Eur Respir J, 1996, 9, 1508–1514
DOI: 10.1183/09031936.96.09071508
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European Respiratory Journal
ISSN 0903 - 1936

Time course of exercise capacity, skeletal and respiratory muscle performance after heart-lung transplantation

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Time course of exercise capacity, skeletal and respiratory muscle performance after heart-lung transplantation. N. Ambrosino, C. Bruschi, G. Callegari, S. Baiocchi, G. Felicetti, C. Fracchia, C. Rampulla. ©ERS Journals Ltd 1996.

ABSTRACT: Recipients of heart-lung transplantation (HLT) show reduced exercise capacity due to several pre- and postsurgical factors. The aim of this study was to evaluate the time course of exercise capacity, and skeletal and respiratory muscle performance in 11 patients (5 females and 6 males; age (mean±SD) 38±13 yrs) undergoing HLT. All of the patients were admitted to our institution for a rehabilitation programme after surgery, and were followed-up for 18 months.

On admission, at discharge after an in-patient rehabilitation programme, and every 6 months, patients underwent evaluation of: lung function values; incremental treadmill exercise, 6 min walking distance (6-MWD); maximal inspiratory and expiratory pressures (MIP and MEP, respectively); and peak torque of isokinetic contraction of leg flexor and extensor muscles (IFX and IEX, respectively).

On admission, patients had: reduced lung volumes as assessed by vital capacity (VC) (60±15% of predicted); reduced exercise capacity as assessed by peak oxygen consumption ($V'_{O_2,peak}$) (40±12% pred); reduced skeletal and respiratory muscle performance as assessed by IEX, IFX (48±16 and 28±12 Newton-metres (N×m), respectively) and by MIP and MEP (54±21 and 58±19 cmH_2O, respectively). Ten patients completed the rehabilitation programme. At discharge, no significant change in dynamic and static lung volumes was observed. However, nonsignificant increases in MIP, MEP, IEX, IFX, 6-MWD and $V'_{O_2,peak}$ were recorded. After 6 and 12 months, indices of skeletal and respiratory muscle function and $V'_{O_2,peak}$ improved further, but still remained lower than normal values.

We conclude that in patients with heart-lung transplantation, skeletal and respiratory muscle function and exercise performance are reduced after surgery, that they may improve with time but are still less than normal after 18 months.
Eur Respir J., 1996, 9, 1508–1514.

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Keywords: Lung function tests
physical training
pulmonary rehabilitation
respiratory muscle training

Received: January 17 1995
Accepted after revision February 2 1996

Heart-lung transplantation (HLT) has been shown to be effective as a treatment for fatal and severe cardiopulmonary diseases [1–3]. In addition to survival, one goal of performing HLT is improvement in quality of life [4]. Several factors contribute to the maximal work capacity achievable after transplantation. Before surgery, patients are usually debilitated from the primary disease and long-term inactivity [5]; and the unavoidable complications of allograft transplantation, mainly lung resection, and toxic effects of immunosuppressant therapy contribute to the reduced exercise capacity [6].

Numerous investigators have described the features of the cardiovascular response to steady-state exercise in heart and HLT recipients [7–11]. However, little information is currently available regarding the expected functional outcome [12–15], and not all studies have focused on results at a well-defined time-point. Even less information is available on skeletal and respiratory muscle function over time [13, 15, 16]. The aim of the present study was to evaluate exercise, skeletal and respiratory muscle performance over time in patients who have received a HLT and were followed-up for 18 months after surgery.

Materials and methods

Patients

From September 1991 until June 1993, 11 patients (5 females and 6 males; age (mean±SD) 38±13 yrs (range 19–50 yrs)) underwent HLT, and 21–100 days (47±23 days) after discharge from the surgical unit were admitted to our institution for a rehabilitation programme. Their mean weight and height were 50±4 kg and 167±6 cm, respectively. The underlying diseases were: Eisenmenger syndrome (4 patients); primary pulmonary hypertension (5); chronic obstructive pulmonary disease (COPD) (1); and bronchiectasis (1). None of the patients had undergone a structured preoperative rehabilitation programme.

