Received: 1 February 2024 | Accepted: 13 February 2024

https://doi.org/10.1016/j.rpth.2024.102366

ORIGINAL ARTICLE

Physical activity following pulmonary embolism and clinical correlates in selected patients: a cross-sectional study

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Handling Editor: Dr V Morelli

Abstract

Background: There is limited knowledge regarding physical activity and clinical correlates among people who have suffered a pulmonary embolism (PE).

Objectives: To assess physical activity levels after PE and potential clinical correlates.

Methods: One hundred forty-five individuals free of major comorbidities were recruited at a mean of 23 months (range, 6-72) after PE diagnosis. Physical activity was assessed by steps/day on the Sensewear monitor for 7 consecutive days, exercise capacity with the incremental shuttle walk test, and cardiac function with left ventricular ejection fraction (LVEF). The association between physical activity and other variables was analyzed by a mixed-effects model.

Results: Participants achieved a mean of 6494 (SD, 3294; range, 1147-18.486) steps/day. The mixed-effects model showed that physical activity was significantly associated with exercise capacity (β-coefficient, 0.04; 95% CI, 0.03-0.05) and LVEF (β-coefficient, −0.81; 95% CI, −1.42 to −0.21). The analysis further showed that men became less physically active with increasing age (β-coefficient, −0.14; 95% CI, −0.24 to −0.04), whereas no change with age could be detected for women.

Conclusion: In selected post-PE patients, physical activity seems to be associated with exercise capacity and LVEF but not with quality of life, dyspnea, or characteristics of the initial PE. Men appear to become less physically active with increasing age.

KEYWORDS
activity, cardiac function, exercise capacity, pulmonary embolism, quality of life, venous thromboembolism

Essentials

- There is limited knowledge regarding physical activity after pulmonary embolism.
- This study measured daily physical activity after pulmonary embolism.
- Higher physical activity levels were associated with better exercise capacity.
- Men were less physically active with increased age.

1 | INTRODUCTION

Pulmonary embolism (PE) is a major cause of hospitalization and morbidity [1]. Moreover, it is well documented that many PE survivors suffer with bothersome symptoms in the aftermath [2,3]. Various grades of persistent, unexplained dyspnea have been observed in up to 50% of patients more than 6 months after the PE diagnosis [2,3]. In addition, reduced exercise capacity and impaired health-related quality of life (HRQoL) have been observed among people with post-PE dyspnea compared with the general population norms and people without post-PE dyspnea [3–5].

Although some patients display persistent physiological changes, such as chronic thromboembolic pulmonary hypertension (CTEPH) after PE, it is likely that inactivity-induced physical deconditioning following venous thromboembolism (VTE) may contribute to the breathlessness some post-PE patients experience [6,7]. The sensation of dyspnea may lead to fear of physical activity, further aggravating the situation and resulting in subsequent muscle weakness and reduced physical capacity [8,9]. Therefore, patients who suffer from persistent symptoms after PE may benefit from daily physical activity and/or rehabilitation [5,10,11].

In general, a large proportion of healthy people fail to achieve the recommended levels of physical activity [12,13]. Therefore, it is fair to assume that those who experience persistent symptoms in the aftermath of PE may be even more likely to have lower physical activity levels than recommended. Self-reported physical inactivity is associated with increased mortality following VTE [9]. A recent longitudinal observational study exploring self-reported changes in physical activity levels following an acute PE showed that 51% of patients had reduced physical activity levels within the first 3 months compared with their self-reported physical activity level prior to the PE event. Reported explanations for this decrease in physical activity were dyspnea on exertion, fatigue, fear of pain, and fear of PE reoccurrence [11]. This reduction in physical activity continued in 24% of the participants at 6 months post-PE and in 15% at 12 months post-PE, suggesting that physical inactivity may become a long-term behavioral change for some patients. Self-reported physical activity, however, may be prone to recall bias and over- or underreporting [14,15]. Therefore, the validity of these findings is uncertain. Objectively measured physical activity may be a more accurate method for measuring physical activity compared with subjective measures in adult populations [16,17]. To date, objectively measured physical activity levels remain unknown in post-PE patients and there is limited knowledge on the clinical correlates of physical activity levels in this patient group. Nevertheless, it may be reasonable to hypothesize that people with persistent symptoms following PE, such as reduced exercise capacity and dyspnea, are less physically active than PE-patients who make a full recovery.

An increased awareness regarding the clinical correlates for physical activity after PE may lead to improved routines for the assessment, treatment, and prevention of physical inactivity in this population. Therefore, the primary aim of this study was to explore objectively measured physical activity levels in post-PE patients. The secondary aim was to identify clinical correlates for physical activity levels in this patient group.

2 | METHODS

2.1 | Study design

This cross-sectional study assessed baseline data from the PE-Rehab study, a 2-center, randomized controlled trial performed at Østfold Hospital and Akershus University Hospital in Norway [18]. Written informed consent was obtained from all participants. The study was approved by the Regional Committee for Medical and Health Research Ethics (2017/1940/REK South-East D) and registered at ClinicalTrials.gov (NCT03405480) and followed the Helsinki declaration.

2.2 | Study population

A sample of post-PE patients both with and without persistent symptoms was identified from the Thrombosis registry at Østfold Hospital [19] or via International Classification of Diseases, 10th Revision, discharge codes (ICD I26.x) (Akershus University Hospital). Patients were invited to participate by postal mail. Based on equipment availability, a selection of the study participants were assigned an activity monitor for the registering of physical activity (Figure 1). Participants were recruited continuously from January 2018 to May 2021.

Inclusion criteria were age 18 to 75 years, objectively diagnosed symptomatic PE (greater than isolated subsegmental PE) by computerized tomography pulmonary angiogram 6 to 72 months prior to inclusion in the study, and the ability to provide written informed

