social functioning and wellbeing, is associated with clinical endpoints and is increasingly considered an important outcome measure in clinical research (1-3). QoL can be assessed by generic QoL instruments, e.g. the Short Form 36 (SF-36), scoring standardized responses to standardized questions. These generic instruments are designed to sample the complete spectrum of function, disability, and distress that is relevant to QoL. In doing so, generic instruments are applicable to a wide variety of populations, irrespective of the illness or condition of the patients, and allow comparison between different patient groups. QoL can also be assessed by disease-specific questionnaires, which assess disease specific elements of quality of life and have been shown to be sensitive in detecting and quantifying changes in QoL that might be relevant to patients with a specific disease (2-5). Although it is known that both the acute event itself as well as the long-term clinical course of acute pulmonary embolism (PE) is frequently complicated by serious adverse events, such as recurrent venous thromboembolism (VTE) or chronic thromboembolic pulmonary hypertension (CTEPH) (6), there is a lack of knowledge on how this translates into QoL, as perceived by PE patients.

Recently, a disease-specific instrument for assessing QoL after PE, called the Pulmonary Embolism Quality of Life (PEmb-QoL), has been developed and validated. The PEmb-QoL assesses pulmonary signs and symptoms in addition to limitations in daily activities, emotional and social complaints and anxiety (7;8). Given that recent data indicates that PE is frequently associated with serious long-term clinical consequences, it would be important to know to what extent the QoL of patients after acute PE compares to the QoL of patients with chronic (cardio-) pulmonary diseases, such as chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF) and to patients with acute cardiopulmonary disease such as a history of acute myocardial infarction (AMI) the previous year (9). Yet, such a comparison has not been performed. The primary objective of this study was to compare QoL as expressed by SF-36 scores in patients with acute PE with general population norms, and to patients with COPD, CHF and in the first year after AMI. The secondary objectives were to evaluate QoL in the short-term and long-term clinical course of patients with acute PE, as expressed the PEmb-QoL, and to investigate whether patients' characteristics impacted their QoL.
Chapter 15

METHODS

Participant, procedure and description of the questionnaires

Dutch PEmb-QoL and SF-36 questionnaires were distributed by post between August 2011 and January 2012, among a consecutive sample of 150 patients with first or recurrent PE between October 2008 and December 2011 in the Academic Medical Center, Amsterdam, Maastricht University Medical Center, and Leiden University Medical Center, the Netherlands. All patients with objectively proven PE by a CT-scan or high probability ventilation perfusion scintigraphy, who were hemodynamically stable and aged above 18 years, were eligible. The only exclusion criterion was impossibility to follow-up. All surviving patients had been contacted by telephone every 6 months from the time of diagnosis of PE to assess the PE recurrence and CTEPH rate, as part of an ongoing observational, prospective follow-up study, which aims to evaluate the natural clinical course of patients with PE.

Patients were treated with vitamin K antagonists, with a target International Normalized Ratio (INR) between 2.0 and 3.0, for at least 6 months (10). Low molecular weight heparin (LMWH) was given until the INR was above the lower target range on 2 consecutive occasions, with a minimum of 5 days. Patients with active malignant disease were treated with LMWH during the first 6 months of anticoagulant treatment (11). Demographic data and additional relevant information were collected on a Case Record Form.

The SF-36 and PEmb-QoL and questionnaire were applied in Dutch and results of the questionnaires were entered manually into a database. Patients filled out the questionnaires at home and returned them by regular mail.

The SF-36 (generic questionnaire) (12) contains eight scales: physical functioning, social functioning, physical role functioning, emotional role functioning, mental health, vitality, bodily pain and general health, scoring 0-100, with higher values indicating a better health status (12).

The PEmb-QoL (disease-specific instrument assessing QoL after PE) (8) includes six scales: frequency of complaints, activity of daily life (ADL) limitations, work-related problems, social limitations, intensity of complaints, and emotional complaints. Higher scores indicate worse outcome.

In case of missing data, we excluded that specific scale in total from further analyses. The residual scales, however, were interpreted.
General population and disease comparison groups

The SF-36 has been administered to a representative sample of the general Dutch population to validate the Dutch version of the SF-36 in the Netherlands (13). We compare QoL reflected in SF-36 scores in patients with PE with general population norms, and with QoL of patients with COPD, CHF and AMI within one year prior to enrolment (9;14).