All patients were receiving maintenance immunosuppression with cyclosporin, azathioprine and prednisone.

Over two consecutive days, anthropometric, haematological, clinical and functional evaluations were performed at admission and at discharge from hospital, and at the nearest time-points to 6, 12 and 18 months after the HLT. Patients were in a clinically stable condition without evidence of airway complications, and without having received therapy for acute rejection or infection during the month preceding the evaluation.

Lung function tests

Forced expiratory flows were evaluated by means of a water-sealed spirometer (Biomedin, Padova, Italy) with the patient in the seated posture. Static lung volumes were assessed using the helium dilution method. The predicted values were according to QUANJER [17], and were calculated in accordance with the recipient's characteristics. The transfer factor of the lungs for carbon monoxide ($T_{L,CO}$) and the carbon monoxide transfer coefficient (K_{CO}) were determined by the single-breath method (Biomedin, Padova, Italy). An automated analyser (Radiometer ABL 300; Copenhagen, Denmark) was used to measure partial pressure of oxygen and carbon dioxide and oxygen saturation in blood samples from the radial artery for baseline assessments and from the ear lobe during exercise testing.

Exercise testing

Patients performed a progressive, incremental exercise test to a symptom-limited maximum on a motorized treadmill (Jaeger, Wurzburg, Germany) whilst breathing room air. Prior to each test, the patients rested standing upright on the treadmill for 5 min with a face mask in place for gas collection. Functional and metabolic data were determined at rest and during exercise by means of a computerized system (EOS-Sprint analyser; Jaeger, Wurzburg, Germany), mixed-expired gas data, minute ventilation (V'_E), tidal volume (V_T), respiratory frequency (f_R), oxygen consumption (V'_{O_2}), carbon dioxide production (V'_{CO_2}) and respiratory exchange ratio (R) were continuously monitored as average values of 30 s intervals. Electrocardiographic activity (ECG) was monitored continuously and systemic arterial blood pressure was registered every 3 min using a sphygmomanometer. Arterial oxygen tension (P_{a,O_2}), arterial carbon dioxide tension (P_{a,CO_2}), and pH were measured at rest and immediately before the end of the exercise test using arterialized blood samples from the ear lobe. After a period of warm-up walking at a comfortable pace (1.6–2 $km \cdot h^{-1}$, 0% gradient), the treadmill was set at 3% gradient (elevation) and the speed increased on the basis of the patient's body weight to obtain a 30 W change. Thereafter, the gradient was increased by 3% every 3 min and the speed adjusted to obtain 30 W increment at each step. At rest (5 min after adaptation to the face mask) and during the last 10 s of each exercise step, the patients were asked to rate the "sense of dyspnoea" using a modified Borg Category Scale [18]. The exercise was stopped when the $V'_{O_2,peak}$ was achieved or when limited by symptoms.

Exercise performance was also assessed by the 6 min walking distance (6-MWD) test according to MCGAVIN *et al.* [19]. Verbal encouragement was given continuously during the test, but the patient was free to stop when desired. Three attempts were made, the best of which was considered in the data analysis. Results are expressed as actual distance walked in metres.

Respiratory muscle strength

Respiratory muscle strength was assessed by measuring maximal inspiratory and expiratory pressures (MIP and MEP, respectively) breathing at the level of functional residual capacity (FRC), according to the method of BLACK and HYATT [20], using a differential pressure transducer (range ±300 cmH_2O; Honeywell, Freeport, IL, USA). The subjects, comfortably seated and wearing a noseclip, performed maximal inspiratory and expiratory efforts, starting from FRC, against an obstructed mouthpiece with a small air leak to prevent closure of the glottis and connected to a tap that allowed the airway to be closed. The subjects were verbally encouraged to achieve maximal strength. The determinations were repeated until five measurements varying by less than 5% and sustained for at least 1 s were obtained; the best value achieved was considered in the data analysis. Normal values were according to BRUSCHI *et al.* [21].