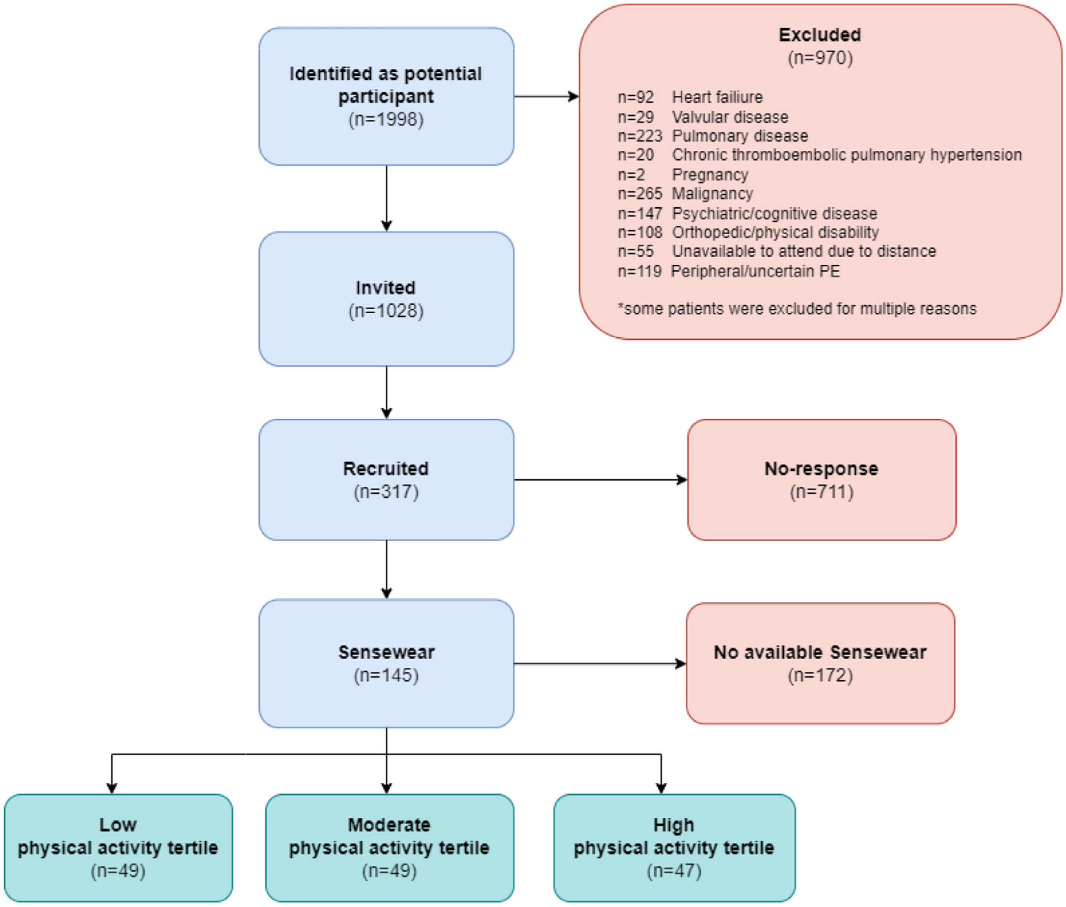


FIGURE 1 Flow chart of the recruitment process. PE, pulmonary embolism.

consent. Exclusion criteria were pulmonary diseases (such as chronic obstructive pulmonary disease [COPD] GOLD stage ≥2 or restrictive pulmonary diseases), heart failure and significant valvular heart disease, CTEPH, other conditions that would interfere with the ability to comply or give informed consent, active malignancy, life expectancy less than 3 months, and/or pregnancy.

2.3 | Physical tests and patient-reported outcome measures on inclusion to the study

2.3.1 | Sensewear activity monitor—daily physical activity

Steps per day, as measured by the Sensewear activity monitor model 7.0 (BodyMedia Inc), were used as proxy of daily physical activity. Sensewear is a lightweight device worn on the upper arm that uses accelometery techniques to estimate energy expenditure [20]. Sensewear is a reliable and valid tool for measuring physical activity in various populations, including people with respiratory disease [21,22]. The participants wore the monitor for 7 consecutive days to measure daily number of steps (daily physical activity).

2.3.2 | Incremental shuttle walk test and Borg scale—exercise capacity

Exercise capacity was assessed using the incremental shuttle walk test (ISWT), which is valid, reliable, and responsive in patients with cardiac and respiratory diseases [23]. ISWT was performed according to standardized guidelines as described in the study protocol [18]. Peripheral oxygen saturation was measured using pulse oximetry. Subjectively perceived dyspnea on exertion was registered using the Borg scale, with participants indicating a score between 6 and 20 before and immediately after the test [24].

2.4 | Patient-reported outcome measures

2.4.1 | Modified Medical Research Council dyspnea scale

The modified Medical Research Council (mMRC) scale is a widely used tool for evaluating the limitation of activities due to dyspnea [25]. Scores range from grade 0 to grade 4, with a higher score indicating worse symptoms of breathlessness.

2.4.2 | Shortness of Breath Questionnaire

The Shortness of Breath Questionnaire (SOBQ) is used for a more in-depth assessment of subjective symptoms of dyspnea associated with activities of daily living [26]. Total scores range from 0 to 120 points, with a higher score indicating a higher degree of dyspnea.

2.4.3 | EQ-5D-5L

The 5-level EQ-5D (EQ-5D-5L) is a questionnaire used to assess generic HRQoL in 5 different dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, as well as a visual analog scale of general health (EQ-VAS). Each dimension ranges from 1 to 5, with a higher score indicating more problems or symptoms [27]. The EQ-VAS ranges from 0 ("worst imaginable state of health") to 100 ("best imaginable state of health"). A transformation of individual dimension scores to EQ-5D index values was performed using crosswalk to the UK 3-level EQ-5D (EQ-5D-3L) Dolan value set [28].

2.4.4 | PE Quality of Life Questionnaire

The PE Quality of Life Questionnaire (PEMB-QoL) is a disease-specific patient-reported outcome measure used to assess HRQoL following PE [29]. PEMB-QoL has 40 items over 6 domains: frequency of complaints, intensity of complaints, social limitations, activities of daily living limitations, work-related problems, and emotional complaints. Scores for each domain were standardized to a 0 to 1 scale. Higher scores indicate poorer HRQoL.

2.5 | Cardiopulmonary tests and data from medical records

2.5.1 | Cardiopulmonary tests at study inclusion

Resting pulmonary function tests (spirometry, whole-body plethysmography, and diffusing capacity of the lung for carbon monoxide [DLCO%]) and resting transthoracic echocardiography (left ventricular ejection fraction [LVEF]) were performed on inclusion in the study.

2.5.2 | PE Severity Index from medical records

Data regarding the severity of the PE at diagnosis was attained retrospectively from medical records. The PE Severity Index (PESI) is a well-validated risk stratification tool that predicts mortality and morbidity [30]. PESI includes 11 variables with higher scores representing higher severity/risk.

2.5.3 | Charlson Comorbidity Index at study inclusion

Charlson Comorbidity Index is a reliable and valid tool used to predict risk of mortality within 1 year of hospitalization in patients with multiple comorbidities. Grading based on total score ranges from 1-2 (mild), 3-4 (moderate), and ≥5 /severe). A higher score indicates higher risk of death [31,32].

