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Article

Investigation of Health-Related Quality of Life, Anxiety and Satisfaction in Patients with Pulmonary Embolism during the COVID-19 Pandemic

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Abstract: Background: Features of post-traumatic stress disorder and anxiety may be present in Pulmonary Embolism (PE) patients along with impaired Quality of Life (QoL). We aim to evaluate health related QoL, anxiety and satisfaction with life, during the pandemic, in patients with a PE. **Methods:** Patients with PE were enrolled during their follow-up. All participants completed the Short Form 36 (SF-36) questionnaire, the State Trait Anxiety Inventory (STAI) X1 and X2 form, and the Satisfaction with Life Scale (SWLS). **Results:** 92 PE patients were included (mean age±SD=62.50±15.33 years, 56.5% males). Most of the mean values of the SF36 subscales were above the normative value except for "physical role functioning") (45.92±42.41). "Emotional role functioning" (51.26±43.31) and "general health perceptions" (GH) (54.02±18.79) were slightly above the normative value of 50. Mean STAIX1 levels were 37.05±11.17 and mean STAIX2 levels were 39.80±10.47. Mean SWLS levels were 23.31±6.58. According to multiple linear regression analysis, mental healthscore (MH) and GH were predictive of SWLS($F(10,76) = 10.576$, $p<0.001$, $R2=0.581$). MH score ($\beta=-0.242$, $p<0.01$), and STAIX1 ($\beta=0.312$, $p<0.001$) ($F(9,77)=26.445$, $p<0.001$, $R2=0.756$) were predictive of STAIX2. **Conclusions:** Patients with PE exhibit light satisfaction with life, borderline anxiety and below the average in some subscales of QoL.

Keywords: anxiety; pulmonary embolism; quality of life; satisfaction with life; thrombosis; thromboembolism

1. Introduction

Venous thromboembolism (VTE) is a common disorder that includes pulmonary embolism (PE) and deep vein thrombosis (DVT) [1,2]. PE is the most serious manifestationof VTE accounting for approximately 300.000 deaths annually in USA [3]. With timely treatment, many of the survivors fully recover within months [1]. However, some of them may experience long term sequelae, such as chronic thromboembolic disease. Interestingly, the long-term psychological consequences of PE are less well understood and only scarcely studied in the literature.

Changes in health-related (HR) QoLis an important outcome in several medical conditions and is related to the presence of chronic disease and/or the associated risk factors; impaired HRQoLis closely linked to mortalityin both chronic diseases and the general population [4,5]. The definition of

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HRQoL encompasses the patients' self-reported impact of the disease and its' associated treatment on his/her physical, mental and social functioning and wellbeing [6]. Satisfaction with life is a broader component of subjective wellbeing through which individuals address the quality of their life as claimed by their own criteria that depend on their personal priorities of life [7]. Life satisfaction can be used as a promising tool for the assessment of positive psychological attributes which may be linked to changes in mortality and life expectancy [8]. Anxiety trait refers to the persons' tendency to present state anxiety. State anxiety mirrors the psychological and physical reactions directly related to demanding situations in a specific moment [9]. The measurement anddistinction between those two aspects is mandatory for the assessment and follow-up of an individuals' anxiety levels, while it may help to effectively manage anxiety [10].

The impact of PE may extend beyond the physical consequences of the disease. PE can be considered as a health-related crisis due to various reasons including: the experience of an acute and life-threatening diagnosis, with potentially invasive treatment, the long-term use of anticoagulants, the fear of recurrences, chronic complications and/or adverse events due to anticoagulant use [11]. Features of post-traumatic stress disorder and anxiety may be present in some PE patients [12], while impaired QoL may be found in most of them following the acute event [13]. The understanding of the effect of PE recovery to psychological and mental wellbeing merits research.

Since the year 2019 that it was first reported, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), is accountable as one of the greater global pandemics in modern history [14]. Despite the governmental restrictions, nationals' lockdowns and safety measures in Greece the virus was spread leading to several hospital admissions and deaths [15]. PE is one severe complication associated with COVID-19 [16] and a pre-existing PE in a patient may complicate the COVID-19 infection [17]. It has been reported that many patients suffering from various diseases have modified their health visits during global pandemic and experienced psychological distress and poor QoL [18–20].

We hypothesized that patients with PE may present impaired HRQoL which may be associated with anxiety and life satisfaction. We chose anxiety and satisfaction with life, since they both present important aspects of mental health in the general population but they have not been examined previously (as for satisfaction with life) or they have not been examined thoroughly (as for anxiety) in the PE population [21]. To this end, we aimed to evaluate HRQoL, anxiety and satisfaction with life in PE patients. Additionally, we sought to address possible correlations between the aforementioned mental health aspects.