For the disease comparison groups, published data of SF-36 outcomes of patients with advanced chronic obstructive pulmonary disease (COPD) (Global Initiative for Chronic Obstructive Lung Disease stage III or IV) (14), severe chronic heart failure (CHF) (New York Heart Association class III or IV) (14), and with a history of AMI < 12 months prior to inclusion were used (9). Patients with COPD and CHF were included in 6 hospitals in the Netherlands in 2008 and 2009 (14) and data of patients with AMI the previous year were assessed from the Medical Outcomes Study (MOS), a survey of 22,462 patients, between the ages of 18 and 97, seen in the practices of 523 physicians in the USA (9).

Diagnosis of thrombus localization and thrombus load on CT-scan

PE was classified in two levels of thrombus occlusion, i.e. central (including central, interlobar vessels) or peripheral (including lobar, segmental and subsegmental vessels) using a scoring system according to Qanadli et al (15). Briefly, this index is defined as the number of segmental artery branches that are blocked, corrected by a factor of one for partial blockage, or a factor of 2 for complete obstructive clots. Using this scoring system, 40 is the highest possible score (thrombus completely obstructing the pulmonary trunk), corresponding with a 100% obstruction index.

Outcome measures

The primary outcome measure of this analysis was SF-36 scores of the patients with PE were compared to Dutch population norms and with patients with other cardiopulmonary diseases: COPD, CHF and the first year after AMI. For this analysis, we excluded patients in our cohort with a history of COPD, CHF and a history of AMI one year prior to exclusion in order to compare these chronic cardio-pulmonary diseases with patients with PE only. Our secondary outcome was QoL, as measured by the PEmb-QoL, after both intermediate and long-term follow-up in patients with a history of acute PE. We arbitrarily denoted follow-up as intermediate if the time frame between the diagnosis of PE and filling out of the questionnaire was shorter than 15 months (which was the 25th
percentile in this cohort), and long-term when the time frame was longer. We analyzed the responses to the questionnaires first in the total cohort and second in two groups of participants, divided by the 25th quartile of the timespan between diagnosis of PE and filling out the questionnaire. In addition, we investigated the impact of the following a priori defined clinical determinants on the QoL in our patient population: age, body mass index (BMI), active malignancy, COPD, CHF, history of venous thromboembolism, smoking habits, time frame between diagnosis and inclusion, Qanadi score and centrally located PE. Active malignancy was defined as cancer with ongoing treatment, treatment within the last 6 months, or in a palliative stage.

**Statistical analyses**

Normally distributed variables are presented as mean and standard deviation (SD), non-normally distributed variables are expressed as medians with ranges.

The scores for the SF-36 dimensions in our patient sample were compared to the published means and SDs for each scale among the general population and the comparison disease subjects, using the standard deviate (z-score). To adjust for age differences between patients and control subjects, the population norms were weighed with the age distribution of our sample.

Because the time frame between PE and measuring QoL ranged between 5 and 46 months, partial bivariate correlations - controlling for the time between PE and filling out questionnaires - were calculated between factors potentially influencing the QoL such as BMI, COPD, CHF, history of VTE, recurrent PE and malignancy and the different scales of the questionnaires. For non-normally distributed data, we used a spearman correlation test.

P-values < 0.05 were considered statistically significant. The calculations of the scores of the PEmb-Qol and SF-36 and all analyses were conducted using statistical software SPSS, version 19.0; (SPSS Inc; Chicago, IL).
RESULTS

Patients
The questionnaires were distributed among 150 patients with a history of acute PE, of whom 109 (73%) completed the questionnaire after a median of 25 months, range 5-46 months. A quarter of the patients filled out the questionnaire within the first 15 months after diagnosis of PE. The clinical characteristics at baseline of the participants are depicted in Table 1. In the time between PE and the questionnaire, 6 patients experienced a recurrent VTE, of which all cases were PE, and 1 patient developed CTEPH.