2.6 | Statistical analysis

Categorical variables are presented as frequencies with percentages. Continuous variables are reported as mean, SD, and range or median and 25th to 75th percentiles, as appropriate. Tertiles were used to categorize the participants as there is no common consensus regarding cutoffs for physical activity levels based on the mean objectively measured steps per day. The tertiles merely serve a descriptive purpose.

The outcome variable for the analysis was the number of steps per day as a measure of daily physical activity. This was measured on a daily basis over a course of 7 consecutive days for each individual. Data are therefore clustered by individuals, with correlations between measurements taken on the same individual and independence between individuals. The proper analysis for such data is a mixed-effects regression analysis, with individuals as random effects. As the mixed model assumes normally distributed data, a Box-Cox analysis was performed, and the optimal power transformation to achieve this was identified as a square root transformation. Estimations were consequently done on the transformed scale. The initial model included SOBQ, EQ-VAS, PEMB-QoL, body mass index, ISWT, DLCO%, LVEF, PESI score, comorbidities, and employment status as explanatory variables. Furthermore, the model was adjusted for age and sex (sex assigned at birth). An interaction term between sex and age allowed for a sex-specific age association with the outcome. The full model was reduced by a number of backward elimination steps, where each step removed the term with the highest *P* value above .05, followed by a re-estimation of the reduced model. This was continued until all terms showed significance.

Unfortunately, the estimates on the transformed scale do not back-transform individually and hence do not allow for interpretation of how changes in individual terms affect the number of steps per day, independently of the value of the other terms. Plots of back-transformed scenarios, where 1 variable varied and the remaining were fixed at their observed mean, were used for communicating the results on the original scale of steps per day. Issues of multicollinearity were assessed by inspection of the variance inflation factors. Quantile-quantile plots and residuals plots were used for checking normality. All analyses were performed using Stata version 17.0 (StataCorp).

3 | RESULTS

3.1 | Study population

In total, 145 participants were recruited at a mean of 23 months (SD, 17.1; range, 6-72 months) post-PE. Mean age was 60 years (SD, 10.7; range, 26-75 years), and 66% were men. The mean number of steps per day was 6494 (median, 6064; SD, 3294), and only 52% of the participants achieved more than 6000 steps per day (Table 1). Men were, on average, slightly more active than women, with a mean number of steps per day of 6516 and 6449, respectively. Compliance was considered acceptable with participants wearing the Sensewear armband for a mean time of 23.5 hours per day for 6 consecutive days, including weekdays and weekends. The level of comorbidities was low, with 25% having 1 to 2 comorbidities and 3% having 3 or more comorbidities (Table 1). Only 31 participants (21%) scored ≥2 points, and no participants scored 4 points on the mMRC, suggesting a low general dyspnea burden (Table 2). There were no significant differences in the proportion of physical activity assessments per season between the physical activity groups (P = .9) (Supplementary Table S1). Participants in the low physical activity tertile had less than 4848 steps per day (mean, 3268; SD, 1142), and those with more than 7390 steps per day (mean, 10,236; SD, 2562) were categorized as having high physical activity level.

3.2 | Mixed-effect regression analysis

The Box Cox analysis suggested a square root transformation of the outcome to be appropriate for normalizing the data. Ten variables were included in the mixed-effect model based on clinical relevance and univariable regression analyses (SOBQ, EQ-VAS, PEMB-QoL, body mass index, ISWT, DLCO%, LVEF, PESI score, comorbidities, and employment status). An exploratory analysis indicated opposite effects of age for men and women, and consequently, the model was adjusted for age and sex, allowing for a potential interaction. Estimated effect is on the scale of the square root transformed number of steps per day. Only ISWT (β-coefficient, 0.04; 95% CI, 0.03-0.05; P < .001) and LVEF (β-coefficient, −0.81; 95% CI, −1.42 to −0.21; P = .008) remained significant in addition to the interaction between age and sex (Table 3). With no main effect of sex, this implies no age effect for women but declining effects for men (β-coefficient, −0.14; 95% CI, −0.24 to −0.04; P = .007). Prediction curves with 95% confidence bands were created for the variables with significant effects and transformed back to the original scale for interpretation (Figure 2).

The allocation of the Sensewear monitor was affected by logistical issues and equipment availability in the present study. When comparing participants who did and did not (n = 172) wear a Sensewear activity monitor (Supplementary Table S2), we found that patients who were assigned a Sensewear had a significantly longer time since diagnosis (mean, 23 months; SD, 17.2 months) compared with those not assigned a Sensewear (mean, 16 months; SD, 12.2 months).

A descriptive analysis comparing patients based on time since PE diagnosis (under and over 12 months) showed that patients diagnosed more than 12 months prior to inclusion were more likely to have 1 or more comorbidities, were less likely to currently use anticoagulants, and had lower dyspnea scores and better HRQoL (Supplementary Table S3).

4 | DISCUSSION

To the best of our knowledge, this study is the first to objectively measure physical activity levels in post-PE patients using an accelerometer. Our findings suggest that following PE, physical activity levels were low and associated with exercise capacity and cardiac function. In addition, we observed that, on average, men became less physically active with increasing age, whereas women stayed at a constant physical activity level.

Although there was large heterogeneity in the number of steps per day, our findings suggest that the physical activity levels were generally low compared with those in other populations [33,34]. A recent meta-analysis recommended 8000 to 10,000 steps per day as sufficient for reducing the risk of all-cause mortality [35]. In the present study, only 15% achieved more than 10,000 steps per day, whereas half achieved 6000 steps or more. According to a recent national report, the normative Norwegian population has a mean of 8712 steps per day in an age group similar to that in the present study [36]. This level of physical activity was only achieved by 1 in 5 (n = 30) of the participants in the present study. In addition, it is possible that participants made adaptions to their behavior in terms of physical activity in the monitoring period due to awareness of being observed (the Hawthorne effect), such as the observed number of steps per day may overestimate the true physical activity level in the population.

The relatively low physical activity level we observed in post-PE patients may be due to some patients reducing physical activity levels in the aftermath of PE, resulting in deconditioning [37] and a number of steps per day in some participants similar to that reported in patients with COPD and severe asthma [38–40]. Therefore, despite PE being an acute event and the generally low symptom burden and good exercise capacity reported by our participants, long-term consequences in terms of physical inactivity among some post-PE patients may be comparable to those among patients with chronic disease. However, as low physical activity is associated with PE in some studies [9,41,42], it may also have been preexisting and potentially contributed to the initial event. As the physical activity levels prior to PE are unknown in the present study, neither explanation can be conclusively ruled out.

