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Original Research

PULMONARY EMBOLISM

Quality of Life in Long-term Survivors of Acute Pulmonary Embolism

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Background: **To our knowledge, studies evaluating the quality of life (QoL) in patients with a history of acute pulmonary embolism (PE) are not available, even though QoL is a key outcome component of medical care and a predictor of disease-specific prognosis.**

Methods: **As part of a large follow-up study, the Short Form 36 (SF-36) was presented to consecutive patients who had survived one or more episodes of acute PE. The results of all nine subscales of the SF-36 were compared with sex- and age-adjusted Dutch population norms. Single and multivariate analyses were performed to identify independent determinants of the QoL in our study population.**

Results: **The SF-36 was completed by 392 patients. Except for the health change subscale, patients had substantially lower QoL than population norms on all eight remaining subscales. After multivariate analysis, the time interval between the last thromboembolic episode 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. Regression models that included all identified significant determinants proved to be quite modest predictors for QoL in the individual patient. Awareness of illness, coping mechanisms, and self-management behavior might be additional important indicators of QoL in our study population but require further investigation.**

Conclusion: **We identified several PE- and non-PE-related determinants of QoL in patients with a history of acute PE, which is impaired compared with sex- and age-adjusted population norms. QoL after acute PE should be studied more extensively and added as a standard measure to outcome studies.**

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Abbreviations: PE = pulmonary embolism; QoL = quality of life; SF-36 = Short Form 36

Evaluating the clinical outcome of acute pulmonary embolism (PE) traditionally involves short-term mortality, thromboembolic recurrence rate, and therapy-related complications.[1,2] In recent years, chronic emboli causing pulmonary hypertension and arterial cardiovascular events (eg, myocardial infarction, stroke), have been added as important prognostic factors in the long-term clinical course of acute PE.[3-6] Until now, no study has reported on quality of life (QoL), its determinants, or its association with long-term prognosis in patients with acute PE. QoL is a multidimensional construct referring to the impact of disease and treatment on the patients' physical, psychologic, and social function and well-being.[7] QoL has emerged as an increasingly important outcome measure in patient management

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because it provides a precise indicator of the overall health status of the individual patient. Higher QoL is associated with improved disease-specific prognosis and increased survival.[8-12] Importantly, several aspects of QoL can be affected by the treating physician and, thus, could be of additional prognostic value for the patient on top of standard treatment regimes and clinical surveillance.[10-13]

The objective of this study was to evaluate QoL in the long-term clinical course of patients with acute PE and to explore its clinical determinants. Accordingly, a generic QoL measurement instrument, the Short Form 36 (SF-36),[14,15] was administered to a large population of consecutive patients who had had one or more episodes of acute PE. In addition, we evaluated correlations between the results from the SF-36 and several apparent clinical characteristics of the acute thromboembolic event as well as other relevant non-PE-related patient demographics.

Materials and Methods

Patients

This study was a subanalysis from a large follow-up study of consecutive patients with a first or recurrent acute PE in the period between January 1, 2001, and July 1, 2007, in an academic (Leiden University Medical Center; Leiden, The Netherlands) and affiliated teaching hospital (Medical Center Haaglanden, The Hague, The Netherlands).[4] The diagnosis of acute PE was confirmed by intraluminal filling defects on pulmonary angiography or CT scan pulmonary angiography, high probability ventilation perfusion scintigraphy, or intermediate probability ventilation-perfusion scintigraphy in combination with objectively diagnosed DVT.[16] All patients were treated initially, according to hospital policy, with at least 5 days of either unfractionated heparin or low-molecular-weight heparin followed by oral anticoagulant therapy for at least 6 months.[17] All surviving patients were invited for a single visit to our vascular medicine outpatient clinic for cardiopulmonary work-up and assessment of QoL. This visit was scheduled between July 1, 2007, and January 1, 2009, and planned at least 1 full year after the thromboembolic episode to rule out the initial effect of acute PE on the study outcome. Patients living abroad or for whom up-to-date contact specifications were not available were excluded. In addition, patients with pulmonary hypertension prior to the start of our study were not invited to participate in the subanalysis because the cardiopulmonary function tests that were one of the primary end points of the follow-up study were already performed in their standard diagnostic work-up.[4] This study was approved by the institutional review boards of both participating hospitals, and all patients provided informed consent.