Table 1. Baseline characteristics of patients with clinically pulmonary embolism.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value N=109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%), Age in years, COPD, n (%)</td>
<td>56 (51), 60 (15)</td>
</tr>
<tr>
<td>CHF, n (%)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>AMI one year prior to enrollment</td>
<td>0 (0)</td>
</tr>
<tr>
<td>History of PE, n (%)</td>
<td>9 (8)</td>
</tr>
<tr>
<td>History of DVT, n (%)</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Active malignancy, n (%)</td>
<td>21 (19)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>18 (17)</td>
</tr>
<tr>
<td>Centrally located PE, n (%)</td>
<td>16 (15)</td>
</tr>
<tr>
<td>Anticoagulant therapy &gt; 6 months, n (%)</td>
<td>28 (26)</td>
</tr>
<tr>
<td>Anticoagulant therapy at time of questionnaire completion, n (%)</td>
<td>17 (16)</td>
</tr>
<tr>
<td>Qanadli score (0-40), median (range)</td>
<td>7 (0-29)</td>
</tr>
<tr>
<td>Time span in months between PE and study inclusions, median (IQR)</td>
<td>25 (15-31)</td>
</tr>
</tbody>
</table>

CHF congestive heart failure, COPD chronic obstructive pulmonary disease, DVT deep venous thrombosis; IQR interquartile range, N number, SD standard deviation, PE pulmonary embolism, VTE venous thromboembolism

SF-36
The number of patients was, per complete SF-36 scale: 105 for physical functioning, 102 for social functioning, 102 for physical role functioning, 100 for emotional role functioning, 105 for mental health, 103 for vitality, 102 for bodily pain and 99 for general health.
The results of physical role functioning, emotional role functioning, mental health, bodily pain, and general health did not differ between the intermediate and the long-term follow-up (data not shown). The results of the scales physical functioning, social functioning, vitality, however, were significantly higher in the group of patients who completed the questionnaire at least 15 months after PE (66 versus 48, 81 versus 67 and 64 versus 54, respectively, p < 0.05)

Results of the SF-36 in PE patients compared to the general population and disease comparison groups

After leaving out the patients with COPD, CHF or AMI the previous year in our cohort, 98 patients with PE only remained for this analysis. We compared patients with PE to the general Dutch population subjects (n=140), which were population-based groups of non-institutionalized individuals with a mean age of 59 years of age in the Netherlands (15). Patients with PE had markedly lower scores than the general population on the scales social functioning and role emotional and general health (p < 0.001) and on the role physical and vitality scale (p < 0.05). On the scales physical functioning, mental health and pain no differences were observed (p=0.40, p=0.96 and p=0.12 respectively) (Table 2 and Figure 1).

Compared to the disease comparison groups, patients with PE were younger than patients with CHF (n=80), but age did not differ in patients with COPD (n=105) and AMI the previous year (n=107) (Table 2). Patients with severe COPD or CHF scored significantly lower compared to patients with PE on all scales. However, scores were not significantly higher or lower than patients with the first year after AMI on most scales; patients with PE scored significantly higher on the vitality scale (p=0.015) and the scale bodily pain (p= 0.018) only (Table 2 and Figure 1).

PEmb-QOL

The numbers of patients per complete PEmb-QoL scales were: 102 for frequency of complaints, 103 for ADL limitations, 102 for work related problems, 108 for social limitations, 104 for intensity of complaints, 92 for emotional complaints. For all dimensions of the PEmb-QoL, a score of 1 point designates no complaints.
Table 2. Demographics and Mean Short Form 36 (SF-36) scores in patients with pulmonary embolism (PE) (leaving out the patients with PE and COPD or CHF), compared to the gender and age adjusted Dutch population norms, patients with severe to very severe Chronic Obstructive Pulmonary Disease (COPD).

