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Functional assessment and quality of life before and after pulmonary endoarterectomy

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ABSTRACT. **Purpose:** ***The study investigates Quality of Life (QOL) and correlation with functional status of patients affected by Chronic Thromboembolic Pulmonary Hypertension who undergo Pulmonary Endoarterectomy.*** **Methods:** ***We investigated with an observational design (before surgery, three and twelve months afterwards) the hemodynamic data (NYHA class, mean pulmonary arterial pressure, cardiac output and pulmonary vascular resistance), the functional status (using the 6-Minute Walk Test) and the QOL, using three questionnaires: Medical Outcome Study Short Form-36 (SF-36), Minnesota Living with Heart Failure Questionnaire (MLHFQ), Saint George Respiratory Questionnaire (SGRQ). We report the results of forty-nine patients.*** **Results:** ***After surgery there was an improvement on functional and hemodynamic parameters and on QOL. The physical domain (PCS) of SF-36 was weakly but significantly associated with all functional parameters. There was no association between functional parameters and mental domain (MCS) of SF-36 or SGRQ. The improvement in 6-Minute Walk Distance was associated with an increase in MLHFQ.*** **Conclusions:** ***Both QOL and submaximal exercise tolerance improve after surgery. However only the physical domains of SF-36 appear to be significantly associated to the functional data.***

Key words: *Quality of Life, pulmonary hypertension, rehabilitation, pulmonary endoarterectomy, Six Minute Walk Test.*

RIASSUNTO. ***Introduzione:*** **Questo studio si propone di indagare la qualità di vita (QOL) e lo stato funzionale, con le relative correlazioni, di pazienti affetti da ipertensione polmonare cronica tromboembolica sottoposti ad intervento di endoarteriectomia polmonare.** ***Materiali & metodi:*** **Mediante uno studio osservazionale sono stati raccolti i parametri relativi all'emodinamica (classe NYHA, pressione arteriosa polmonare media, gittata cardiaca, resistenze vascolari polmonari), allo stato funzionale (con l'esecuzione del test del cammino di 6 minuti o 6MWT) e alla qualità di vita di 49 pazienti. La qualità di vita è stata valutata attraverso tre questionari: il Medical Outcome Study Short Form-36 (SF-36), il Minnesota Living with Heart Failure Questionnaire (MLHFQ), il Saint George Respiratory Questionnaire (SGRQ). Tali dati sono stati rilevati prima del momento chirurgico e a distanza di tre e dodici mesi dopo l'intervento.** ***Risultati:*** **In seguito ad endoarteriectomia polmonare è stato riscontrato un miglioramento dei parametri emodinamici, funzionali e di QOL. Il dominio fisico dell'SF-36 (PCS) risulta significativamente associato, se pur in maniera debole, a tutti i parametri funzionali. Non risulta alcuna associazione tra i parametri funzionali e l'SGRQ né con il dominio mentale dell'SF-36 (MCS). Il miglioramento nella distanza percorsa al 6MWT è associato ad un incremento del punteggio totale ottenuto all'MLHFQ.** ***Conclusioni:*** **Dopo l'intervento chirurgico si è riscontrato un miglioramento sia della QOL che della tolleranza all'esercizio submassimale. Tuttavia solo il dominio fisico dell'SF-36 risulta essere associato in maniera statisticamente significativa ai dati relativi alla funzionalità.**

Parole chiave: Qualità di Vita, ipertensione polmonare, riabilitazione, endoarteriectomia polmonare, test del cammino di 6 minuti.