Procedure

Patients who responded to our invitation for a visit underwent medical questioning, physical examination, and a cardiopulmonary screening that included pulmonary function tests and echocardiography. The SF-36 questionnaire (in Dutch) was used to measure QoL. It comprises 36 items and evaluates general well-being in nine subscales.[14,15,18] Eight subscales refer to perceptions of QoL in the previous 30 days (ie, physical functioning, social functioning, physical role limitations, emotional health limitations, mental health, vitality, bodily pain, general health perceptions), and the ninth subscale (health change) covers changes in the preceding full year. The SF-36 is the most widely used application of QoL assessment and has been shown to excellently represent the individual's psychologic characteristics and to have high reproducibility and clinical relevance.[15,18,19] Prior to their visit, patients received the SF-36 by mail and were asked to return the completed questionnaire. Unfinished questionnaires were completed during the visit. Study participants who could not complete the SF-36 because of language barriers were excluded from this analysis.

Outcome

The primary study end point was QoL, as measured by the SF-36 and represented by its predefined subscales, after long-term follow-up in patients with a history of acute PE. The results were compared with Dutch population norms that were established during the validation of the Dutch version of the SF-36 in The Netherlands.[20]

The secondary study end point was the identification of significant clinical determinants of the QoL in our patient population: age, sex, obesity (BMI $>30 kg/m^2$), active malignancy, cardiopulmonary comorbidity, centrally located PE, recurrent VTE (ie, objectively confirmed recurrent DVT or PE before or after the patients were included in the current analysis), and the duration of follow-up from the most recent thromboembolic event to study inclusion. Active malignancy was defined as cancer with ongoing treatment, with treatment within the past 6 months, or in the palliative stages. Cardiopulmonary comorbidity was considered present if the cardiopulmonary work-up revealed either clinically relevant obstructive or restrictive pulmonary function impairment or systolic or diastolic ventricular dysfunction.

Statistical Analysis

The demographics of patients who participated in the study were compared with the demographics of the patients who did not participate, using independent-sample *t* tests for normally distributed continuous variables and χ^2 tests for categorical variables. Results of the SF-36 were entered manually into a database by one researcher who was blinded to the clinical condition of the patients. The SF-36 results were compared with the population norms by Wilcoxon rank sum test with Bonferroni correction, which indicates that the allowable significance level for each SF-36 subscale was $P < .0056$ (.05 per nine subscales). To adjust for sex and age differences between patients and control subjects, the population norms were weighed with the age and sex distribution of our sample. For the assessment of clinical determinants of QoL in our patient cohort, univariate relations between all predefined potential determinants and the SF-36 subscales were determined by calculating regression coefficients with standard errors and associated *P* values. A $P < .05$ was used to define statistical significance in the linear regression analyses. A backward conditional linear regression analysis, including all possible determinants that were both significant and nonsignificant in the univariate analysis, was performed to identify independent determinants of QoL. The coefficient of determination (r^2) was used to estimate the goodness of fit, which represents the percentage of effect that is predicted by the linear model. All analyses were conducted using statistical software SPSS, version 14.02; (SPSS Inc; Chicago, IL).

Results

Patients

In total, 877 patients were given a diagnosis of acute PE between January 1, 2001, and July 1, 2007,

in the two participating hospitals. Of these patients, 259 (30%) had died before they were able to participate in the study, 11 (1.3%) were excluded for geographical reasons, 19 (2.2%) had pulmonary hypertension prior to the subanalysis, and 10 (1.1%) could not complete the SF-36 due to a language barrier (Fig 1). Finally, 186 (21%) patients declined visiting our outpatient clinic for several reasons: 51 were unable to visit because of advanced age or severe comorbid conditions, 38 recently visited our hospital for clinical reasons and declined revisiting the hospital, and 97 declared to be in good health and to have no time to be involved in clinical studies.

The final sample to complete the SF-36 (n = 392; response rate, 67%) (Fig 1) was aged 55 ± 15 years and included 201 (51%) men, 60 (15%) patients with active malignancy, 190 (48%) patients with cardiopulmonary comorbidity, 125 (32%) patients with obesity, 134 (34%) patients with centrally located PE, and 64 (16%) patients with recurrent VTE (Table 1). The demographics of the study population not included in this analysis also are shown in Table 1. The fraction of patients with a transient risk factor for PE (eg, immobility > 3 days or recent long flight, trauma, recent surgery, fracture of extremity, pregnancy or peripartum period, hormone replacement therapy, use of oral contraception) was higher in the 392 patients who completed the SF-36 (47% vs 36%, respectively) mainly because of a higher rate of active malignancy at the time of the registration PE in the entire study population.