<table>
<thead>
<tr>
<th></th>
<th>Total PE N=98</th>
<th>Dutch population N=140</th>
<th>COPD N=105</th>
<th>Heart failure N=80</th>
<th>AMI N=107</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female n (%)</td>
<td>50 (51)</td>
<td>91 (65)</td>
<td>40 (38)</td>
<td>26 (32.5)</td>
<td>33 (31)</td>
</tr>
<tr>
<td>Age mean (SD)</td>
<td>60.4 (15.0)</td>
<td>59 (range 55-64)</td>
<td>66.3 (9.2)</td>
<td>76.2 (8.3)</td>
<td>59.2 (11.4)</td>
</tr>
<tr>
<td>Care</td>
<td>secondary</td>
<td>N.A.</td>
<td>secondary</td>
<td>secondary</td>
<td>primary</td>
</tr>
<tr>
<td>Physical functioning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>70.6 (32.4)</td>
<td>72.7 (24.4)</td>
<td>21.0 (21.1)</td>
<td>24.7 (23.0)</td>
<td>69.7 (26.1)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.40</td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>Social functioning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>79.3 (25.8)</td>
<td>86.6 (21.4)</td>
<td>65.0 (26.1)</td>
<td>58.6 (31.6)</td>
<td>81.6 (21.1)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.0008</td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>Role physical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>64.5 (45.1)</td>
<td>76.5 (38.1)</td>
<td>37.1 (42.8)</td>
<td>37.8 (43.0)</td>
<td>72.8 (1252)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.002</td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Role emotional</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>79.6 (38.6)</td>
<td>90.1 (24.5)</td>
<td>62.9 (44.9)</td>
<td>67.1 (42.9)</td>
<td>73.5 (38.0)</td>
</tr>
<tr>
<td>p-value*</td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>0.004</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Mental</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>77.0 (17.5)</td>
<td>77.1 (18.7)</td>
<td>68.6 (19.9)</td>
<td>71.3 (21.2)</td>
<td>75.8 (15.7)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.96</td>
<td>&lt;0.00001</td>
<td>0.003</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>62.7 (21.3)</td>
<td>67.0 (21.3)</td>
<td>51.1 (18.9)</td>
<td>48.7 (19.8)</td>
<td>57.7 (19.0)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.046</td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>0.015</td>
<td></td>
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<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>78.6 (25.5)</td>
<td>74.7 (25.0)</td>
<td>70.9 (29.5)</td>
<td>61.1 (31.4)</td>
<td>72.8 (25.2)</td>
</tr>
<tr>
<td>p-value*</td>
<td>0.089</td>
<td>0.02</td>
<td>&lt;0.00001</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>General health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>55.4 (26.8)</td>
<td>64.4 (22.2)</td>
<td>29.7 (19.1)</td>
<td>37.2 (17.3)</td>
<td>59.2 (19.3)</td>
</tr>
<tr>
<td>p-value*</td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>0.14</td>
<td></td>
</tr>
</tbody>
</table>

Congestive Heart Failure (CHF), and myocardial infarction (AMI). SD standard deviation
*2-sided p-value for Z score, patients with PE versus general population, and patients with COPD, CHF and AMI versus patients with PE.
Figure 1: Mean SF-36 scores of patients with a history of acute Pulmonary Embolism, compared to a Dutch general population and disease comparison groups: COPD chronic obstructive pulmonary disease, CHF congestive heart failure, and AMI acute myocardial infarction.

The total score per patient had a median of 7.1 (IQR 6.1-10.8). The median scores of the 6 dimensions of the PEmb-QoL were 1.7 (interquartile range (IQR) 1.0-2.1; max 5 points) for frequency of complaints, 1.5 (IQR 1.0-1.9; max 3 points) for limitations in ADL, 1.3 (IQR 1.0-1.5; max 2 points) for work-related problems, 1.5 (IQR 1.0-2.0; max 5 points) for social limitations, 2.0 (IQR 1.0-3.0; max 6 points) for intensity of complaints and 1.7 (IQR 1.0-3.0 max 6 points) for emotional complaints.

The scores of the patients who completed the questionnaires within 15 months after diagnosis of PE did not differ from the results of the patients who filled out the questionnaires longer than 15 months after diagnosis of PE (data not shown), except for the scales emotional complaints: 2.1 (IQR 1.2-3.2) versus 1.6 (IQR 1.0-1.9) respectively, p=0.028 and limitations in ADL 1.7 (IQR 1.1-2.2) versus 1.5 (IQR 1.0-1.7) respectively, p=0.03.
Associations between clinical characteristics and the PEmb-QoL

The total PEmb-QoL score did not correlate with age, BMI, COPD, CHF, history of VTE, recurrent PE, malignancy, smoking habits (partial correlations as we adjusted for time between PE and filling out the questionnaires). PEmb-QoL was neither related to localization of PE, thrombus load expressed as Qanadli score, nor the time span between PE and inclusion.

Of the 6 PEmb-QoL dimensions, modest correlations were found between COPD and intensity of complaints (r=0.23, p=0.02) and social limitations (r=0.28, p=0.025), CHF and social limitations (r=0.28, p=0.003), malignancy and emotional complaints (r=0.24, p=0.023), time span between PE and inclusion and emotional complaints (r=-0.2, p=0.04), and ADL limitations (r=-0.20, p=0.008).