2. Materials and Methods

Patients with PE with or without DVT were enrolled consecutively between April 2020 and June 2021 during their follow-up at the PE Outpatient Clinic of the Respiratory Medicine Department of the University Hospital of Larissa, Greece. All participants had confirmed PE by Computed Tomography Pulmonary Angiography (CTPA). Concurrent DVT was diagnosed with whole leg compression ultrasonography. Demographic and clinical characteristics of the patients were recorded. Unprovoked PE was defined as PE occurring in the absence of transient or persistent major or intermediate risk factors [1,22]. Acute right heart dysfunction was diagnosed according to current guidelines [1]. High risk PE was defined as PE occurring in the context of hemodynamic instability [1]. All participants completed the SF-36 questionnaire, the State Trait Anxiety Inventory (STAI) form X-1 (STAIX1) and form X-2 (STAIX2) and the Satisfaction with Life Scale (SWLS). We used the Short Form 36 (SF-36) questionnaire that addresses HRQoL. SF-36 provides an accurate estimate of the impact of illnesses on a patient's quality of life [23] and is considered the most extensively validated measure of QoL in various populations [24]. The Short Form 36 (SF-36) questionnaire is validated in the Greek language [25]. SF-36 consists of eight subscales: vitality (VT), physical functioning (PF), bodily pain (BP), general health perceptions (GH), physical role functioning (RP), emotional role functioning (RE), social role functioning (SF) and mental health (MH). Each subscale is rated between 0-100 with higher scores indicating better health status. A mean score of 50 has been considered a normative value for all subscales [13,26].

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We administered the STAIX1 and X2 form that assesses state and trait anxiety, respectively. The instrument presents high inner validity for the clinical diagnosis [27]. Trait anxiety was assessed by the STAIX2 that refers to anxiety as a personality trait [28]. The STAI-X2 includes questions relating to how one feels generally. State anxiety was assessed by the STAIX1 that refers to anxiety as a condition. The STAIX1 asks respondents about how they currently feel and STAIX2 about they generally feel. Scores range from 20–80. Higher scores suggest higher trait or state anxiety. Clinically significant anxiety corresponds to scores over 39 [29]. The STAI questionnaire is validated in the Greek language [30].

Finally, we used the SWLS which measures subjective cognitive judgments of satisfaction with one's life and is considered a valid and reliable instrument in various populations [7]. The SWLS is a 5-item instrument designed to measure global cognitive judgments of satisfaction with one's life [31,32]. The total score ranges from 5 to 35. Subjects with higher scores present higher satisfaction with life. Scores between 5-9 suggest that the respondent is "extremely dissatisfied" with life, scores of 10-14 indicate the respondent is "dissatisfied", score between 15-19 suggest the respondent is "slightly dissatisfied", a score of 20 is considered "neutral", a score between 21-25 indicates the respondent is "slightly satisfied", score of 26-30 suggests the respondent is "satisfied" whereas scores between 31-35 indicate the respondent is "extremely satisfied" [31].

Statistical Analysis

Data are presented as mean±SD or as percentages. Normal distribution was assessed by the Kolmogorov-Smirnov test. Univariate correlations were performed by Pearson's correlation coefficient or by Spearman's correlation coefficient according to the variable's distribution. Chi-square test, Fischer's exact test or Student's t-test was used for the univariate analysis. The results of the SF36 subscales were categorized as "below average" when the value was ≤50 and "over average" when the value was >50 since the cut-off of 50 is considered a normative value for all subscales [13,26]. For STAIX1 and STAIX2 we used the cut off 39 and categorized participants as having "high score" if the value was >39 and "low score" if the values was ≤39 [29]. We performed multiple linear regression analysis with SF36 subscales, STAIX1, STAIX2 and SWLS scores as the dependent variable. Variables with a significance level below <0.05 were retained for the analysis and served as possible independent predictors. The coefficient of determination (R squared, R^2) was used to estimate the percentage of effect explained by the model. The significance level was set at $p<0.05$. The sample size was calculated to provide a power of 80% (a=0.05 by two-sided test), with a 10% margin error. For our sample (92 subjects) the margin of error is 2.84 (https://www.enterprise-development.org/measuring-results-the-dced-standard/sample-size-calculator/). Analysis was performed using the SPSS 20 statistical package (SPSS Chicago, IL).

3. Results

The study included 92 PE patients. The patients' sociodemographic characteristics are summarized in Table 1. Mean age (±SD) was 62.50±15.33 years and 56.5% were male. Mean disease duration was 9.58±12.43 months. Most patients (52.2%) reported dyspnea at diagnosis,8.7% of subjects had a history of recurrence, 43.5% had unprovoked VTE, 92.4% were on direct oral anticoagulant therapy and 8.7% reported minor hemorrhagic complications. Right heart dysfunction was evident in the acute event in 23.9% and 8.7% experienced high-risk PE. Of the patients included, 8.7% had previous diagnosis of mental disease (depression, anxiety disorder). Hereditary thrombophilia (FV Leiden heterozygous or prothrombin G20210A heterozygous) was present in 7 out of the 61 patients examined. PE occurring in the setting of COVID19 was observed in 4.4% of the study population (Table 1).