Introduction

Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is one of the most common form of pulmonary hypertension; its precise prevalence is not yet known: in the US, 0.1-0.5% of patients surviving acute pulmonary embolism are estimated to develop CTEPH (1, 2); on the other hand, it has been noted that 63% of patients with CTEPH have no previous clinical history of acute pulmonary embolism (3). CTEPH is characterized by chronic obstruction of pulmonary arteries by pulmonary emboli and by vascular remodelling in small blood vessels, similar to that observed in other forms of pulmonary hypertension. Both proximal obstruction of the pulmonary arteries and small-vessel arteriopathy lead to an increase in pulmonary vascular resistance with a mean pulmonary pressure (mPAP)>25mmHg, right ventricular overload, possible reduction of cardiac output and a reduction in oxygen saturation (2, 3). The most common symptoms in patients with CTEPH are progressive exertional dyspnea, reduced exercise tolerance (they tire easily and experience muscle weakness) and signs of right-heart failure which compromise functional status (3). Factors such as dyspnea, reduced physical functioning, social isolation, anxiety and depression determine a reduced Quality of Life (QOL). Pulmonary endoarterectomy (PEA), which was originally considered as a bridge to lung or heart-lung transplantation, is nowadays the treatment of choice for patients with CTEPH (1, 4, 5). Peri-operative mortality ranges from between 4,4% and 11% (3, 4). Current survival rates after PEA are 90.9% (6) after three years and 75% after six years (1, 5). Patients who do not undergo surgery have a median survival of 2-3 years after diagnosis (3). Moreover, in CTEPH, surgery (PEA) improves hemodynamic parameters and tolerance to exercise (3, 7). Reduced exercise tolerance is normally monitored by maximal exertion testing (cardiopulmonary test) and by submaximal testing like the 6-Minute Walk Test, which reproduces daily activities. For several years now, QOL has been considered crucial in assessing the effectiveness of various courses of treatment as well as a significant outcome in healthcare (8, 9). Since PEA reduces pulmonary artery pressure and improves symptoms (5, 8), QOL and functional status should show a marked improvement even in the early stages after

surgery. There are few studies on QOL in CTEPH (6-8) and to best of our knowledge there are no studies systematically assessing QOL before and after PEA and correlating it with functional outcome.

The aim of this observational longitudinal study was to investigate, over a 12 months follow-up, the quality of life in CTEPH patients undergoing PEA, and its correlation with functional parameters.

Materials and methods

Patients selection

From July 2003 to July 2006, our cooperation with the Cardiac Surgery Unit led to the consecutive observation of 65 adults who were diagnosed with CTEPH and indicated for PEA surgery. We assessed their functional capacity and quality of life in three different time periods: before surgery (in the week prior to surgery), three and twelve months afterwards. Inclusion criteria for this study were evaluation before surgery and PEA surgery. Sixteen patients were excluded because they did not have the evaluation before surgery. Forty-nine patients met inclusion criteria. Four patients (8%), two males and two females, died after the operation before the three-month follow-up assessment. Causes of death were: 1 cardiogenic shock, 1 case of multiorgan failure, 1 case of bleeding (hemoptysis), 1 case of bilateral pneumonia. These patients were older, with higher mPAP and lower cardiac output than the surviving population, but with similar BMI, 6-Minute Walk Distance and QOL before PEA. The study protocol was approved by the local Ethics Committee and was a part of a wide research project on QOL. Patients agreed to participate to the study.

Measures

Clinical assessment of functional capacity included: age, gender, BMI, NYHA functional classification, mean pulmonary arterial pressure (mPAP), cardiac output (CO), pulmonary vascular resistance (PVR) and the 6-Minute Walk Test (6MWT), performed using ATS guidelines (10). These parameters were recorded in the Cardiac Surgery clinical data-base. Heart rate and hemoglobin oxygen percent saturation were measured (albeit not recorded) continuously during the 6MWT using a battery-powered finger pulse oximeter (a 200gr 180x80x25mm ALPApulse2) attached to the patient's waist with a sensor worn on the forefinger of the left hand. The test was stopped whenever marked dyspnea or chest pain occurred, or, in the absence of symptoms, in the event of marked desaturation by pulse oximeter (a cut-off value of oxygen percent saturation <86 was considered for safety reasons) (11). To establish the patient's subjective perception of dyspnea, the Modified Borg Scale (12) were administered immediately before and after the 6MWT. Any pre-existing walking difficulty or need to discontinue the 6MWT for any reason were noted. Patients on oxygen therapy performed the 6MWT carrying the same oxygen canister with the same oxygen flow used by the patient when going about normal daily activities (10). We also quantified the distance walked as a percentage of predicted based on previous reports (13, 14), which studied the performance of healthy subjects during the 6MWT.

QOL assessment included three self-administered questionnaires (one generic and two specific): MOS 36-Item Short Form-36 (SF-36) (15, 16), Minnesota Living with Heart Failure Questionnaire (MLHFQ) (17), Saint George Respiratory Questionnaire (SGRQ) (18). The Italian version of these questionnaires had already been validated. The questionnaires were administered before the 6MWT.