The 392 patients for current analysis were followed for a mean period of 3.6 ± 1.7 years, with a range of 0.99 to 6.48 years to the registration PE. None of these latter patients were suspected of or had been diagnosed with chronic thromboembolic pulmonary hypertension after the cardiopulmonary work-up was completed.[4]

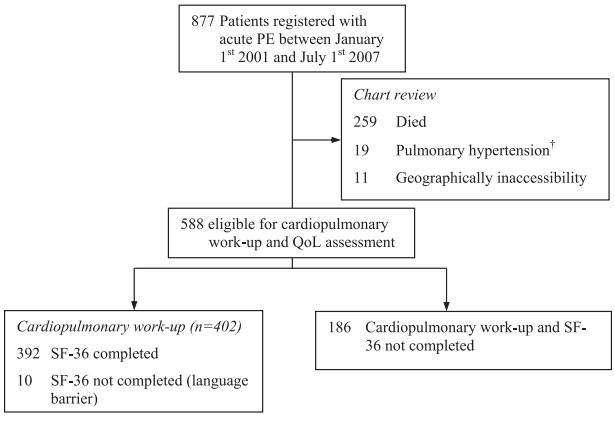

FIGURE 1. Flowchart. †Patients with pulmonary hypertension prior to the start of our study were not invited for the cardiopulmonary work-up for logistic reasons. PE = pulmonary hypertension; QoL = quality of life; SF-36 = Short Form 36.

Results From SF-36

All 392 patients completed the SF-36. After Bonferroni correction for multiple tests, health change over 1 year and mental health were not different between the patients and age- and sex-adjusted Dutch population norms (Fig 2, Table 2). In contrast, the study patients scored significantly lower than the adjusted population norms with respect to the other seven subscales (Fig 2, Table 2).[19] This contrast was most distinct in the physical role limitation scale (difference, 15.5 points). Closely related to this subscale is physical functioning (difference, 6.3 points). For illustration, the observed decrease for both physical SF-36 subscales could mean the difference between being able to fully comply with one's job, walk up one or more stairs, and take care of the household or personal hygiene and not being able to do so.

Univariate Determinants of QoL

Univariate analysis indicated that recurrent VTE was associated with decreased physical functioning, vitality and health change, and increased bodily pain after at least 1 year and not > 6.5 years of follow-up (Table 3). The disease-free interval was positively related to physical and social functioning and physical role limitations; longer time span from the last acute PE to study inclusion led to improvement of these three SF-36 subscales. On the other hand, we found an inverse relation between disease-free interval and health change, indicating that a more recent PE was associated with increased health improvement. Centrally located PE was not associated with QoL. In contrast to the PE etiology, QoL was decreased after unprovoked PE or PE caused by a permanent risk factor compared with PE caused by a transient risk factor. Age, obesity, and cardiopulmonary comorbidity also were significantly correlated to the results of the SF-36 (Table 3).

Multivariate Determinants of QoL

After multivariate analysis, obesity, active malignancy, and cardiopulmonary comorbidity proved to be independent determinants of decreased QoL on several SF-36 subscales (Table 4). Longer disease-free interval was an independent predictor of increased physical role performance, physical and social functioning, and decreased health change. In addition, recurrent VTE was found to be an independent determinant of decreased physical functioning and health change and of increased bodily pain. Finally, PE associated with transient risk factors proved to be an independent predictor of better QoL compared with PE occurring with permanent risk factors or without risk factors. We evaluated possible interactions in

Table 1—*Patient Demographics and Characteristics of the Registration Thromboembolic Event*