Skeletal muscle function

The peak torque of isokinetic contraction at a test speed of 120° per second of flexor (hamstring) and extensor (quadriceps) muscles of the leg (IFX and IEX, respectively) was measured by means of an isokinetic dynamometer (Cybex; Lumex Inc., Bay Shore, NY, USA) according to standard procedure, taking into account data from the dominant leg [22, 23]. The better of two testing sequences was considered for analysis. Peak torque is measured in Newton-metres (N×m). Twenty two sex-matched subjects, who had recently experienced a myocardial infarction without left ventricular dysfunction, served as controls. In these subjects, mean values of IEX and IFX were 117±22 and 74±11 N×m, respectively.

Rehabilitation programme

The in-hospital rehabilitation programme consisted of: 1) supervised incremental exercise, until achieving twice daily 30 min sessions of continuous treadmill walking at 70% of the load achieved on the incremental exercise test carried out at entry; 2) inspiratory muscle training: 10 min four times a day of inspiratory resistive breathing against a threshold device (Threshold; HealthScan Inc., USA), increasing the inspiratory load until a mouth pressure equal to 50% of MIP was attained [24]; and 3) abdominal muscle training and upper and lower limb training lifting a progressively increasing weight [25]. Nutritional programmes were prescribed when appropriate. After discharge, the patients were instructed to perform exercise (walking, cycling *etc.*) but no structured exercise programme was prescribed.

Statistical analysis

An analysis of variance (ANOVA) test for repeated measurements was employed: 1) to evaluate differences in the indices considered compared with admission; and 2) to test a time effect during follow-up period. A linear regression analysis corrected for multiple comparisons was performed to correlate changes in lung, skeletal and respiratory muscle function and exercise capacity with duration of rehabilitation programme and hospitalization, changes in body weight and haemoglobin (Hb) concentration. A p-value of less than 0.05 was considered to be significant.

Results

One patient died soon after admission due to cytomegalovirus pneumonia, before having performed any functional evaluation. One patient was found at admission to have bilateral phrenic nerve injury and was treated with nocturnal intermittent negative pressure ventilation using a poncho-wrap ventilator for 1 month. Ten patients performed the rehabilitation programme and after discharge were followed-up for 18 months. Hospitalization averaged 75±28 days (range 28–106 days), during which patients performed the rehabilitation programme for 41±19 days (range 20–70 days), *i.e.* 59±18% (range 20–76%) of their stay in hospital.

Lung function

Preoperative lung function data of patients in the study were not available. The time course of lung function tests is presented in table 1. At admission, patients showed reduced static and dynamic volumes and $T_{L,CO}$. At discharge from hospital, no significant changes in dynamic or static volumes, or in $T_{L,CO}$ were observed. A significant increase in VC was observed over time after discharge. At admission, patients were mildly hypoxaemic. P_{a,O_2} was significantly increased at discharge and did not change throughout the follow-up.

Exercise and muscle performance

Changes in body weight, Hb concentration, respiratory and skeletal muscle performance and exercise tolerance are presented in table 2. On admission, patients were underweight and mildly anaemic. They showed reduced exercise capacity as assessed by $V'_{O_2,peak}$ and 6-MWD and in comparison to predicted or control values, and reduced respiratory and skeletal muscle performance as assessed by MIP, MEP, IEX and IFX. The single patient affected by bilateral phrenic nerve injury showed basal values of 17 and 16 cmH_2O (24 and 19% pred) for MIP and MEP, respectively.

Both body weight and Hb concentration progressively increased over time. In comparison to admission, this increase was significant starting from 1 yr after HLT. Maximal body weight and Hb concentration (26 and 22% increase in comparison to admission, respectively) were observed at 18 months.

At discharge, patients showed an increase in MIP, MEP, IEX, IFX, 6-MWD and in $V'_{O_2,peak}$ which did not reach statistical significance. No significant relationship was found between changes in any functional parameter and duration of the rehabilitation programme or hospitalization, or changes in body weight or Hb concentration. Six months after HLT, improvement in IEX, IFX, 6-MWD and $V'_{O_2,peak}$ ($mL \cdot kg \cdot min^{-1}$) became significant and $V'_{O_2,peak}$ reached its highest level (a 38% increase in comparison to admission). The highest values of skeletal and respiratory muscle function indices were observed at 12 months (38, 72, 71 and 50% increase in comparison to admission for MIP, MEP, IEX and IFX, respectively). At that time, changes in MIP and MEP became significant. At 18 months, only 6-MWD showed a further increase to 51% of admission value.