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Table 1. Sociodemographic characteristics of the study population.

Characteristic	Mean ±SD or %
Age (years)	62.5±15.33
Gender	
Male	56.5%
Female	43.5%
Smoking status	
Non-smoker	45.7%
Ex-smoker	40.2%
Current smoker	14.1%
Comorbidities	
None	17.4%
≥1	82.6%
Comorbidities diagnosis	
Arterial hypertension	35.9%
Dyslipidemia	32.6%
Hashimoto thyroiditis	14.1%
Coronary artery disease	10.9%
Diabetes mellitus type II	10.9%
Mental disease	8.7%
COVID19	4.4%
Chronic Obstructive Pulmonary Disease	3.3%
Osteoporosis	2.2%
Obstructive sleep apnea hypopnea syndrome	1.1%
Idiopathic thrombocytosis	1.1%
Dementia	1.1%
Sarcoidosis	1.1%
Ulcerative colitis	1.1%
BMI	
Healthy weight/Overweight/Obesity	15.2%/40.2%/44.6%
Educational level	
Primary school	41.1%
3 years of high school	25.6%
6 years of high school	23.3%
university graduates	8.9%
Working status	
Unemployed/Retired/Currently working	15.2%/56.5%/27.2%
Marital status	
Married/In a relationship	78.3%
Single	9.8%
Widower	10.9%

Health Related Quality of Life, Anxiety and Life Satisfaction

Table 2 presents the results the SF36, STAIX1, STAIX2 and SWLS. Most of the mean values of the SF36 subscales were above the normative value except for PR (45.92±42.41). RE (51.26±43.31) and GH (54.02±18.79) were slightly above the normative value of 50. Mean STAIX1was 37.05±11.17 and mean STAIX2was 39.80±10.47. Mean SWLS was 23.31±6.58.

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Table 2. Results of SF36, STAI and SWLS in our population.

	Minimum	Maximum	Mean	Standard Deviation
Age	18	88	62.50	15.33
Duration of the disease	1	36	8.60	8.28
Physical functioning	0	100	57.77	25.76
Role physical functioning	0	100	45.92	42.41
Emotional role	0	100	51.26	43.31
Vitality	10	95	57.11	21.27
Mental health	16	100	66.70	19.49
Social role functioning	0	100	61.95	31.49
Bodily pain	0	100	72.44	28.40
General health perceptions	15	100	54.02	18.79
Change in health	0	100	58.42	30.62
STAIX1	20	75	37.05	11.17
STAIX2	24	71	39.80	10.47
SWLS	5	35	23.31	6.58

Bivariate Correlations

Table 3 presents the bivariate correlations of the SF36 subscales, STAIX1, STAIX2 and SWLS and demographic variables of the sample. Age of diagnosis was statistically significantly negatively correlated with PF, RP, VT, SF and GH (Table 3). Disease duration was statistically significantly positively correlated with RP, RE, SF and "change in health" (Table 3). BMI was statistically significantly negatively correlated with PF, VT and BP (Table 3).

Table 3. Bivariate correlations of demographical parameters and SF36 subscales scores, STAI X1, STAI X2 and SWLS. Abbreviations: PF, physical role functioning; RP, role physician; RE, emotional role fuctioning; VT, vitality; MH, mental health; SF, social role functioning; BP, bodily pain; GH, general health perceptions.

Parameters	**SF36 subscales**											
	PF	**RP**	**RE**	**VT**	**MH**	**SF**	**BP**	**GH**	**Change in health**	**STAIX1**	**STAI X2**	**SWLS**
Age (years)	p<0.001 R=-0.445	p=0.003 r=-0.307	p>0.05	p=0.009 r=-0.270	p>0.05	p<0.001 r=-0.363	p>0.05	p=0.05 r=-0.293	p>0.05r	p>0.05	p>0.05	p>0.05
Disease duration (years)	p>0.05	p=0.006 r=0.292	p=0.031 r=0.229	p>0.05	p>0.05	p=0.010 r=0.270	p>0.05	p>0.05	p=0.001 r=0.347	p>0.05	p>0.05	p>0.05
BMI (Kg/m²)	p<0.001 r=-0.515	p>0.05	p>0.05	p=0.048 r=-0.281	p>0.05	p>0.05	p=0.009 r=-0.368	p>0.05	p>0.05	p>0.05	p>0.05	p>0.05

We observed significant correlations between the SF36 subscales (Table 4). PF was statistically significantly correlated with RP, RE, VT, MH, SF, BP, GH (Table 4). RP was significantly positively correlated with RE, VT, MH, SF, BP, GH and "change in health" (Table 4). RE was statistically significantly positively correlated with VT, MH, SF, BP, GH, and statistically significantly negatively correlated with "change in health" (Table 4). VT was statistically significantly positively correlated with MH, SF, BP, GH and "change in health" (Table 4). MH was statistically significantly positively correlated with SF, GH and "change in health" (Table 4). SF was statistically significantly positively correlated with BP (Table 4).