The exclusion criteria in the main randomized controlled trial were CTEPH and other comorbidities, such as cardiac disease and pulmonary disease [18]. Furthermore, participants in the present study had few comorbidities, a low symptom burden, and relatively good HRQoL. As multimorbid patients may struggle to be physically active, our findings may underestimate the true magnitude of physical

TABLE 1 Characteristics for all participants and low, moderate, and high physical activity groups based on steps per day (*N* = 145).

Background variables	All participants *N* = 145	Low PA group *n* = 49 ≤4848 steps/d	Moderate PA group *n* = 49 4849-7331 steps/d	High PA group *n* = 47 ≥7332 steps/d
Steps per day	6494, 6064 (3294) [1147-18,486]	3268, 3363 (1142) [1147-4848]	6130, 61,410 (700) [4915-7331]	10,236, 9768 (2561) [7390-18,486]
Age (y)	60, 60 (10.7) [26-75]	62, 68 (11.4) [318-75]	60, 61 (8.9) [36-75]	57, 57 (11.4) [27-75]
18-44	12 (8)	4 (8)	2 (4)	6 (13)
45-54	33 (23)	9 (18)	11 (22)	13 (28)
55-66	52 (36)	11 (22)	23 (47)	18 (38)
≥67	48 (33)	25 (51)	13 (27)	10 (21)
Sex, men	95 (66)	31 (63)	34 (69)	30 (64)
Body mass index (kg/m^2)	29.8, 28.7 (5.7) [19.6-51.4]	30.2, 29.1 (6.5) [19.6-51.4]	30.8, 29.0 (6.4) [20.2-46.3]	28.4, 27.2 (3.6) [22.6-38.2]
Smoking status				
Never smoked	59 (41)	23 (47)	19 (39)	17 (36)
Former smoker	76 (52)	22 (45)	28 (57)	26 (55)
Current smoker	8 (6)	3 (6)	2 (4)	3 (6)
Missing	2 (1)	1 (2)	0 (0)	1 (2)
Employment status				
Employed/student	68 (47)	14 (29)	24 (49)	30 (64)
Unemployed	16 (11)	6 (12)	7 (14)	3 (6)
Retired	48 (33)	24 (49)	13 (27)	11 (23)
Sick leave	12 (8)	4 (8)	5 (10)	3 (6)
Missing	1 (1)	1 (2)	0 (0)	0 (0)
Charlson Comorbidity Index				
0	105 (72)	29 (59)	39 (80)	37 (79)
1-2	34 (25)	17 (35)	10 (20)	8 (17)
≥3	6 (3)	3 (6)	0 (0)	2 (4)
Incremental shuttle walk test (m)	739, 750 (236) [140-1020]	612, 590 (245) [140-1020]	755, 750 (220) [290-1020]	855, 880 (174) [450-1020]
Missing	1 (1)	0 (0)	1 (2)	0 (0)
Lung function tests				
FEV1%	77 (72.5-80.7)	78 (72.6-82.5)	76.2 (71.7-79.1)	77.9 (74.3-79.7)
Missing	28 (19)	10 (20)	10 (20)	8 (17)
DLCO%	90 (78-99)	87 (76-98)	90 (78-96)	95 (81-102)
Missing	29 (20)	11 (22)	10 (20)	8 (17)
Echocardiography				
Left ventricular ejection fraction (%)	61.5 (58.7-65.0)	62.4 (59.8-65.1)	61.5 (58.8-64.8)	61.2 (56.9-64.1)

Continuous variables are reported as mean, median (SD) [range] or median (25th to 75th percentile) as appropriate. Categorical variables are reported as number (percentage).

DLCO%, diffusing capacity of the lungs for carbon monoxide percent predicted; FEV1%, forced expiratory volume in 1 second percent predicted; PA, physical activity.

inactivity following PE, and physical inactivity may be more common than the current paper shows. Farmakis et al. [37] recently demonstrated that cardiopulmonary exercise limitation is highly prevalent in post-PE patients with and without pre-existing cardiac and respiratory disease. This was particularly prevalent in those with persistent manifestations such as dyspnea.

TABLE 2 Variables related to pulmonary embolism events and patient-reported outcomes measures for all participants and low, moderate, and high physical activity groups based on steps per day (*N* = 145).

Background variables	All participants *N* = 145	Low PA group *n* = 49	Moderate PA group *n* = 49	High PA group *n* = 47
Time since PE (mo)	23, 19 (17.2) [6 to 72]	23, 20 (16.1) [6 to 67]	22, 14 (18.7) [6 to 72]	25, 21 (17.0) [6 to 62]
PESI score	69 (58 to 77)	73 (63 to 78)	68 (61 to 76)	63 (54 to 79)
Missing	12 (8)	4 (8)	4 (8)	4 (9)
Previous venous thromboembolism	29 (20)	8 (16)	11 (22)	10 (21)
Current anticoagulant use	92 (63)	31 (63)	33 (67)	28 (60)
Time anticoagulant used (mo)	6 (6 to 9)	6 (6 to 10)	7 (6 to 9)	6 (6 to 8)
Missing	1 (1)	0 (0)	1 (2)	0 (0)
Time from symptom onset to diagnosis (d)	17, 3 (67) [0 to 700]	10, 3 (17) [0 to 75]	11, 2 (23) [0 to 120]	29, 3 (112) [0 to 700]
Missing	25 (17)	7 (14)	12 (24)	6 (13)
Provoked PE	45 (31)	14 (29)	16 (33)	15 (32)
mMRC, (range, 0 to 4)				
0	34 (23)	13 (27)	7 (14)	14 (30)
1	80 (55)	23 (47)	30 (61)	27 (57)
2	27 (19)	11 (22)	12 (25)	4 (9)
≥3	4 (3)	2 (4)	0 (0)	2 (4)
Shortness of Breath Questionnaire				
Total score (range, 0 to 120)	18, 14 (17) [0 to 96]	20, 15 (21) [2 to 96]	20, 16 (17) [0 to 64]	15, 13 (13) [0 to 49]
EQ-5D-5L				
EQ-5D index (range, −0.594 to 1.000)	0.83 (0.72 to 1)	0.86 (0.74 to 1)	0.80 (0.68 to 0.84)	0.84 (0.74 to 1)
EQ-VAS (range, 0 to 100)	70 (52.5 to 80.0)	68 (60.0 to 80.0)	60 (50.0 to 77.5)	75 (60.0 to 85.0)
Missing	1 (1)	0 (0)	1 (2)	0 (0)
PEMB-QoL				
Total score (range, 0 to 1)	0.29 (0.26 to 0.35)	0.30 (0.26 to 0.36)	0.30 (0.26 to 0.36)	0.28 (0.25 to 0.33)
Missing	1 (1)	0 (0)	1 (2)	0 (0)

Continuous variables are reported as mean, median (SD) [range] or median (25th to 75th percentile) as appropriate. Categorical variables are reported as number (percent).