Characteristic	Included Patients (n = 392)	Not Included Patients (n = 485)	χ^2 Test[a]	*P* Value
Male sex	201 (51)	209 (43)	5.83	.016
Age, y[b]	55 ± 15	57 ± 19	…	.090 (875 *df*, individual samples *t* test)
Cardiopulmonary comorbidity[c]	190 (48)	NA	NA	NA
Active malignancy[d]	60 (15)	NA	NA	NA
Obesity[b,e]	125 (32)	164 (34)	0.546	.55
Centrally located PE[b]	134 (34)	172 (35)	0.156	.69
Unprovoked PE[b]	142 (36)	168 (35)	0.238	.63
Transient risk factor for PE[b]	184 (47)	133 (27)	35.8	< .001
Permanent risk factor for PE[b]	66 (17)	184 (38)	47.4	< .001
Recurrent VTE	64 (16)	100 (21)	2.63	.11
Disease-free interval, d[f]	1,313 ± 637	NA	NA	NA

Data are presented as No. (%) or mean ± SD. *df* = degrees of freedom; NA = not applicable; PE = pulmonary embolism.
[a]Number of *df* was 1.
[b]At time of the registration PE.
[c]Determined by cardiopulmonary work-up during the follow-up visit.
[d]At time of follow-up visit.
[e]BMI > 30 kg/m^2.
[f]Time span between most recent acute PE and study inclusion.

the multivariate model and corrected our models with relevant interaction terms. The results of our multivariate model before and after this correction were very much comparable: Not any predictor variable became nonsignificant after significant interaction terms were entered, and the corrections of the models were associated with small r^2 increases between 0.2% and 2.9% of points. The specific results of the multivariate analysis, including interactions, are not reported.

Models including only the independent determinants of the individual SF-36 subscales performed poorly when predicting the overall observed results of the subscales of the SF-36. These models for physical and social functioning, physical role limitations, emotional health limitations, mental health, vitality, bodily pain, general health perceptions, and health change predicted only 1.1% to 12% (mean ± SD, 4.1 ± 3.3%) of the observed effect (r^2) (Table 4).

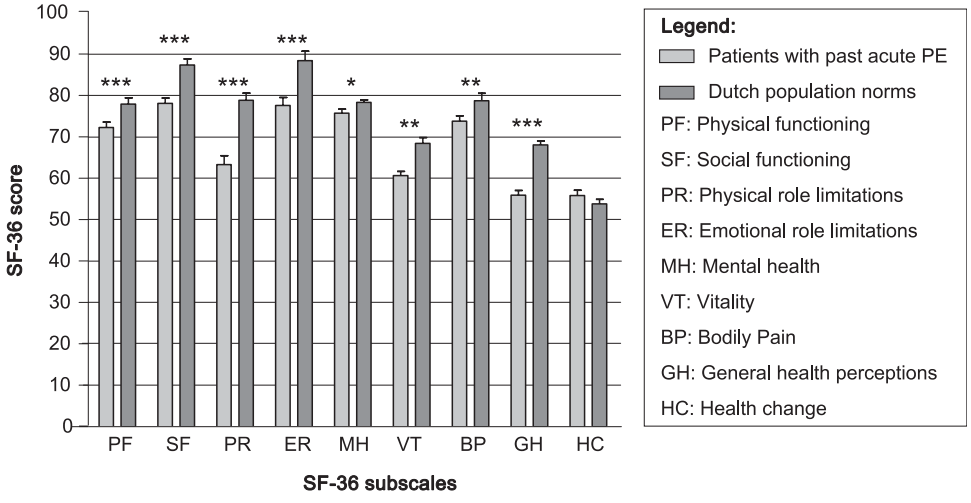

FIGURE 2. Mean SF-36 scores of patients with past acute PE compared with sex- and age-adjusted Dutch population norms.[19] Error bars represent SEM. Higher SF-36 scores are associated with better QoL. *$P < .05$. **$P < .01$. ***$P < .001$ (Wilcoxon rank sum test). $P < .0056$ considered significant after Bonferroni correction. BP = bodily pain; ER = emotional role limitations; GH = general health perceptions; HC = health change; MH = mental health; PF = physical functioning; SF = social functioning; PR = physical role limitations; VT = vitality. See Figure 1 legend for expansion of other abbreviations.