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Table 4. Bivariate correlations between the SF36 subscales, STAI X1, STAI X2 and SWLS score. Abbreviations: PF, physical functioning; RP, physical role functioning; RE, emotional role functioning; VT, vitality; MH, mental health; SF, social role functioning; BP, bodily pain; GH, general health perceptions.

Parameters	**SF36 subscales**											
	PF	**RP**	**RE**	**VT**	**MH**	**SF**	**BP**	**GH**	**Change in health**	STAIX1	STAI X2	SWLS
Sex Male female	-	p<0.001 r=0.553	p=0.001 r=0.336	p<0.001 r=0.530	p=0.036 r=0.219	p<0.001 r=0.515	p<0.001 r=0.481	p<0.001 r=0.380	p>0.05	p=0.016 r=-0.252	p=0.010 r=-0.270	p=0.017 r=0.251
Symptoms Dyspnea (Yes/No) Hemoptysis (Yes/No)	p<0.001 r=0.553	-	p<0.001 r=0.595	p<0.001 r=0.444	p=0.048 r=0.207	p<0.001 r=0.603	p=0.015 r=0.252	p=0.010 r=0.268	p=0.029 r=0.228	p=0.030 r=-0.228	p=0.007 r=-0.281	p=0.032 r=0.229
Prior VTE (Yes/NO)	p=0.001 r=0.336	p<0.001 r=0.595	-	p<0.001 r=0.490	p<0.001 r=0.411	p<0.001 r=0.481	p=0.024 r=0.235	p<0.001 r=0.357	p=0.035 r=0.220	p<0.001 r=-0.438	p<0.001 r=-0.447	p<0.001 r=0.412
Anticoagulants (yes/No)	p<0.001 r=0.530	p<0.001 r=0.444	p<0.001 r=0.490	-	p<0.001 r=0.655	p<0.001 r=0.649	p<0.001 r=0.404	p<0.001 r=0.628	p=0.003 r=0.310	p<0.001 r=-0.607	p<0.001 r=-0.639	p<0.001 r=0.591
MH	p=0.036 r=0.219	p=0.048 r=0.207	p<0.001 r=0.411	p<0.001 r=0.655	-	p<0.001 r=0.450	p>0.05	p<0.001 r=0.401	p=0.028 r=0.229	p<0.001 r=-0.660	p<0.001 r=-0.789	p<0.001 r=0.667
SF	p<0.001 r=0.515	p<0.001 r=0.603	p<0.001 r=0.481	p<0.001 r=0.649	p<0.001 r=0.450	-	p<0.001 r=0.383	p>0.05	p>0.05	p<0.001 r=-0.379	p<0.001 r=-0.429	p<0.01 r=0.431
BP	p<0.001 r=0.481	p=0.015 r=0.252	p=0.024 r=0.235	p<0.001 r=0.404	p>0.05	p<0.001 r=0.383	-	p=0.003 r=0.302	p>0.05	p>0.05	p>0.05	p=0.009 r=0.275
GH	p<0.001 r=0.380	p=0.010 r=0.268	p<0.001 r=0.357	p<0.001 r=0.628	p<0.001 r=0.401	p>0.05	p=0.003 r=0.302	-	p>0.05	p<0.001 r=-0.541	p<0.001 r=-0.534	p<0.001 r=0.572
Change in health	p>0.05	p=0.029 r=0.228	p=0.035 r=0.220	p=0.003 r=0.310	p=0.028 r=0.229	p>0.05	p>0.05	p>0.05	-	p>0.05	p>0.05	p>0.05
STAIX1	p=0.016 r=-0.252	p=0.030 r=-0.228	p<0.001 r=-0.438	p<0.001 r=-0.607	p<0.001 r=-0.660	p<0.001 r=-0.379	p>0.05	p<0.001 r=-0.541	p>0.05	-	p<0.001 r=0.761	p<0.001 r=-0.569
STAIX2	p=0.010 r=-0.270	p=0.007 r=-0.281	p<0.001 r=-0.447	p<0.001 r=-0.639	p<0.001 r=-0.789	p<0.001 r=-0.429	p>0.05	p<0.001 r=-0.534	p>0.05	p<0.001 r=0.761	-	p<0.001 r=-0.669
SWLS	p=0.017 r=0.251	p=0.032 r=0.229	p<0.001 r=0.412	p<0.001 r=0.591	p<0.001 r=0.667	p<0.01 r=0.431	p=0.009 r=0.275	p<0.001 r=0.572	p>0.05	p<0.001 r=-0.569	p<0.001 r=-0.669	-

We observed significant correlations between SF36 subscales, STAI and SWLS results which are presented in Table 4. STAIX1 was statistically significantly negatively correlated with PF, RP, RE, VT, MH, SF and GH (Table 4). STAIX2 was statistically significantly negatively correlated with PF, RP, RE, VT, MH, SF and GH (Table 4). SWLS was statistically significantly positively correlated with RP, RE, VT, MH, SF, BP, GH and statistically significantly negatively with PF (Table 4). STAIX1 was statistically significantly positively correlated with STAIX2 and negatively with SWLS. STAIX2 was statistically significantly negatively correlated with SWLS (Table 4).