EQ-5D-5L, 5-level EQ-5D; EQ-VAS, visual analog scale of general health; mMRC, modified Medical Research Council dyspnea scale; PA, physical activity; PE, pulmonary embolism; PEMB-QoL, Pulmonary Embolism Quality of Life Questionnaire; PESI, Pulmonary Embolism Severity Index.

We observed an inverse relationship between steps per day and LVEF. However, we excluded all participants with known heart failure at inclusion, including heart failure with reduced LVEF and preserved LVEF [43]. A mildly reduced or borderline resting LVEF can sometimes be seen in athletes due to increased cardiac volumes but is unlikely to be the explanation in our study [44]. Furthermore, due to our exclusion criteria, all participants had an LVEF within the normal range. Thus, the small association between LVEF and steps per day in the present study was considered to be of limited clinical relevance. Focus in future studies could be variables other than LVEF that may better explain the effect of cardiac function on daily physical activity.

Our findings showed that higher levels of physical activity were associated with better exercise capacity. Although other clinical correlates, such as symptoms of dyspnea, did not have statistically significant associations with physical activity, they may still be clinically significant. Due to our response rate and inclusion and exclusion criteria, we may have been unable to explore the potential associations between physical activity and clinical correlates in less healthy patients with PE. In post-PE patients observed from acute hospitalization, Danielsbacka et al. [11] showed that patients with more severe dyspnea scores were less physically active than those with lower dyspnea scores. In contrast, we recruited patients from 6 months after the acute PE event and found no significant association between self-reported dyspnea and physical activity. Furthermore, participants tended to have low levels of dyspnea as measured on mMRC and SOBQ. Our findings may suggest that even post-PE patients with less dyspnea are more physically inactive compared with normative populations.

TABLE 3 Estimated coefficients of significant effects from the mixed model analysis of the transformed number of steps per day.

Background variables	Estimate/β-coefficient	SE	95% CI	P value
Incremental shuttle walk test	0.04	0.006	0.03 to 0.05	<.001
Left ventricular ejection fraction	−0.81	0.309	−1.42 to −0.21	.008
Age effect males	−0.14	0.051	−0.24 to −0.04	.007

Note that the estimated coefficients apply linearly on the transformed scale (the square root of the daily number of steps). They do not have individual interpretations on the original scale but act as a compound in the back transformation.

The relationship between daily physical activity levels and exercise capacity in other patient groups, such as COPD, is somewhat unclear. Some studies show a positive correlation between physical activity and walking tests [45,46]. However, Zwerink et al. [47] demonstrated a moderate to weak correlation between steps per day and exercise capacity on the ISWT. Several studies have explored the association between exercise capacity and the effect of pulmonary rehabilitation on physical activity levels [45,48,49], with higher exercise tolerance being associated with an increase in daily physical activities following rehabilitation [48]. Furthermore, it has been suggested that people with better exercise tolerance may have greater potential to improve physical activity levels due to higher functional reserve than those with poorer exercise capacity and lower reserves [50].

In concurrence with previous studies, our findings support the hypothesis that exercise capacity may be related to physical activity, suggesting that rehabilitation, including structured exercise training, may be beneficial in improving exercise capacity and reducing dyspnea in patients who suffer persistent symptoms following PE [5,10,11]. Similarly, a study investigating the safety of exercise in patients who have experienced VTE showed an increase in time spent performing physical activity in favor of the intervention group [51]. However, an increase in physical capacity following pulmonary rehabilitation did generally not translate into improved physical activity levels in people with COPD [45,49]. Specific behavioral interventions and physical activity coaching in combination with exercise training may be required to achieve long-term changes in lifestyle and physical activity habits [47]. Previous findings regarding sex differences and physical activity are somewhat inconclusive [52–55], and in the current study, low levels of physical activity were seen in both sexes. Interestingly, our analyses also showed that men became less physically active with increasing age, whereas women had no change in physical activity. This may suggest that interventions for behavioral change and physical activity following PE should particularly be targeted toward aging men.

Chronic thromboembolic disease (CTED) and residual perfusion defects may potentially be important contributors to functional limitations. However, due to the lack of a clear diagnostic definition, we did not collect data regarding patients who may have had CTED. A prospective study into impairment in patients with CTEPH after PE found that 94% reported lower HRQoL and presented a combination of echocardiographic and clinical signs of cardiopulmonary limitation. In addition, patients with CTEPH had a higher risk of hospitalization and death [56]. All participants in the current study were assessed for CTEPH and CTED by echocardiography and ventilation/perfusion scintigraphy and were referred for right heart catheterization if CTEPH was suspected. Patients with CTEPH were excluded; thus, it is likely that our findings may underestimate the true presentation of this subgroup of patients with more severe complications after PE.

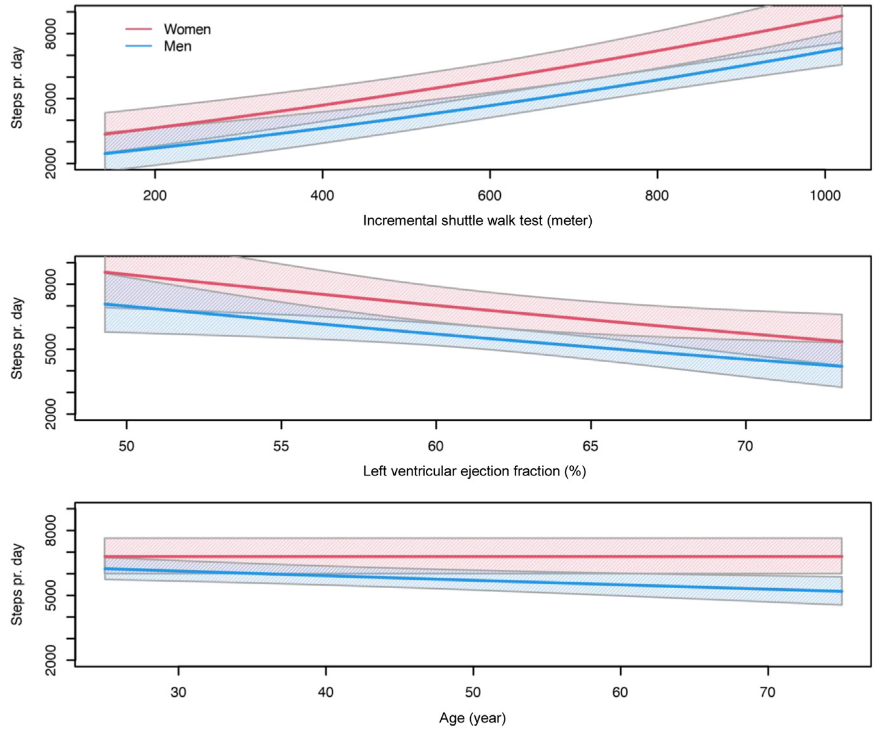
Factors related to the initial PE event, such as time from symptom onset to diagnosis, unprovoked PE, and the radiological extent of the initial PE, have in other studies been linked to residual perfusion defects [57,58]. We initially hypothesized an association between factors related to the initial PE event and physical activity, as this association could have been mediated by residual perfusion defects, but no association was observed. However, the lack of association could be explained by recall bias due to long length of time since diagnosis or poor quality of or lack of compliance to anticoagulation [59,60], but data on this were not collected.