Table 2—*Mean Short Form 36 Scores of Patients With Past Acute PE Compared With Sex- and Age-Adjusted Dutch Population Norms*[19]

Subscale	Patients (n = 392)	Norms (n = 1,053)	*P* Value
Physical functioning	72 ± 1.3	78 ± 0.95	< .001
Social functioning	78 ± 1.2	87 ± 0.97	< .001
Physical role limitations	63 ± 2.1	79 ± 0.96	< .001
Emotional health limitations	77 ± 1.9	88 ± 0.95	< .001
Mental health	76 ± 0.91	78 ± 0.95	.046
Vitality	61 ± 1.1	68 ± 0.95	.004
Bodily pain	74 ± 1.2	79 ± 0.96	.003
General health perceptions	56 ± 1.1	67 ± 1.0	< .001
Health change	56 ± 1.2	54 ± 1.1	.15

Data are presented as mean ± standard error. Higher SF-36 scores are associated with better quality of life. Mean scores were compared by using the Wilcoxon rank sum test. SF-36 = Short Form 36. See Table 1 legend for expansion of other abbreviation.

[a]*P* < .0056 is considered significant after Bonferroni correction.

Discussion

This study evaluated QoL in patients with a history of acute PE and has two important novel findings. First, our results indicate that patients who survive the acute thromboembolic event and do not suffer from chronic thromboembolic pulmonary hypertension have a significantly lower QoL than age- and sex-adjusted population norms, implying moderate to severe impairment of social activities and physical performance for patients with a history of acute PE. Second, we identified several demographics in disease-specific factors associated with better or worse QoL.

The question arises about to what extent our observations are caused by the acute thromboembolic episode itself or by other factors. The results from the multivariate regression analyses clearly demonstrate that both PE-related and non-PE-related patient characteristics are independent determinants of QoL. Longer duration of the disease-free interval was associated with increased likelihood of higher QoL, and patients with more recent PE showed more health improvement over the past year. In addition, recurrent thromboembolic events were associated with increased bodily pain and decreased health change and physical functioning. Finally, the PE etiology proved to be a predictor of QoL because patients who survived a PE caused by transient risk factors had higher scores on the general health perceptions subscale than those who survived PE caused by permanent risk factors or not associated with any risk factors. This observation can be explained best by the more complicated clinical course of patients after unprovoked PE (higher rates of myocardial infarction and other serious cardiovascular events, higher rates of recurrent VTE, and newly diagnosed malignancies) and of patients after provoked PE with permanent risk factors (higher rates of recurrent VTE and malignancy-related mortality) than of patients with PE after transient risk factors.[6,21] Age, obesity, and severe comorbid conditions such as active malignancy and pulmonary or cardiac function impairment were strong determinants of QoL as well. These last findings concur with current knowledge because several previous studies in other patient cohorts have demonstrated the importance of these factors for the well-being of individual patients.[20,22] Furthermore, a previous study demonstrated that the QoL after DVT of the lower extremities was not determined at all by severity of the acute clinical event.[23] This observation also was confirmed by our results because centrally located emboli were not associated with any of the nine SF-36 subscales.

Although we were able to identify several significant determinants of QoL in our patient population, combining these in multivariate prediction models did not result in precise prediction of the QoL for individual patients because our models predicted only 1.1% to 12% of the observed effect (Table 4). One explanation for this finding is the likely lack of specificity for PE-related QoL of the SF-36. In addition to the use of generic QoL tools, disease-specific questionnaires can be applied when evaluating the QoL associated with a certain condition. Disease-specific questionnaires are likely to detect and quantify small, but relevant QoL changes. Recently, the PEmb-QoL questionnaire was proposed and validated.[24,25] Further studies should evaluate this questionnaire in a larger patient population to study the specificity and predictive value of the PEmb-QoL for QoL after PE. A second explanation for the low predictive value of SF-36 in our population is the lack of other crucial determinants of QoL in the current analysis. Potential candidates for these determinants are educational, financial, social, and geographic factors as well as social support systems, although it is not likely that these are different in the study patients compared with the population norms. More interesting determinants are illness cognitions, coping behaviors, and self-management. All three concepts have been reported to have strong relationships with psychologic well-being in patients with different diseases.[10-13] Furthermore, interventions by specific patient management programs might lead to notable improvement of QoL and, thus, clinical outcome.[10-13] Unfortunately, studies in patients with acute PE reporting on these three key concepts of QoL are lacking.