Statistical analysis

Data were described as mean and standard deviation (SD) or median and interquartile range (IQR) if continuous and as counts and percent if categorical. A Student t test was used to compare QOL and distance at the 6MWT against the norm. GEE equations (with either gaussian or logit link) were used to assess changes over time of the measured functional and QOL parameters. Robust standard errors were computed. The association between changes at one year in the functional performance and changes in QOL was evaluated by means of the Pearson correlation, the Fisher exact test or the Mann Whitney U test for continuous or categorical variables or their combination. Stata 10 (StataCorp, College Station, TX, USA) was used for computation. All tests were 2-sided. A p-value<0.05 was considered statistically significant.

Results

The 49 patients included in the study had a mean age of 56 (±15 years), 27 were males (55%), 22 females (45%).

As shown in Table I, there was an improvement of all functional parameters over time, which was highest between the pre PEA and the third month follow-up, and remained stable up to 12 months. Particularly, at 3 months mPAP had dropped by 24mmHg (95% CI 21-27), CO had increased by 1.61 l/min (95% CI 1.25-1.97) (and by further 1.43 l/min thereafter), and PVR was reduced by 711 Dyn/s/cm^{-5} (95% CI 607-815). Before PEA, one patient did not perform the 6MWT as he was too weak to walk; two patients refused to perform the test three months after surgery and one at twelve-months follow-up. If patients need oxygen therapy, they performed 6MWT with this support (11 at pre PEA, 4 after three months, 2 after 12 months). The number of patients who had to interrupt the test decreased during the postoperative period: 23 patients at pre PEA (1 due to chest pain, 6 to dyspnea and 16 to desaturation), 10 patients at three and twelve months (1 due to dyspnea, 1 to fatigue, 8 to desaturation). As we introduced in a previous preliminary report (19), following surgery, a significant increase was recorded in the distance covered in the 6MWT (Table I). Before surgery, the difference in the distance actually walked and the expected

distance was 316 metres (44%) (95%CI 284-348); this difference dropped to 181 metres (69%) (95% CI 149-212) at the third month follow-up assessment (p<0.001) and remained unchanged at 12 months. Before surgery 24 (53%) patients perceived, at rest, dyspnea; under exertion the number of patients with dyspnea increased (43 patients-96%) and as did the intensity of the experienced dyspnea. Three months after PEA, 7 (16%) patients reported resting dyspnea, which increased to 29 (65%) after exercise. At 12 months, a slight increase in the number of patients complaining of dyspnea before and after the test was recorded (20% and 79%). Dyspnea measured using Modified Borg Scale was significantly lower before the 6MWT both at three (-0.5; 95% CI 0.1-0.9) and 12 months. Perception of dyspnea after the test was reduced at the three-month follow-up assessment (-2; 95% CI 1.3-2.6) and was maintained at twelve months (Table I).

One generic and two specific self-administered questionnaires were used to assess QOL. Before surgery 80% of patients filled in all the questionnaires and at three and twelve months 90% did so. The scores from the generic and specific questionnaires indicated a poor quality of life before surgery, which markedly improved during subsequent controls both in physical and mental domains (Table II).

SF-36

Before surgery the mean value of the Physical Component (PCS) was very low; considering the single domains, scores were particularly low for Physical Functioning (PF), Physical Role (RP) and General Health (GH), while Bodily Pain (BP) was closer to the normal mean value. At three- and twelve-months assessments scores increased, approaching near normal values for the healthy Italian population. The mental component score (MCS)