Discussion

This study demonstrates that the QoL status, as assessed with SF-36, of patients who experienced PE is comparable to patients with a history of AMI the previous year and significantly better compared to patients with COPD and CHF. Second, the QoL in patients with PE as assessed with the disease-specific pemb-QoL questionnaire, was not influenced by severity of PE, as expressed in thrombus location and thrombus load.

Until now, only few studies addressed the QoL of patients with acute PE. Klok and colleagues (3) assessed the SF-36 in 392 patients with a history of PE and compared their SF-36 scores to Dutch population norms. Consistent with our findings, demonstrating that patients with a recent history of acute PE have an impaired QoL, they found significant differences on all scales, indicating a decreased QoL in PE patients. The time interval between PE and study inclusion was inversely related to QoL, and significant determinants of poor QoL were prior PE, age, obesity, active malignancy, and cardiopulmonary comorbid conditions (3). In the current study, we found only a modest correlation between COPD, CHF, malignancy and time span between PE and inclusion, and no correlation was found for all other clinical characteristics. An explanation for these differences could be that the current study represents a healthier population as reflected by the lower rates of cardiopulmonary comorbidity (8% versus 48%). Also, the current analysis had a smaller time-window between the PE episode and QoL-measurement, which has been demonstrated to be inversely related with QoL (17).

The PEmb-QoL has been validated in 2010 in 90 patients with a history of PE (7). The median time between PE and inclusion in that study was 3 years and 2 months,
(range 10 months -approximately 8 years). The median PE
db-QoL scores were all slightly lower in the previous cohort, indicating a better QoL, possibly due to the larger
time gap between PE and inclusion.

As recent data reveal that a large proportion of patients with acute PE experience
an adverse clinical course (6), it could be debated whether PE should be considered an
acute or a chronic disease. We therefore investigated to what extent the QoL of patients
with acute PE compares to the QoL reported by patients with chronic cardiopulmonary
diseases, including COPD and CHF, using the generic SF-36 questionnaire. Notably, the
QoL of patients with acute PE was significantly better on all SF-36 subscales. Furthermore,
no clear differences were seen when we compared the QoL status of our patients to that
of patients with a history of AMI the previous year. Thus, the QoL in patients with acute
PE resembles more as an acute, than a chronic cardiopulmonary disease. These findings
may be supported by the fact that for some scales in both questionnaires, we observed
that the longer the period between the diagnosis and the QoL measurement, the better
the QoL outcome.

To our knowledge, this is the first study that investigated the correlation between
thrombus-load, as expressed by the Qanadli score and the location of the thrombus (i.e.,
central or lobar, segmental and subsegmental), and the QoL, as assessed with the PE
db-QoL questionnaire, in patients with PE. More centrally located PE or a higher thrombus
load did not appear to affect QoL on the long-term. Although thrombus load has clearly
been established as an important predictor for the short term clinical outcome (18), its
implications for the long term clinical course, including the risk of developing CTEPH,
have yet to be established.

The conclusions of this study are strengthened by the high response rate of 73%.
A limitation includes the fact relatively low sample size, as a consequence, this study
might have been underpowered to detect significant correlations between baseline
characteristics and QoL. Additionally, our patient sample represents a relative healthy
population, which is likely inherent to the fact that the patients had to survive the first
months following PE to enter the study. In our view, however, this does represent the
population of PE patient in whom assessing the QoL after PE is relevant. Furthermore,
we measured both questionnaires once, which might give a bias as symptoms might
change over time. Besides, for 84% of our population the question “Would you have
been worried if you had to stop taking anticoagulant medication?” was not relevant.
This question was then interpreted as “were you worried when you had to stop taking
anticoagulants”. Last, we have assessed statistical differences in QoL scores between
Quality of life after pulmonary embolism as assessed with SF-36 and PEmb-QoL
different groups. However, a clinically meaningful difference is defined for SF-36, not yet
for PEmb-QoL. Consequently, it is unknown whether such differences are meaningful to
the patients even if p < 0.05.

In summary, QoL in our cohort of Dutch patients with a history of acute PE is
impaired compared to the general population, irrespective of clinical characteristics
such as age, comorbidity, or severity of PE. The presented population of patients with a
history of acute PE report better QoL scores compared to patients with COPD and CHF,
whereas the QoL of PE patient was comparable to patients with AML.

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