As far as we are aware, this report is the first to compare the QoL in patients with a history of acute PE to population norms, which seems surprising

Table 3—*Univariate Linear Regression Analysis of Absolute SF-36 Scores: Unstandardized Regression Coefficients and Standard Errors of PE and Not-PE-Related Determinants of the SF-36 Subscale Scores*

Subscale	Age, y	Sex[a]	Obesity[b,c]	Malignancy[c]	Cardiopulmonary Comorbidity[c]	Disease-Free Interval, d	Recurrent VTE[c]	Centrally Located PE[c]	Unprovoked PE[c]	Transient Risk Factor for PE[c]	Permanent Risk Factor for PE[c]
PF	-0.46 ± 0.084[d]	4.8 ± 2.7[d]	-9.9 ± 2.9[d]	-12 ± 4.3[d]	-14 ± 2.6[d]	0.005 ± 0.02[d]	-6.3 ± 2.9[d]	0.52 ± 2.8	-3.52.8	1.4 ± 2.7	3.2 ± 3.6
P	< .001[d]	.042[d]	< .001[d]	.004[d]	< .001[d]	.015[d]	.032[d]	.85	.21	.60	.37
t	-5.5[d]	2.0[d]	-3.5[d]	-2.9[d]	-5.5[d]	2.4[d]	-2.2[d]	0.18	-1.2	0.52	0.90
SF	0.72 ± 0.79	2.5 ± 2.2	-8.2 ± 2.6[d]	-0.43 ± 4.0	-4.5 ± 2.5[d]	0.003 ± 0.02[d]	-3.8 ± 2.7	0.88 ± 2.6	1.0 ± 2.6	-2.4 ± 2.5	2.7 ± 3.3
P	.63	.37	.002[d]	.91	.044[d]	.042[d]	.16	.74	.70	.32	.41
t	0.91	0.89	-3.1[d]	-0.11	-2.0[d]	-2.0[d]	-1.4	0.34	0.39	-0.99	0.82
PR	-0.37 ± 0.14[d]	4.3 ± 4.3	-5.7 ± 4.6	-14 ± 7.0[d]	-16 ± 4.3[d]	0.009 ± 0.03[d]	-5.5 ± 4.7	7.6 ± 4.6	0.73 ± 4.5	-3.7 ± 4.3	5.5 ± 5.8
P	.008[d]	.33	.22	.043[d]	< .001[d]	.002[d]	.25	.095	.87	.39	.35
t	-2.7[d]	0.98	-1.2	2.0[d]	-3.7[d]	3.1[d]	-1.2	1.7	0.16	-0.86	0.94
ER	-0.12 ± 0.048	0.73 ± 3.8	-9.1 ± 4.1[d]	-1.9 ± 6.2	-7.0 ± 3.8[d]	0.002 ± 0.003	1.1 ± 4.2	1.1 ± 4.0	0.84 ± 4.0	-2.2 ± 3.8	2.6 ± 5.1
P	.35	.85	.027[d]	.75	.043[d]	.54	.78	.79	.83	.56	.61
t	-0.94	0.19	-2.2[d]	0.31	-2.0[d]	0.62	0.28	0.27	0.21	-0.58	0.51
MH	0.12 ± 0.058[d]	1.5 ± 1.8	-2.5 ± 2.0	-0.82 ± 3.0	1.4 ± 1.8	0.001 ± 0.001	-0.41 ± 2.0	-0.80 ± 1.9	0.63 ± 1.9	-0.67 ± 1.8	0.16 ± 2.4
P	.035[d]	.41	.20	.78	.43	.58	.83	.68	.74	.71	.95
t	2.1[d]	0.83	-1.3	0.28	0.79	0.55	-0.21	-0.42	0.33	-0.37	0.066
VT	0.74 ± 0.069	0.34 ± 2.1	-6.2 ± 2.3[d]	-1.8 ± 3.4	-2.3 ± 2.1	0.001 ± 0.001	-4.3 ± 2.3[d]	-2.2 ± 2.2	0.59 ± 2.2	-0.39 ± 2.1	0.60 ± 2.8
P	.28	.88	.007[d]	.60	.29	.37	.042[d]	.34	.98	.85	.83
t	1.1	0.16	-2.7[d]	0.53	-1.1	0.89	-2.0[d]	-0.96	0.03	-0.18	0.21
BP	0.17 ± 0.079	2.2 ± 2.5	-7.0 ± 2.6[d]	-0.64 ± 4.0	-2.4 ± 2.4	0.002 ± 0.002	-8.0 ± 2.6[d]	-0.56 ± 2.6	0.51 ± 2.6	-2.6 ± 2.5	3.8 ± 3.3
P	.83	.38	.008[d]	.87	.34	.36	.002[d]	.83	.84	.29	.25
t	-0.21	0.88	-2.7[d]	-0.16	-0.96	-0.92	-3.0[d]	-0.22	0.20	-1.1	1.2
GH	-0.15 ± 0.071[d]	-0.41 ± 2.2	-6.2 ± 2.4[d]	-7.3 ± 3.6[d]	-5.8 ± 2.2[d]	0.001 ± 0.002	-2.2 ± 2.4	-0.60 ± 2.3	-5.0 ± 2.5[d]	4.2 ± 2.2[d]	-3.7 ± 2.0[d]
P	.038[d]	.85	.009[d]	.041[d]	.009[d]	.41	.36	.80	.042[d]	.041[d]	.046[d]
t	-2.1[d]	-0.19	-2.6[d]	-2.1[d]	-2.6[d]	0.83	-0.93	-0.26	-2.0[d]	-2.0[d]	-2.0[d]
HC[e]	-0.16 ± 0.077[d]	1.4 ± 2.4	-2.8 ± 2.6	6.6 ± 3.9[d]	-0.63 ± 3.4	-0.004 ± 0.002[d]	-5.9 ± 2.6[d]	-0.83 ± 2.5	-3.4 ± 2.3	2.5 ± 2.4	4.0 ± 3.2
P	.041[d]	.57	.28	.043[d]	.79	.016[d]	.024[d]	.44	.14	.31	.21
t	-2.1[d]	0.57	-1.1	2.0[d]	-0.26	-2.4[d]	-2.3[d]	-0.33	-1.5	1.0	1.2