This is, to our best knowledge, the first study to explore objective physical activity following PE, where all participants underwent a comprehensive clinical assessment. Use of the Sensewear accelerometer has previously been shown to be reliable and valid when measuring physical activity levels [17,61]. However, objective measuring of physical activity has some limitations, such as high cost, difficulties with administration, and the risk that the monitor does not register all forms and intensities of movement [17].

Previous findings show that participants in research studies may have fewer symptoms and better physical function and health literacy compared with those in nonresponders [62–64]. The main limitations of the current study include the lack of a control group and baseline characteristics of nonresponders. We had no reports on physical activity levels prior to the PE event, and we were unable to evaluate changes in physical activity levels in the post-PE phase. Moreover, we did not collect data on participants' race and ethnicity and are unable to consider sociocultural determinants of health. Due to the wide time frame since PE diagnosis (6-72 months) and the lack of a fixed time point for the follow-up assessment, our findings must be interpreted with caution. Our descriptive analysis comparing patients based on time since PE diagnosis showed that these patients differed in terms of baseline characteristics, which may be explained by the natural development of the condition.

Additionally, although the cross-sectional nature of the study may identify potential associations between physical activity and other variables, it cannot define direct causation due to the nonrandomized nature. Although participants were recruited from 2 centers, national and international generalizability may be limited by cultural and geographical differences potentially affecting health and physical activity profiles [65]. In order to explore the true magnitude of physical

FIGURE 2 Predicted mean number of steps per day with 95% confidence bands by explanatory variables, retrieved by back transformation from the square root scale. For each of the 3 variables depicted, the 2 other variables were kept fixed at their observed median values.



activity behaviors in this patient group, future studies should have larger sample sizes and include patients with multiple comorbidities. The current statistical analysis aimed to address the clinical questions by use of a backward elimination approach on the mixed-effects model. It is well known that obtaining a final model this way is not unambiguous and may be subject to various pitfalls. We have strived at avoiding these by checking model assumptions, independence of covariates, inspecting potential and relevant interaction effects, and refraining from automatic variable selection. The model was built to capture all major variation in physical activity by means of a minimal set of variables related to the clinical question.

5 | CONCLUSION

Our findings suggest that physical inactivity is prevalent after PE in selected patients with various grades of persistent complaints. We found no associations between physical activity and PE characteristics or pulmonary function. However, physical activity levels appear to be related to exercise capacity, and a sex effect was observed, with men becoming less physically active with increasing age. Interventions aimed at increasing exercise capacity and reducing dyspnea may be beneficial in maintaining and improving physical activity levels in these patients.

ACKNOWLEDGMENTS

The authors wish to thank all the patients who participated in the study and the health professionals who contributed to the collection of data, especially Mats Grensemo, Trude Støver, Anna Roger Heranger, and Amalie Berg Riise for their contributions to data collection and Hanne Fjåll Larssen, Eva Engen, and Janne Katrin Gundersen for performing the pulmonary function tests.

FUNDING

The PE-Rehab study is funded by the Østfold Hospital.

ETHICS STATEMENT

The study was approved by the Regional Committee for Medical and Health Research Ethics (2017/1940/REK South-East D) and registered at ClinicalTrials.gov (NCT03405480) and followed the Declaration of Helsinki. Written informed consent was obtained from all participants.

AUTHOR CONTRIBUTIONS

All authors were responsible for the design of the study. S.H.-P. and Ø.J. were responsible for data collection. S.H.-P. and R.H. performed the statistical analyses. S.H.-P. drafted the manuscript. All authors have contributed to the interpretation of the results, revision of the text, and approved the final version of the manuscript.

RELATIONSHIP DISCLOSURE

W.G. reports fees for participation in advisory board from Amgen, Novartis, Pfizer, Principia Biopharma Inc–a Sanofi Company, Sanofi, SOBI, Grifols, UCB, Argenx, Cellphire; lecture honoraria from Amgen, Novartis, Pfizer, Bristol Myers Squibb, SOBI, Grifols, Sanofi, and Bayer; and research grants from Bayer, BMS/Pfizer, and UCB. M.A.S. has obtained research grants from Netherlands Lung Foundation and Stichting Astma Bestrijding, outside the scope of the current study; research grants from AstraZeneca, TEVA, Chiesi, and Boehringer Ingelheim outside the scope of the current study; and consultancy fees from AstraZeneca and Boehringer Ingelheim for advisory boards outside the scope of the current study. All research grants and consultancy fees were paid to CIRO+. The remaining authors declare that they have no conflict of interest.

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REFERENCES

[1] Huisman MV, Barco S, Cannegieter SC, Le Gal G, Konstantinides SV, Reitsma PH, et al. Pulmonary embolism. *Nat Rev Dis Primers*. 2018;4:18028. https://doi.org/10.1038/nrdp.2018.28

[2] Klok FA, Tijmensen JE, Haeck ML, van Kralingen KW, Huisman MV. Persistent dyspnea complaints at long-term follow-up after an episode of acute pulmonary embolism: results of a questionnaire. *Eur J Intern Med*. 2008;19:625–9.

[3] Tavoly M, Utne KK, Jelsness-Jørgensen LP, Wik HS, Klok FA, Sandset PM, et al. Health-related quality of life after pulmonary embolism: a cross-sectional study. *BMJ Open*. 2016;6:e013086. https://doi.org/10.1136/bmjopen-2016-013086

[4] Ghanima W, Wik HS, Tavoly M, Enden T, Jelsness-Jørgensen LP. Late consequences of venous thromboembolism: measuring quality of life after deep vein thrombosis and pulmonary embolism. *Thromb Res*. 2018;164:170–6.

[5] Kahn SR, Hirsch AM, Akaberi A, Hernandez P, Anderson DR, Wells PS, et al. Functional and exercise limitations after a first episode of pulmonary embolism: results of the ELOPE prospective cohort study. *Chest*. 2017;151:1058–68.