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Comparison between Patient Characteristics and Psychometric Scores

We observed that men had higher levels of PF versus women (63.55±24.66 vs 50.25±25.51, respectively, p=0.013) (Supplementary Figure S1). Patients presenting dyspnea at diagnosis had higher levels of GH versus those without (58.12±18.26 vs 49.54.18.54, respectively, p=0.028) (Supplementary Figure S1). Patients presenting hemoptysis at diagnosis had higher levels of BP than those without (91.25±10.45 vs 71.13±28.82, respectively, p=0.003) (Supplementary Figure S1). BP was lower in patients with prior VTE recurrence (50.00±36.47) versus those without (74.58±26.82) (p=0.037) (Supplementary Figure S1). PF was higher in patients receiving anticoagulants than in patients that were not under anticoagulant therapy (59.52±26.65 vs 36.42±16.76, respectively, p=0.022) (Supplementary Figure S1). Patients with at least one comorbidity versus those without had lower SWLS (22.51±6.81 vs 27.26±3.19, respectively, p<0.001), lower SF (58.88±32.26 vs 76.56±23.21, respectively, p=0.041) and reduced GH (51.90±17.98 vs 64.06±19.93, respectively, p=0.018) (Supplementary Figure S2).

Patients with known mental disease versus those without, had increased STAIX1 (45.53± 9.65 vs 35.36±10.72, respectively, p=0.001), increased STAIX2(50.33±10.16 vs 37.69±9.23, respectively, p<0.001), reduced SWLS (17.60±6.08 vs 24.47±6.09, respectively, p<0.001), reduced VT (42.50±17.88 vs 6.02±20.73, respectively, p=0.002), lower MH (50.0±18.81 vs 70.22±17.83, respectively, p<0.001) and reduced GH (38.75±9.21 vs 57.23±18.75, respectively, p<0.001). Patients with PE associated with COVID19 versus those that their event was not associated with SARSCoV2, had lower levels of "change in health" (25.00±20.41vs59.77±30.34, respectively, p=0.026) (Supplementary Figure S1). Patients with diabetes mellitus, versus those without, had lower levels of RE (23.32±35.30 vs 54.67±43.13, respectively, p=0.023), lower MH (51.60±21.74 vs 68.54±17.93, respectively, p=0.009), lower GH (42.50±18.59 vs 55.42±18.54, respectively, p=0.039), higher STAIX1 (44.50±15.46 vs 36.12±10.27, respectively, p=0.025) and lower SWLS (18.30±7.61 vs 23.94±6.21, respectively, p=0.010). Patients with thyroid disease, when compared to those without, had lower PF (43.07±23.14 vs 60.18±25.50, respectively, p=0.026) and lower BP (54.03±25.50 vs 75.47±27.85, respectively, p=0.013). Finally, patients with hereditary thrombophilia, versus those without, had higher levels of PF (82.14±25.95 vs, 60.83±24.52, respectively, p=0.036), higher RE (95.23±12.60 vs 50.30±43.97, respectively, p<0.001), higher SF (98.21±4.72 vs 63.19±28.95, respectively, p<0.001) and higher BP (94.28±9.75 vs 72.03±27.87, respectively, p<0.001).

Subjects that had attended only primary school had the lowest score of PF (46.48±25.72) versus those that had attended the 3 first years of high school (68.47±21.37), those had attended all 6 years of high school (66.42±21.80) and those that were university graduates (54.37 ±32.12) (p=0.006). Similarly, patients that had attended only primary school had the lowest GH score (48.37±16.60) versus those that had attended the 3 first years of high school (54.56±17.63), those had attended all 6 years of high school (65.23±19.45) and those that were university graduates (55.62± 19.16) (p=0.0.20). Retired patients exhibited the lowest PF score (19.51±24.95) versus unemployed subjects (63.57±20.60) and those that were currently working (70.00±23.80) (p=0.002).

Former smokers exhibited the lowest SWLS score (19.15±8.56) followed by non-smokers (23.28±6.49) and current smokers (24.81±5.33) (p=0.027).

Patients with below average level of PF had increased age of diagnosis (67.74±14.12) versus those with over average score (57.20±15.09) (p=0.001). Patients that had high risk PE more often had an over average PF score (8.69%) than those with below average PF (0%).