Changes in these variables expressed as percentage of predicted (or control for IEX and IFX) are presented in

Table 1. – Ventilatory function, carbon monoxide transfer coefficient, transfer factor of the lung for carbon monoxide and arterial blood gas values at admission and discharge, and during follow-up

	Admission	Discharge	6 months	12 months	18 months
VC L	2.3±0.5	2.4±0.4	2.6±0.7	3±0.8*	3.1±0.8*
VC % pred	60±15	60±15	70±17	77±12*	81±11*
FEV1/FVC %	82±18	78±15	77±16	75±18	78±17
FEV1 L	2±0.4	2±0.4	2±0.4	2.3±0.5	2±0.6
FEV1 % pred	56±12	63±17	64±15	68±10	67±28
FRC % pred	85±15	84±14	87±17	86±18	83±29
TLC % pred	70±11	75±9	71±15	84±12	78±12
K_{CO} $mmol \cdot min \cdot kPa^{-1} \cdot L^{-1}$	1.07±0.3	1.15±0.4	1.04±0.17	1.09±0.17	1.27±0.24
% pred	52±13	55±2	49±8	53±9	62±12
$T_{L,CO}$ $mmol \cdot min \cdot kPa^{-1}$	3.6±0.8	3.6±0.8	3.8±0.6	4.3±0.9	5.2±1.3
% pred	37±6	41±16	39±6	46±10	54±14
P_{a,O_2} kPa	10.4±1.3	11.6±1.3*	11.6±1.3*	11.7±1.4*	11±1.8
P_{a,CO_2} kPa	4.8±0.8	4.7±0.6	4.9±0.8	4.7±0.5	4.6±0.5
S_{a,O_2} %	95.4±0.4	96.5±1	97±1.3*	96±1.3*	96±2

Values are presented as mean±SD. VC: vital capacity; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; FRC: functional residual capacity; TLC: total lung capacity; K_{CO}: carbon dioxide transfer coefficient; $T_{L,CO}$: transfer factor of the lung for carbon monoxide; P_{a,O_2} and P_{a,CO_2}: arterial oxygen and carbon dioxide tension, respectively; S_{a,O_2}: arterial oxygen saturation; % pred: percentage of predicted value. *: $p<0.05$, compared with value at admission.

Table 2. – Body weight, haemoglobin concentration, muscle and exercise performance at admission and discharge, and during follow-up

	Admission	Discharge	6 months	12 months	18 months
Hb g·dL^{-1}	9.3±0.7	10.2±3.5	10.5±1.4	11±2.2*	13±2*
Weight kg	50±5	50±4	54±7	60±7***	63±9***
MIP cmH_2O	54±21	60±23	69±26	75±17*	65±16
MEP cmH_2O	58±19	70±18	78±9	100±49***	82±31***
IEX N×m	48±16	55±16	86±18***	82±16***	78±20***
IFX N×m	28±12	33±11	35±10*	44±7***	42±10***
6-MWD m	351±66	422±69	481±76***	511±100***	530±91***
$V'_{O_2,peak}$ mL·kg·min^{-1}	14.2±4	18.2±6	19.6±6*	18.9±3.5	15.7±4
$V'_{O_2,peak}$ % pred	40±13	55±4	56±18	51±20	48±14

Values are presented as mean±SD. Hb: haemoglobin concentration; MIP: maximal static inspiratory pressure; MEP: maximal static expiratory pressure; IEX: peak torque of isokinetic contraction of extensor leg muscles; IFX: peak torque of isokinetic contraction of flexor leg muscles; 6-MWD: 6 min walking distance; $V'_{O_2,peak}$: peak oxygen consumption; % pred: percentage of predicted value. *: p<0.05; and ***: p<0.001, compared with value at admission.