[6] Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): the Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Respir J*. 2019;54:1901647. https://doi.org/10.1183/13993003.01647-2019

[7] Klok FA, Zondag W, van Kralingen KW, van Dijk AP, Tamsma JT, Heyning FH, et al. Patient outcomes after acute pulmonary embolism. A pooled survival analysis of different adverse events. *Am J Respir Crit Care Med*. 2010;181:501–6.

[8] Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med*. 2013;188:e13–64.

[9] Evensen LH, Isaksen T, Braekkan SK, Hansen JB. Physical activity and risk of recurrence and mortality after incident venous thromboembolism. *J Thromb Haemost*. 2019;17:901–11.

[10] Klok FA, Barco S. Follow-up after acute pulmonary embolism. *Hamostaseologie*. 2018;38:22–32.

[11] Danielsbacka JS, Hansson PO, Mannerkorpi K, Olsén MF. Physical activity and respiratory symptoms after pulmonary embolism. A longitudinal observational study. *Thromb Res*. 2020;189:55–60.

[12] Guthold R, Stevens GA, Riley LM, Bull FC. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1.9 million participants. *Lancet Glob Health*. 2018;6:e1077–86.

[13] Kohl 3rd HW, Craig CL, Lambert EV, Inoue S, Alkandari JR, Leetongin G, et al. The pandemic of physical inactivity: global action for public health. *Lancet*. 2012;380:294–305.

[14] Pitta F, Troosters T, Spruit MA, Decramer M, Gosselink R. Activity monitoring for assessment of physical activities in daily life in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil*. 2005;86:1979–85.

[15] Prince SA, Adamo KB, Hamel ME, Hardt J, Connor Gorber S, Tremblay M. A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *Int J Behav Nutr Phys Act*. 2008;5:56. https://doi.org/10.1186/1479-5868-5-56

[16] Dyrstad SM, Hansen BH, Holme IM, Anderssen SA. Comparison of self-reported versus accelerometer-measured physical activity. *Med Sci Sports Exerc*. 2014;46:99–106.

[17] Tudor-Locke CE, Myers AM. Challenges and opportunities for measuring physical activity in sedentary adults. *Sports Med*. 2001;31:91–100.

[18] Haukeland-Parker S, Jervan Ø, Johannessen HH, Gleditsch J, Stavem K, Steine K, et al. Pulmonary rehabilitation to improve physical capacity, dyspnea, and quality of life following pulmonary embolism (the PeRehab study): study protocol for a two-center randomized controlled trial. *Trials*. 2021;22:22. https://doi.org/10.1186/s13063-020-04940-9

[19] Jørgensen CT, Tavoly M, Pettersen HH, Førsund E, Roaldsnes C, Olsen MK, et al. The venous thrombosis registry in Østfold Hospital (TROLL registry) - design and cohort description. *Res Pract Thromb Haemost*. 2022;6:10.1002/rth2.12770. https://doi.org/10.1002/rth2.12770

[20] Langer D, Gosselink R, Sena R, Burtin C, Decramer M, Troosters T. Validation of two activity monitors in patients with COPD. *Thorax*. 2009;64:641–2.

[21] Vooijs M, Alpay LL, Snoeck-Stroband JB, Beerthuizen T, Siemonsma PC, Abbink JJ, et al. Validity and usability of low-cost accelerometers for internet-based self-monitoring of physical activity in patients with chronic obstructive pulmonary disease. *Interact J Med Res*. 2014;3:e14. https://doi.org/10.2196/ijmr.3056

[22] Farooqi N, Slinde F, Håglin L, Sandström T. Validation of SenseWear armband and ActiHeart monitors for assessments of daily energy expenditure in free-living women with chronic obstructive pulmonary disease. *Physiol Rep*. 2013;1:e00150. https://doi.org/10.1002/phy2.150

[23] Parreira VF, Janaudis-Ferreira T, Evans RA, Mathur S, Goldstein RS, Brooks D. Measurement properties of the incremental shuttle walk test. A systematic review. *Chest*. 2014;145:1357–69.

[24] Borg G, Linderholm H. Exercise performance and perceived exertion in patients with coronary insufficiency, arterial hypertension and vasoregulatory asthenia. *Acta Med Scand*. 1970;187:17–26.

[25] Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. *Chest*. 1988;93:580–6.

[26] Eakin EG, Resnikoff PM, Prewitt LM, Ries AL, Kaplan RM. Validation of a new dyspnea measure: the UCSD Shortness of Breath Questionnaire. University of California, San Diego. *Chest*. 1998;113:619–24.

[27] Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20:1727–36.

[28] Dolan P. Modeling valuations for EuroQol health states. *Med Care*. 1997;35:1095–108.

[29] Klok FA, Cohn DM, Middeldorp S, Scharloo M, Büller HR, van Kralingen KW, et al. Quality of life after pulmonary embolism: validation of the PEmb-QoL Questionnaire. *J Thromb Haemost*. 2010;8:523–32.

[30] Aujesky D, Obrosky DS, Stone RA, Auble TE, Perrier A, Cornuz J, et al. Derivation and validation of a prognostic model for pulmonary embolism. *Am J Respir Crit Care Med*. 2005;172:1041–6.

[31] Charlson ME, Carrozzino D, Guidi J, Patierno C. Charlson Comorbidity Index: a critical review of clinimetric properties. *Psychother Psychosom*. 2022;91:8–35.

[32] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–83.

[33] Tudor-Locke C, Bassett Jr DR. How many steps/day are enough? Preliminary pedometer indices for public health. *Sports Med*. 2004;34:1–8.