Patients with below average RP had increased age of diagnosis (65.5±13.79) versus those with over average (55.89+16.20) (p=0.004). Similarly, disease duration was reduced in those with below average RP (6.91±7.36) versus those with over average (12.17±17.14) (p=0.046). Patients with below average VT had higher age of diagnosis (67.34±12.34) when compared to those with over average (58.19±16.25) (p=0.003). Patients with known mental disease rarely had VT over average (5.43%) than those without mental disease (11.95%) (p=0.009). Patients with mental disease had below average MH more frequently (6.52%) than over average (10.86%) and those without mental disease had more frequently over average MH (73.91%) than below average (8.69%) (p=0.014). Patients with over average BP had an increased age of diagnosis (67.61±12.23) when compared to those with below

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average BP (60.22±15.90) (p=0.039). Similarly, patients with below average SF versus those with over average score had increased age of diagnosis (63.37±10.31 vs 57.28±17.34, respectively, p=0.001) and reduced disease duration (5.88± 6.46 vs 12.48±15.02 months, respectively, p=0.007). Patients with below average GH differed significantly to those with over average in terms of age of diagnosis (65.97 ±14.74 vs 57.89±15.25, respectively, p=0.012). Patients with over average GH suffered more rarely from mental disease (1.08%) than those with below average (16.30%) (p<0.001).

Patients with known mental disease had high STAIX1 levels more frequently than those with low levels (11.95% vs 4.34%, respectively, p=0.001). Similarly, patients with mental disease had more frequently high STAIX2 levels (15.21%) than those with low levels (1.08%) (p<0.001).

Patients with comorbidities had high SWLS more frequently (51.08%) than those without (16.30%) (p=0.005). Patients with mental disease had high SWLS less frequently (5.43%) than low SWLS (61.95%) (p=0.001).

Predictors of HRQoL, Anxiety and Satisfaction with Life

We performed multiple linear regression analysis toassess predictors of HRQoL, anxiety and satisfaction with life and the results are summarized in Table 5 and Table 6. In the multiple linear regression analysis, age (β=-0.469, p=0.027) and BMI (β=-1.988, p=0.001) significantly predicted PF score (F (12,32)=4.623, p<0.001, R2=0.634) (Table 3). SF score (β=0.457, p=0.006), RE score (β=0.404, p<0.001) and PF score (β=0.460, p=0.014) were predictive of RP (F (13,70)=7.749, p<0.001, R2=0.590).Analysis for the prediction of RE demonstrated that only RP score (β=0.493, p<0.001)was predictive (F (12,71)=6.295, p<0.001, R2=0.515).

For VT score prediction, MH score (β=0.715, p=0.001) and GH score (β=0.361, p=0.017) served as independent variables (F (13,31)=9.424, p<0.001, R2=0.798). We observed that GH score (β=-0.235, p=0.008), VTscore (β=0.296, p=0.011), STAIX2 score (β=-0.972, p<0.001) and SWLS score (β=0.642, p=0,019)were predictive of MH score (F (10,76)=20.182, p<0.001, R2=0.726).Only PR score (β=0.229 p=0.006) served as an independent variable for SF score (F (10,76)=11.015, p<0.001, R2=0.611).

In multiple linear regression analysis, only PF score(β=0.413, p=0.024) was significantly predictive of BP(F (10,81)=4.904, p<0.001, R2=0.546).For GH score, age (β=-0.236, p=0.043) and SWLS score (β=0.811, p=0.019) were independent variables(F (10,76)=8.242, p<0.001, R2=0.520).Finally, for change in health score, only disease duration(β=0.801, p=0.011) served as an independent variable (F (6,82)=3.457, p<0.001, R2=0.202).

In the multiple linear regression model, only MH score (β=0.113, p=0.015) and GH (β=0.105, p=0.00) were independent variables for the prediction of SWLS (Table 4)(F (10,76)=10.576, p<0.001, R2=0.581).For STAIX1, only STAIX2served as an independent variable(β=0.549, p<.001) (F (9,77)=14.915, p<0.001, R2=0.635).The following variables were independently predictive of STAIX2: MH score (β=-0.242, p<0.01), and STAIX1(β=0.312, p<0.001) (F (9,77)=26.445, p<0.001, R2=0.756).

Table 5. Multivariate linear regression model for possible predictors of the subscales of SF36. Abbreviations: PF, physical role functioning; RP, role physician; RE, emotional role functioning; VT, vitality; MH, mental health; SF, social functioning; BP, bodily pain; GH, general health perceptions.