Table I. ***Variation overtime in functional and hemodynamic data***

PARAMETERS		P value	Time change p value Post-hoc comparison
6MWD (m)		<0.001	
pre-PEA	260 ± 128.7		<0.001 (3 months vs pre PEA)
3 months	404 ±106.1		<0.001 (12 months vs pre-PEA)
12 months	389 ± 106.9		=0.227(12 months vs 3 months)
% pred (Δm, 95%)		<0.001	
Pre-PEA	44% [316 (95%CI284-348)]		<0.001 (3 months vs pre PEA)
3 months	69% [181 (95%CI149-212)]		<0.001 (12 months vs pre-PEA)
12 months	69% [181 (95%CI149-212)]		=0.831 (12 months vs 3 months)
mPAP (mmHg)		<0.001	
pre-PEA	46.1 ±10.4		<0.001 (3 months vs pre PEA)
3 months	22.1 ± 9.6		<0.001 (12 months vs pre-PEA)
12 months	22.3 ± 8.9		=0.856 (12 months vs 3 months)
CO (lt/min)		<0.001	
pre-PEA	3.54 ± 1.19		<0.001 (3months vs pre PEA)
3 months	5.22 ± 1.13		<0.001 (12 months vs pre-PEA)
12 months	5.03 ± 1.11		=0.151(12 months vs 3 months)
PVR (Dyn/s/cm $^{-5}$)		<0.001	
pre-PEA	1008 ± 409		<0.001 (3 months vs pre PEA)
3 months	282 ± 164		<0.001 (12 months vs pre-PEA)
12 months	301 ± 204		=0.443 (12 months vs 3months)
BORG dyspnea pre-6mwt		<0.001	
pre-PEA	0.86 ± 1.19		<0.001 (3 months vs pre PEA)
3 months	0.31 ± 0.82		<0.001 (12 months vs pre-PEA)
12 months	0.23 ± 0.51		=0.373(12 months vs 3 months)
BORG dyspnea post-6mwt		<0.001	
pre-PEA	3.50 ± 1.90		<0.001 (3 months vs pre PEA)
3 months	1.53 ± 1.77		<0.001 (12 months vs pre-PEA)
12 months	1.56 ± 1.46		=0.935 (12 months vs 3 months)
NYHA III-IV		<0.001	
pre-PEA	43 (89.5%)		<0.001 (3 months vs pre PEA)
3 months	2 (4.4%)		<0.001 (12 months vs pre-PEA)
12 months	1 (2.1%)		=0.316 (12 months vs 3 months)
BMI (Kg/m^2)		<0.001	
Pre-PEA	24.71 ± 5.02		=0.537 (3 months vs pre PEA)
3 months	24.59 ± 4.58		<0.001 (12 months vs pre-PEA)
12 months	26.44 ± 5.56		<0.001 (12 months vs 3months)

6MWD = six minute walk distance; % pred = percentage of predicted walk distance; mPAP = mean pulmonary arterial pressure; CO = cardiac output; PVR = pulmonary vascular resistance; NYHA = New York Heart Association Class; BMI = body mass index.

Table II. ***Variation over time in QOL***

		P value	Time change p value Post hoc comparison
PCS (SF-36)		<0.001	
pre-PEA	32 ± 8		<0.001 (3 months vs pre PEA)
3 months	46 ± 8		<0.001 (12 months vs pre PEA)
12 months	48 ± 8		=0.091 (12 months vs 3 months)
MCS (SF-36)		<0.001	
pre-PEA	43 ±11		<0.001 (3 months vs pre PEA)
3 months	52 ±10		<0.001 (12 months vs pre PEA)
12 months	54 ±8		=0.261 (12 months vs 3 months)
MLHFQ score		<0.001	
pre-PEA	52 ± 21		<0.001 (3 months vs pre PEA)
3 months	21 ± 19		<0.001 (12 months vs pre PEA)
12 months	17 ± 17		=0.087 (12 months vs 3 months)
SGRQ Total		<0.001	
pre-PEA	53 ± 15		<0.001 (3 months vs pre PEA)
3 months	22 ± 16		<0.001 (12 months vs pre PEA)
12 months	19 ± 13		=0.072 (12 months vs 3 months)
SGRQ Symptom		<0.001	
pre-PEA	45 ± 16		<0.001 (3 months vs pre PEA)
3 months	30 ± 12		<0.001 (12 months vs pre PEA)
12 months	29 ± 13		=0.549 (12 months vs 3 months)
SGRQ Activity		<0.001	
pre-PEA	68 ± 16		<0.001 (3 months vs pre PEA)
3 months	30 ± 25		<0.001 (12 months vs pre PEA)
12 months	26 ± 23		=0.126 (12 months vs 3 months)
SGRQ Impact		<0.001	
pre-PEA	48 ± 19		<0.001 (3 months vs pre PEA)
3 months	16 ± 17		<0.001 (12 months vs pre PEA)
12 months	12 ± 12		=0.107 (12 months vs 3 months)

SF-36 = MOS 36-Item Short Form-36; PCS = Physical Component Summary; MCS = Mental Component Summary; MLHFQ = Minnesota living with heart failure Questionnaire; SGRQ = Saint George Respiratory Questionnaire.

and the corresponding single domain scores were all compromised before PEA. They increased at the three- and twelve-months assessments, reaching near normal values for the healthy Italian population. Particularly PCS significantly improved by 13.7 (95% CI 11.16-16.39) at three months and remained stable up to 12 months after surgery. The MCS score also showed a similar significant improvement at three (8.9; 95% CI 5.5-12.41) and twelve months (Table II).