[34] Tudor-Locke C, Craig CL, Aoyagi Y, Bell RC, Croteau KA, De Bourdeaudhuij I, et al. How many steps/day are enough? For older adults and special populations. *Int J Behav Nutr Phys Act*. 2011;8:80. https://doi.org/10.1186/1479-5868-8-80
[35] Paluch AE, Bajpai S, Bassett DR, Carnethon MR, Ekelund U, Evenson KR, et al. Daily steps and all-cause mortality: a meta-analysis of 15 international cohorts. *Lancet Public Health*. 2022;7:e219–28.
[36] Helsedirektoratet. Nye råd om fysisk aktivitet og stillesitting – hvert eneste minutt teller; 2022. https://www.helsedirektoratet.no/nyheter/nye-rad-om-fysisk-aktivitet-og-stillesitting–hvert-eneste-minutt-teller; 2023. [accessed March 19, 2024].
[37] Farmakis IT, Valerio L, Barco S, Alsheimer E, Ewert R, Giannakoulas G, et al. Cardiopulmonary exercise testing during follow-up after acute pulmonary embolism. *Eur Respir J*. 2023;61:2300059. https://doi.org/10.1183/13993003.00059-2023
[38] Neale J, Orme MW, Majd S, Chantrell S, Singh SJ, Bradding P, et al. A comparison of daily physical activity profiles between adults with severe asthma and healthy controls. *Eur Respir J*. 2020;56:1902219. https://doi.org/10.1183/13993003.02219-2019
[39] Blondeel A, Demeyer H, Janssens W, Troosters T. The role of physical activity in the context of pulmonary rehabilitation. *COPD*. 2018;15:632–9.
[40] Wickerson L, Mathur S, Singer LG, Brooks D. Physical activity levels early after lung transplantation. *Phys Ther*. 2015;95:517–25.
[41] Kunutsor SK, Mäkikallio TH, Seidu S, de Araújo CGS, Dey RS, Blom AW, et al. Physical activity and risk of venous thromboembolism: systematic review and meta-analysis of prospective cohort studies. *Eur J Epidemiol*. 2020;35:431–42.
[42] Evensen LH, Brækkan SK, Hansen JB. Regular physical activity and risk of venous thromboembolism. *Semin Thromb Hemost*. 2018;44:765–79.
[43] McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al, ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42:3599–726.
[44] Baggish AL, Wood MJ. Athlete's heart and cardiovascular care of the athlete: scientific and clinical update. *Circulation*. 2011;123:2723–35.
[45] Kanao K, Shiraishi M, Higashimoto Y, Maeda K, Sugiya R, Okajima S, et al. Factors associated with the effect of pulmonary rehabilitation on physical activity in patients with chronic obstructive pulmonary disease. *Geriatr Gerontol Int*. 2017;17:17–23.
[46] Johnson-Warrington V, Harrison S, Mitchell K, Steiner M, Morgan M, Singh S. Exercise capacity and physical activity in patients with COPD and healthy subjects classified as Medical Research Council dyspnea scale grade 2. *J Cardiopulm Rehabil Prev*. 2014;34:150–4.
[47] Zwerink M, van der Palen J, van der Valk P, Brusse-Keizer M, Effing T. Relationship between daily physical activity and exercise capacity in patients with COPD. *Respir Med*. 2013;107:242–8.
[48] Osadnik CR, Loeckx M, Louvaris Z, Demeyer H, Langer D, Rodrigues FM, et al. The likelihood of improving physical activity after pulmonary rehabilitation is increased in patients with COPD who have better exercise tolerance. *Int J Chron Obstruct Pulmon Dis*. 2018;13:3515–27.
[49] Mesquita R, Meijer K, Pitta F, Azcuna H, Goërtz YMJ, Essers JMN, et al. Changes in physical activity and sedentary behaviour following pulmonary rehabilitation in patients with COPD. *Respir Med*. 2017;126:122–9.
[50] Langer D, Demeyer H. Interventions to modify physical activity in patients with COPD: where do we go from here? *Eur Respir J*. 2016;48:14–7.
[51] Lakoski SG, Savage PD, Berkman AM, Penalosa L, Crocker A, Ades PA, et al. The safety and efficacy of early-initiation exercise training after acute venous thromboembolism: a randomized clinical trial. *J Thromb Haemost*. 2015;13:1238–44.
[52] Li W, Procter-Gray E, Churchill L, Crouter SE, Kane K, Tian J, et al. Gender and age differences in levels, types and locations of physical activity among older adults living in car-dependent neighborhoods. *J Frailty Aging*. 2017;6:129–35.
[53] Liao YH, Kao TW, Peng TC, Chang YW. Gender differences in the association between physical activity and health-related quality of life among community-dwelling elders. *Aging Clin Exp Res*. 2021;33:901–8.
[54] Azevedo MR, Araújo CL, Reichert FF, Siqueira FV, da Silva MC, Hallal PC. Gender differences in leisure-time physical activity. *Int J Public Health*. 2007;52:8–15.
[55] Oliveira AJ, Lopes CS, Rostila M, Werneck GL, Griep RH, Leon AC, et al. Gender differences in social support and leisure-time physical activity. *Rev Saude Publica*. 2014;48:602–12.
[56] Valerio L, Mavromanoli AC, Barco S, Abele C, Becker D, Bruch L, et al. Chronic thromboembolic pulmonary hypertension and impairment after pulmonary embolism: the FOCUS study. *Eur Heart J*. 2022;43:3387–98.
[57] Jervan Ø, Dhayyat A, Gleditsch J, Haukeland-Parker S, Tavoly M, Klok FA, et al. Demographic, clinical, and echocardiographic factors associated with residual perfusion defects beyond six months after pulmonary embolism. *Thromb Res*. 2023;229:7–14.
[58] Sanchez O, Helley D, Couchon S, Roux A, Delaval A, Trinquart L, et al. Perfusion defects after pulmonary embolism: risk factors and clinical significance. *J Thromb Haemost*. 2010;8:1248–55.
[59] Spyropoulos AC, Preblick R, Kwong WJ, Lingohr-Smith M, Lin J. Is adherence to the American College of Chest Physicians recommended anticoagulation treatment duration associated with different outcomes among patients with venous thromboembolism? *Clin Appl Thromb Hemost*. 2017;23:532–41.
[60] Speed V, Auyeung V, Patel JP, Cooper D, Miller S, Roberts LN, et al. Adherence to rivaroxaban for the treatment of venous thromboembolism-results from the FIRST registry. *Res Pract Thromb Haemost*. 2021;5:e12614. https://doi.org/10.1002/rth2.12614
[61] McNamara RJ, Tsai LL, Wootton SL, Ng LW, Dale MT, McKeough ZJ, et al. Measurement of daily physical activity using the SenseWear armband: compliance, comfort, adverse side effects and usability. *Chron Respir Dis*. 2016;13:144–54.
[62] Atkinson G, Williamson P, Batterham AM. Issues in the determination of 'responders' and 'non-responders' in physiological research. *Exp Physiol*. 2019;104:1215–25.
[63] Johnson TP, Wislar JS. Response rates and nonresponse errors in surveys. *JAMA*. 2012;307:1805–6.
[64] Barriball KL, While AE. Non-response in survey research: a methodological discussion and development of an explanatory model. *J Adv Nurs*. 1999;30:677–86.
[65] Pitta F, Breyer MK, Hernandes NA, Teixeira D, Sant'Anna TJ, Fontana AD, et al. Comparison of daily physical activity between COPD patients from Central Europe and South America. *Respir Med*. 2009;103:421–6.

SUPPLEMENTARY MATERIAL

The online version contains supplementary material available at https://doi.org/10.1016/j.rpth.2024.102366.