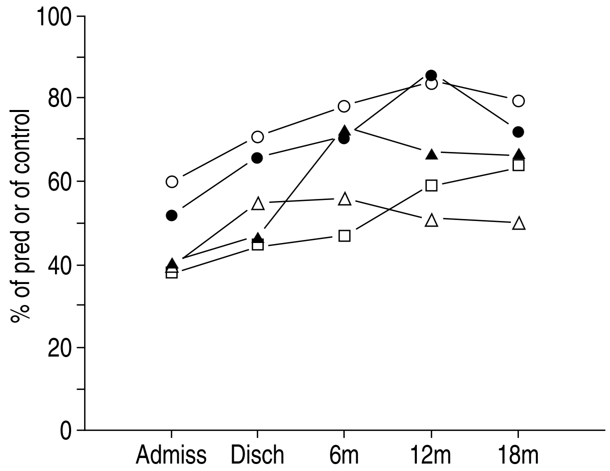

Fig. 1. – Time course of exercise and muscle performance. Values in percentage of predicted (% pred) or of control (see text). —○—: MIP; —●—: MEP; —△—: $V'_{O_2,peak}$; —▲—: IEX; —□—: IFX. Admiss: values assessed at hospital admission; Disch: values assessed at discharge; 6m, 12, and 18m: values assessed at 6, 12 and 18 months after surgery, respectively. MIP: maximal static inspiratory pressure; MEP: maximal static expiratory pressure; IEX: peak torque of isokinetic contraction of extensor leg muscles; IFX: peak torque of isokinetic contraction of flexor leg muscles; $V'_{O_2,peak}$: peak oxygen consumption.

figure 1. The highest increases with time were observed at 12 months in MIP and MEP (to 84 and 86% pred, respectively). At all time-points, all of these measurements were reduced in comparison to predicted or control values.

In table 3, the time course of cardiopulmonary parameters at rest and at maximum exercise are presented. At admission, patients had a more elevated mean resting heart rate (HR) than predicted. All patients stopped the exercise test due to leg muscle fatigue. Maximum HR and V'_E were reduced. Maximum HR, but not V'_E, significantly increased at discharge and further increased 6 and 12 months after surgery. No significant desaturation with exercise occurred at any time.

Discussion

To our knowledge, this is the first report on changes of skeletal and respiratory muscle function over time in recipients of heart-lung transplantation. After HLT, cardiorespiratory function, respiratory and skeletal muscle performance and exercise tolerance were below the predicted or control values. Although, after hospitalization, these parameters showed an improvement which was well-maintained for at least 18 months, they were still significantly below predicted values.

Lung function tests

Dynamic flows, TLC (% pred) and $T_{L,CO}$ were low compared with earlier reports [13, 16, 26–28]. This poor lung function after transplantation may have affected the exercise and muscle performance.

Exercise tolerance

Maximal tolerable exercise capacity has been shown to be reduced in HLT patients. Despite the fact that they were studied in stable clinical condition, HLT patients only achieved $V'_{O_2,peak}$ values of approximately 40–60% predicted. On admission, the patients showed a reduced exercise capacity, in keeping with the literature [6, 11, 12]. A less severe reduction in aerobic work capacity has been found in heart transplant patients [8–10, 29, 30], suggesting that cardiovascular function poses the greater restraining influence on muscular effort in these patients, but other factors may be involved. At discharge, $V'_{O_2,peak}$ increased to 55±4% pred, which is in keeping with the values found by KIMOFF *et al.* [15], and by LEVY *et al.* [31]. In this latter series, the exercise evaluation was performed 7.4±2.2 months after surgery, their patients also having performed a supervised graded aerobic exercise programme. Interestingly enough $V'_{O_2,peak}$ did not return to normal values after 18 months. Similar results have recently been found by ORENS *et al.* [32] in single and double lung transplantation recipients.