	PF		**RP**		**RE**		**VT**		**MH**		**SF**		**BP**		**GH**		**Change in health**	
	β	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**
Disease duration	-	-	0.166	0.603	0.067	0.847	-	-	-	-	0.346	0.124	-	-	-	-	0.801	**0.003**
Age	-0.469	**0.027**	-0.060	0.821	-	-	-0.219	0.118	-	-	-0.235	0.210	-	**-**	-0.236	**0.043**	-	-
BMI	-1.988	**0.001**	-	-	-	-	-0.787	0.052	-	-	-	-	-	-	-	-	-	-
MH	0.446	0.220	-0.508	0.125	0.114	0.750	0.715	**0.001**	-	-	0.276	0.240	-	-	-	-	0.029	0.892
GH	0.084	0.729	-0.198	0.495	-0.121	0.685	0.361	**0.017**	-0.235	**0.008**	0.071	0.729	0.038	0.846	-	-	-	-
SF	0.014	0.914	0.457	**0.006**	0.099	0.589	0.109	0.193	0.063	0.271	-	-	0.153	0.235	-0.050	0.506	0.044	0.764
BP	0.150	0.225	-0.194	0.182	0.062	0.694	0.033	0.683	-	-	0.172	0.094	-	-	0.057	0.389		
RP	0.186	0.063	-	-	0.493	**<0.001**	0.008	0.903	-0.056	0.185	0.229	**0.006**	-0.082	0.393	-0.005	0.934	-0.002	0.986
RE	-0.019	0.848	0.404	**<0.001**	-	-	0.006	0.926	0.012	0.764	0.039	0.615	-0.001	0.991	-0.023	0.650	<0.001	0.998
PF	-	-	0.460	**0.014**	-0.071	0.726	-0.093	0.425	-0.056	0.363	-0.003	0.980	0.413	**0.024**	0.040	0.643	-	-
Vitality	-0.232	0.404	0.220	0.473	-0.066	0.846	-	-	0.296	**0.005**	0.411	0.056	0.190	0.381	0.222	0.091	0.365	0.116
Change in health	-	-	0.034	0.783	0.024	0.854	0.005	0.944	0.032	0.431	0.038	0.666	-	-	-	-	-	-
STAIX1	-0.239	0.532	0.746	0.147	-0.788	0.162	-0.248	0.317	-0.109	0.532	-0.236	0.520	-	-	-0.317	0.165	-	-
STAIX2	0.322	0.596	-0.897	0.200	-0.622	0.400	0.193	0.624	-0.972	**<0.001**	0.569	0.252	-	-	-0.190	0.473	-	-
SWLS	-0.832	0.292	-0.018	0.982	0.641	0.465	-0.982	0.050	0.642	**0.019**	0.033	0.953	-	-	0.811	**0.019**	-	-
R squared	0.634		0.590		0.515		0.798		0.726		0.611		0.546		0.520		0.202	

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Table 6. Multivariate linear regression model for possible independent predictors of STAIX1, STAIX2 and SWLS. Abbreviations PF, physical role functioning; RP, role physician; RE, emotional role functioning; VT, vitality; MH, mental health; SF, social functioning; BP, bodily pain; GH, general health perceptions.

	SWLS		STAIX1		STAIX2	
	β	p	β	p	β	p
MH	0.113	**0.015**	-0.042	0.579	-0.242	**<0.001**
GH	0.105	**0.003**	-0.077	0.193	-0.071	0.108
SF	0.011	0.654	-0.009	0.802	0.034	0.226
BP	0.027	0.189	-	-	-	-
RP	-0.003	0.876	0.033	0.233	-0.020	0.335
RE	0.011	0.491	-0.034	0.188	-0.016	0.410
PF	-0.022	0.404	0.022	0.591	-0.003	0.922
VT	-0.002	0.971	-0.089	0.199	0.010	0.851
STAIX1	-0.014	0.851	-	-	0.312	**<0.001**
STAIX2	-0.095	0.312	0.549	**<0.001**	-	-
SWLS	-	-	0.13	0.942	-0.145	0.293
R squared	0.581		0.635		0.756	

4. Discussion

In the present study we examined HRQoL, anxiety and life satisfaction in a cohort of PE. Our patients presented a rather preserved HRQoL (besides RP which was below the normative value), a slightly increased anxiety trait and were slightly satisfied with life. Age was inversely correlated with several factors of HRQoL and served as an independent variable for the prediction of PF and GH. Increased disease duration displayed positive correlations with some SF36 subscales and was a significant variable for the prediction of "change in health", suggesting that HRQoL may improve over time.

Life satisfaction has emerged as a distinct construct that reflects a cognitive evaluation of one's life [32] and a potential target to improve one's health and use of preventive strategies [33]. Reduced life satisfaction has been associated with lower mortality and life expectancy and may serve as a potentially promising tool for the follow-up of various chronic diseases [8]. To our knowledge this is the first study assessing life satisfaction inPE patients. We demonstrated an average of "slight satisfaction" with life in our cohort. Mental disease, comorbidities and increased age were more frequently associated with life dissatisfaction while anxiety trait and state were correlated with satisfaction with life. Only MH andGH were independent variables of SWLS. Studies have previously show that Life satisfaction is lower in patients with mental diseases [34], while anxiety has beeninversely correlated with life satisfaction in other respiratory diseases [35]. Our results agree with the latter observations and provide insight in the understanding of the late psychological consequences of PE as far as life satisfaction is concerned.