Minnesota (MLHFQ)

Variation in MLHFQ scores over time (Table II) highlights an improved quality of life with a 31 points reduction in score at three months (95% CI 24-38), which was maintained at 12 months.

St George's

Scores were significantly reduced at three months, overall and for the single domains, denoting an improved quality of life. In particular, there was a 30 points reduction in the overall score at three months (95% IC 26-30). There was no substantial variation at 12 months.

The reduction in mean pulmonary arterial pressure values and vascular resistance significantly correlated with an improvement in the PCS component in the SF-36 (R from 30% to 52%) (Table III), as did the ability to exercise (metres walked in the 6MWT and its percentage value). On the contrary, no correlation was found between the mental component of the SF-36 and clinical and functional data. Scores on the Minnesota questionnaire correlated with the distance covered, but not with hemodynamic data. None of the components of the Saint George's questionnaire correlated with clinical and functional data. The extent of dyspnea (Borg Scale) perceived before the 6MWT correlated with the MCS component of the SF-36 as well as with scores recorded by the Minnesota questionnaire and all components in the St George's questionnaire. After performing the test, values on the Borg Scale only correlated with the components in the St George's questionnaire.

Discussion

The main results of this observational longitudinal study are an improvement of functional status and of QOL three and twelve months after PEA. Improvement in functional status is confirmed by a lower number of patients who required oxygen therapy during their daily activities

Table III. *Association of changes in functional performance and changes in QOL*

	SF-36 PCS	SF-36 MCS	MLHF	SGRQ total	SGRQ symptom	SGRQ activity	SGRQ impact
	R(95%IC)	R(95%IC)	R(95%IC)	R(95%IC)	R(95%IC)	R(95%IC)	R(95%IC)
Δ 6MWD meters	39% (6 to 64) p=0.012	15% (-19to 46) p=0.363	-54% (-74to-27) p=0.001	-30% (-57 to 24) p=0.072	-13% (-33 to 31) p=0.936	-17% (-47 to 15) p=0.198	-34% (-60 to -25) p=0.085
% Pred	36% (21 to 27) p=0.018	21% (-14to 52) p=0.187	-52% (-73to-24) p<0.001	-29% (-57 to 37) p=0.075	11% (-32 to 34) p=0.947	-13% (-44 to 21) p=0.408	-38% (-63 to -59) p=0.047
PAPm	-52% (-73to-23) p=0.001	14% (-19to 45) p=0.420	25% (-6 to 53) p=0.119	24% (-80 to 52) p=0.174	9% (-22 to 40) p=0.552	33% (12 to 58) p=0.024	11% (-21 to 41) p=0.546
CO	31% (-31to 58) p=0.126	-32% (-59to 17) p=0.091	-9% (-40to 24) p=0.660	-20% (-49 to 12) p=0.366	85% (-24 to 40) p=0.565	-20% (-49 to 13) p=0.253	-19% (-49 to 14) p=0.351
PVR	-40% (-65to-71) p=0.032	22% (-13to 52) p=0.281	21% (-12to 50) p=0.290	22% (-11 to 50) p=0.310	19% (-30 to 34) p=0.926	22% (-10 to 51) p=0.223	17% (-16 to 46) p=0.387
Borg pre	-21% (-51to 13) p=0.079	-59% (-77to-31) p=0.0000	42% (11 to 65) p=0.0013	52% (24 to 72) p=0.0000	27% (-5 to 55) p=0.052	36% (5 to 61) p=0.0004	47% (17 to 69) p=0.0000
Borg post	-23% (-53to 10) p=0.159	-33% (-60 to 0) p=0.092	32% (-0 to 58) p=0.086	51% (23 to 72) p=0.0006	41% (10 to 64) p=0.076	33% (1 to 59) p=0.015	43% (12 to 66) p=0.006

Δ 6MWD meters = ;% pred = percentage of predicted of walk distance; SF-36 = MOS 36-Item Short Form-36; PCS = Physical Component Summary; MCS = Mental Component Summary; MLHFQ = Minnesota living with heart failure Questionnaire; SGRQ = Saint George Respiratory Questionnaire; mPAP = mean pulmonary arterial pressure; CO = cardiac output; PVR = pulmonary vascular resistance.