Higher SF-36 scores are associated with better quality of life. Number of *df* was 1 for all calculations. BP = bodily pain; ER = emotional role limitations; GH = general health perceptions; HC = health change; MH = mental health; PF = physical functioning; SF = social functioning; PR = physical role limitations; VT = vitality. See Table 1 and Table 2 legends for expansion of other abbreviations.

[a]0 = male; 1 = female.

[b]BMI > 30 kg/m^2.

[c]0 = not present; 1 = present.

[d]Statistically significant.

[e]Compared with 1 year ago.

Table 4—*Multivariate Linear Regression Analysis of Absolute SF-36 Scores: Unstandardized Regression Coefficients and Standard Errors of Independent PE and Not-PE-Related Determinants of the SF-36 Subscales Scores*

Subscale	Age, y	Sex	Obesity[ab]	Active Malignancy[b]	Cardiopulmonary Comorbidity[b]	Disease-Free Interval, d	Recurrent VTE[b]	Centrally Located PE	Unprovoked PE[b]	Transient Risk Factor for PE[b]	Permanent Risk Factor for PE[b]	r^2, %	*df*	*F*[c]
PF	-0.25 ± 0.094	…	-7.6 ± 1.7	-9.8 ± 4.4	-8.7 ± 2.9	0.004 ± 0.002	-4.8 ± 2.7	…	…	…	…	12	6/385	9.5
P	.009	…	.006	.028	.003	.026	.045	…	…	…	…	…	…	< .001
t	-2.6	…	-2.8	-2.2	-3.0	2.2	-2.0	…	…	…	…		…	…
SF	0.19 ± 0.080	…	-7.8 ± 2.6	…	-6.1 ± 2.7	0.003 ± 0.002	…	…	…	…	…	4.9	4/387	5.0
P	.031	…	.003	…	.027	.038	…	…	…	…	…	…	…	.001
t	2.2	…	-3.0	…	-2.2	2.1	…	…	…	…	…	…	…	…
PR	…	…	…	-13 ± 7.2	-14 ± 4.3	0.009 ± 0.003	…	…	…	…	…	3.6	3/388	7.0
P	…	…	…	.042	.001	.003	…	…	…	…	…	…	…	< .001
t	…	…	…	-2.0	-3.4	2.9	…	…	…	…	…	…	…	…
ER	…	…	-9.1 ± 4.1	…	…	…	…	…	…	…	…	1.3	1/390	4.9
P	…	…	.027	…	…	…	…	…	…	…	…	…	…	.027
t	…	…	-2.2	…	…	…	…	…	…	…	…	…	…	…
MH	0.12 ± 0.058	…	…	…	…	…	…	…	…	…	…	1.1	1/390	4.5
P	.03	…	…	…	…	…	…	…	…	…	…	…	…	.035
t	2.1	…	…	…	…	…	…	…	…	…	…	…	…	…
VT	…	…	-6.2 ± 2.3	…	…	…	…	…	…	…	…	1.9	1/390	7.4
P	…	…	.007	…	…	…	…	…	…	…	…	…	…	.007
t	…	…	-2.7	…	…	…	…	…	…	…	…	…	…	…
BP	…	…	-6.1 ± 2.6	…	…	…	-7.3 ± 2.6	…	…	…	…	3.7	2/389	7.5
P	…	…	.019	…	…	…	.006	…	…	…	…	…	…	.001
t	…	…	-2.4	…	…	…	-2.8	…	…	…	…	…	…	…
GH	…	…	-5.5 ± 2.4	-6.1 ± 3.5	-4.4 ± 2.2	…	…	…	-3.3 ± 2.0	2.8 ± 2.7	-2.1 ± 1.7	3.8	6/385	5.1
P	…	…	.021	.044	.048	…	…	…	.043	.049	.046	…	…	.002
t	…	…	-2.3	-2.0	-2.0	…	…	…	-2.0	-2.0	-2.0	…	…	…
HC[d]	-0.19 ± 0.078	…	…	8.1 ± 3.9	…	-0.004 ± 0.002	-5.6 ± 2.6	…	…	…	…	5.0	4/387	5.1
P	.013	…	…	.037	…	.011	.030	…	…	…	…	…	…	.001
t	-2.5	…	…	2.1	…	-2.6	-2.2	…	…	…	…	…	…	…