PE is a potentially life-threatening state, mostly during the acute phase of the disease; PE patients commonly experience worrying symptoms such as dyspnea, hemoptysis, and syncope [1]. The stress of hospitalization and application of (invasive) treatment in PE patients, may serve as potential stressors and lead to mood and psychological impairments. We observed suboptimal state anxiety and borderline clinically significant trait anxiety in our cohort. MH score was an independent variable of anxiety trait. In the same context, others [36] have reported higher levels of anxiety in a small cohort of PE subjects. Arterial partial oxygen pressure (PaO_2), disease severity and age influenced the level of anxiety. The lower level of anxiety experienced by our patients (when compared to Liu et al.) may be associated with lower age and more comorbidities in their cohort that may lead to increased anxiety.

QoL after PE has not been extensively studied in the literature. Impaired HRQoL in PE has been reported previously [6,37]. Mean SF36 subscales of patients with PE are statistically significantly

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lower than age and sex matched controls as well as when compared to patients with severe/very severe COPD and congestive heart failure [37]. In our cohort, we observed that mean RP was below the normative value and RE and GH were marginally above the average of the general population. HRQoL in our cohort of patients seems lower than those reported by other groups studying PE patients [6,37]. One possible explanation is the discrepancies in the time span between the study inclusion and the acute event which is higher than ours when compared to the previously published studies. As discussed later, disease duration is possibly associated with improved outcomes in QoL. Alternatively, the reduced HRQoL may reflect the effect of the COVID19 pandemic, which may have affected the mental state of our sample.

Reduced disease duration was correlated with worse HRQoL while patients with worse score in SF36 subscales had significant higher disease duration when compared to those with better HRQoL. Disease duration served as an independent variable for "change in health" prediction. Our results may indicate that when patients are close to the event, they experience a decline in QoL that is followed by an improvement; our data strengthen those of other studies in VTE population [6,36–39] Lukas et al [40] studied a mixed PE/DVT population and reported that increased time since the diagnosis was statistically significantly correlated with improved physical QoL. In the same context, others have demonstrated that the PF, SF and VTSF36 subscales are higher (i.e., reflecting better QoL) in patients with longer duration since the event [6] although when QoL was assessed with other instruments (i.e.PEmb-Qol) this finding was not replicated.

In contrary to traditional perceptions, PE is now acknowledged as a "chronic" disease that in most of patients requires chronic attention and close follow up [41]. The mental and physical recovery in some patients may not be complete and studies have reported increased use of psychotropic drugs in VTE patients up to 5 years following the acute event [42]. Although some have reported that average QoL scores in PE improve and approach the values of healthy subjects' norms by 1 year [43], others have demonstrated significant signs of post traumatic syndrome >9 months following diagnosis [12]. The aforementioned findings suggest that long term mental health of PE patients may be impaired and merits attention. Long term interventions to support the mental health of this group of patients may have a beneficial health impact.

Age served as an independent variable for the prediction of some aspects of HRQoL(including PF and GH). In our cohort, older patients had lower scores of SF36 reflecting impaired HRQoL. Our findings strengthen those of others reporting similar results [38]. In the same context, Kahn et al [39] reported that age was predictive of SF36 physical component score in a cohort of patients with DVT. Older patients may experience more adverse events, have more complications during hospitalization and have frequently comorbidities which may collectively influence QoL.

Our study was performed during the COVID19 pandemic. Ahigh frequency of PE has been reported in COVID19 patients with some studies reporting increased severity and worse outcomes [44]. We observed that patients with PE associated with COVID19had lower"change in health" score when compared to patients that their event was not COVID19 related. COVID19 pandemic affects medical aspects of health while it has social and economic effects. Restrictive and safety measures that were implied during the COVID19 pandemic have proven impact on mental health and QoL of patients suffering from various diseases [19,20,45,46] of general population [47] and of frontline healthcare workers [48]. Our findings are consistent with previous studies and indicate the effect that COVID19 may have on mental health. We must acknowledge that the strength of our findings is limited since only 4.4% of our cohort were COVID19-related events. Due to the absence of previous assessment of the HRQoL, anxiety and satisfaction, no definite conclusion can be drawn. In addition, one must acknowledge that the pandemic itself may have an impact on various aspects of mental health and impacts with our results. Since COVID19 may further complicate the mental health of various chronic conditions [19,20] individuals with comorbidities may be more susceptible to mental health impairments.

This study is not without limitations. We acknowledge that we applied the psychometric questionnaires during the patients' follow up at the PE Outpatient Clinic of Larissa, Greece, and we did not perform longitudinal assessments, therefore we cannot address potential differences in QoL,

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life satisfaction and anxiety over time. Additionally, we used convenience sampling and there is a potential selection bias. We have included a small sample size. We acknowledge that our findings may be implicated by the assessment of patients during the COVID19 pandemic that may affect the mental burden of our patients.

In conclusion, we demonstrated that patients with PE exhibit light satisfaction with life, borderline anxiety and below the average in some subscales of HRQoL. Our results provide further insight to the mental consequences of PE. Additionally, our data strengthen the concept that PE is a disease that requires a structured follow-up and chronic attention.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

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