(10% after 3 months, 5% after 12 months), percentage that is lower than which reported by Matsuda (75% after 1 year) (6) and Archibald (11% after 3 years) (8). In the recent literature, the 6MWT is proposed as a test to evaluate and monitor the outcome of a treatment even in thromboembolic pulmonary hypertension (6, 19-22). The increase in the distance walked by our patients after surgery is in agreement with the literature (6, 21, 22) and points to an improved exercise tolerance and good functional recovery; in our cohort we observed that the increase in distance walked is associated both with a reduced percentage of patients with dyspnea after test and with a lower level of perceived dyspnea.

Symptoms of pulmonary hypertension and the functional impairment that characterizes the disease worsen both the physical and emotional aspects of QOL (12). Most studies on QOL have been carried out on PAH patients as part of pharmacological trials (23-25). In patients with CTEPH after PEA, Archibald reports, in a retrospective study, an improvement of health status and quality of life (8) and Yoshimi observed an improved QOL in all components of the SF-36, which correlates with the reduced percentage of PVR, especially for PVR reduced by more than 50% (7). Before surgery, in our population, the physical component (PCS) as assessed by the SF-36, scored much lower than the normal expected values, overall and in all its domains (Physical Functioning, Role Function, General Health, Bodily Pain). As a fact, QOL is influenced by the patient's overall perception of his health status and by poor physical conditions involving a limited functional capacity. Moreover, health status has a negative impact on relationships with family and friends. This is shown by the fall in "vitality" as demonstrated by MCS, and all its domains in the SF-36 (Social Functioning, Mental Health, Vitality, Role Function-emotion related).

When considering correlation with functional parameters, we observed that the patients' perception of health is correlated, as regards PCS, with an improved hemodynamic picture and with an increase in the number of metres walked. An improvement in physical functioning has a positive influence on the patient's subjective perception of QOL. However, the changes in QOL are only partially explained by the changes in the functional parameters, as shown by the correlation coefficients, which, although statistically significant, never reach values higher than 60%. The emotional component also improves after PEA; however, the improvement does not correlate (according to our data) with hemodynamic and functional data (except for the level of dyspnea before performing the test). This may be explained by the difficulty in defining quality of life, by the emotional, psychological and behavioural implications that this involves and that may therefore not be included among objective categories. The improvement both in the total score and in the single domains of Saint George's Respiratory Questionnaire is significant after PEA, but the scores do not correlate with hemodynamic parameters.

However, the SGRQ correlates with values on the pre and post-6MWT Borg Scale, confirming that this questionnaire is specific for the impact of respiratory disease on QOL. Taichman also found abnormally high values on the SGRQ, both for the overall score and for the single domains, that do not correlate with hemodynamic parameters (24). We are in agreement with these authors in claiming that patients' overall functional status is of greater importance than actual hemodynamic values in determining QOL. Previous studies have used the MLHF Questionnaire in PAH (23, 25). Chua claims that the MLHF Questionnaire correlates with the 6MWT and with NYHA functional class, but not with hemodynamic parameters (25). In a multivariate analysis, Cenedese demonstrated that the overall score of the MLHFQ is the only factor able to predict outcome in PAH patients (23). Also in our study the MLHFQ pointed to a poorer quality of life before surgery. After PEA, the levels fall steadily (improved QOL) and are stable after 12 months. The Minnesota score correlates with the distance walked in the 6MWT and with the pre-6MWT on Borg Scale, while correlations with hemodynamic data are not significant. This result is in line with data in the literature.

Conclusion

The limit of this study includes not being able to use a disease specific questionnaire for Pulmonary Hypertension. A specific questionnaire has recently been implemented to assess QOL in PAH but we started to collect data for the present study in July 2003 (i.e. before publication of the aforesaid) (9). Moreover, to our knowledge, the Italian version has not yet been published. In conclusion PEA, above its ability to increase the hemodynamic performance, is able to induce an improvement of both the functional capacity and the QOL.

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