Higher SF-36 scores are associated with better quality of life. See Table 1, 2, and 3 legends for expansion of other abbreviations.

[a]BMI > 30 kg/m^2.

[b]0 = not present; 1 = present.

[c]Analysis of variance.

[d]Compared with 1 year ago.

given that several studies on QoL in patients with conditions closely related to PE, such as DVT, have been published.[23,26] Despite the literature gap on this subject, our study shows that QoL is affected by acute PE and, therefore, should be incorporated in future outcome studies. From all subscales of the SF-36, physical condition (SF-36 subscales physical functioning and role limitations) was affected most by a history of acute PE compared with population norms. Hence, these outcome studies might include cardiopulmonary rehabilitation programs to improve QoL after acute PE. Such programs to improve clinical outcome and QoL have been shown to be very effective after other serious acute cardiovascular events (eg, acute myocardial infarction).[27,28]

The strengths of the study are the novelty of reporting on this issue in this specific group of patients, the sample size of our study population, and the high response rate, making the data broadly generalizable. Even so, patient selection may have influenced our results. The SF-36 was completed by 67% of the surviving patients who were not excluded because of geographical inaccessibility precluding follow-up, language barriers, or the impossibility of providing informed consent. The remaining patients did not participate because they were in excellent health or, in contrast, suffered from severe morbidity. These factors possibly would restrict the range of scores available, which in turn would restrict the associations found using regression coefficients. Nonetheless, because the demographics at initial PE diagnosis of the 392 patients who completed the SF-36 were not different from those of the entire study population, except for the etiology of PE, these former patients are likely to be reasonably representative of a more general PE population. One additional point is that the results of the univariate analysis should be interpreted with caution because they were not corrected for multiple testing.

One specific group of patients requires additional comment. Unfortunately, this analysis did not include patients with chronic thromboembolic pulmonary hypertension because patients with this condition were not invited for a study visit for logistical reasons, and no new cases of this disease were identified by our cardiopulmonary work-up. For this reason, we could not compare QoL in patients with established chronic thromboembolic disease to patients who clinically recovered from the acute event and to population norms. Yet, QoL in patients with pulmonary hypertension has been shown previously to be considerably impaired.[29]

In summary, QoL in patients with a history of acute PE is impaired compared to sex- and age-adjusted population norms. This observation is partly caused by the thromboembolic event itself and by age, obesity, and comorbid conditions. Nonetheless, these independent determinants of QoL cannot explain the total measured effect in our patient population. There is a great need for additional studies on QoL in patients with a history of acute PE concerning such important matters as illness cognitions, coping mechanisms, and self management; the effect of intervening in these; or the effect of other interventions, such as cardiopulmonary rehabilitation programs, on the clinical outcome and QoL of the individual patient. In general, QoL should be incorporated into future studies reporting on the clinical course of acute PE.

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