The levels of the V'_E/V'_{O_2} ratio at maximal work found in our study are similar to those of LEVY *et al.* [31] and THEODORE *et al.* [12], and showed a constant trend to decrease over the follow-up. Exercise in HLT is associated with excessive hyperventilation in relation to the rate of oxygen uptake [15, 33]. This may represent an effect of prolonged confinement to bed. In HLT, GRASSI *et al.*

Table 3. – Exercise test values at admission and discharge, and during follow-up

	Admission		Discharge		6 months		12 months		18 months	
	Basal	Max	Basal	Max	Basal	Max	Basal	Max	Basal	Max
Work W		33±31		59±36		90±51*		121±50*		109±58*
fR breaths·min^{-1}	23±4	36±6	22±5	32±4	22±5	38±7	20±3	33±5	21±5	35±7
R		1±0.1		1±0.1		1±0.1		0.9±0.1		1.9±1.6
V'E L·min^{-1}	12±2.8	32±16	13±6	34±16	14.6±5.4	40±16*	13±5	41±14*	11±4	38±10**
V'_{O_2} L·min^{-1}	0.3±0.08	0.6±0.2	0.3±0.06	0.9±0.3	0.34±0.1	1±0.4**	0.29±0.07	1.1±0.27**	0.3±0.12	1±0.3**
V'_{O_2} mL·kg·min^{-1}	5.6±1	14.2±4	5.9±1.7	18.2±6	4.5±1.8	19.6±6*	4.6±1.91	18.9±3.5	4.6±1.1	15.7±4
V'_{O_2} mL·kg·HR^{-1}		0.1±0.05		0.1±0.04		0.15±0.05*		0.15±0.02		0.12±0.03
V'_{CO_2} L·min^{-1}	0.24±0.05	0.7±0.2	0.26±0.05	0.9±0.3	0.3±0.09	1.03±0.4**	0.24±0.07	1.01±0.25*	0.26±0.11	1.02±0.35**
F'_{CO_2} %		3.2±0.6		3.7±1.06		3.5±1		3.6±1.4		3.7±0.9*
V'E/V'_{CO_2}	55.2±14	44.8±9	50.2±15	39±9	50.8±16	39.9±9	54.4±19	42±15	52±25	38.9±10*
V'E/V'_{O_2}	47.1±12	46.5±15	42.9±14	37.2±9	44.4±13	40.2±9	42±9	36.3±7.5	48±25	38.5±8
VT L	0.5±0.12	1±0.5	0.5±0.1	1.1±0.4	0.67±0.24	1.45±0.6	0.6±0.3	1.4±0.6	0.56±0.17	1.3±0.5*
HR beats·min^{-1}	106±13	117±13	107±6	125±13*	108±6.4	123±11*	103±6	123±9*	106±9	128±12*
BP (median) mmHg	98±11	98±11	98±8	110±15	97±12	107±17	107±15	112±31	102±8	116±18
Borg scale score	0.1±0.3	0.1±0.3	0.1±0.2	3±2.2	0.1±0.2	2.6±2.2	0±0	1.4±1.5	0±0	2.6±2

Values are presented as mean±SD. fR: breathing frequency; R: respiratory exchange ratio; V'E: minute ventilation; V'_{O_2}: oxygen consumption; V'_{CO_2}: carbon dioxide production; F'_{CO_2}: carbon dioxide expiratory fraction; VT: tidal volume; HR: heart rate; BP: systemic blood pressure. *: p<0.05; and **: p<0.01, compared to value at admission.

[11] found that the ventilatory response is substantially preserved despite lung denervation, confirming a previous study by CERRETELLI *et al.* [8] in heart transplantation recipients. These authors found that the limitation of peak exercise appeared to be imposed by a reduced maximal cardiac performance. The proportional contributions of VT and fR were within normal limits both at rest and at maximal exercise levels and did not change with time. In some, but not all, HTL recipients studied by GRASSI *et al.* [11], breathing pattern during steady-state exercise was similar to that of heart transplantation recipients and to normal untrained subjects. A previous suggestion that there is an inco-ordination of VT and fR resulting from the loss of intrapulmonary receptors was not confirmed when HLT patients were compared with normal subjects during peak exercise [13, 15].

Arterial blood gas values during maximum exercise can be used as an index of the efficiency of pulmonary gas exchange. Under these conditions, the transplanted lungs of our patients were essentially normal, perhaps indicating that the integrating function required for matching ventilation and perfusion is intrapulmonary and autoregulatory in nature, and that an external nerve supply is not a crucial requirement for regulating gas exchange within the lung.

Many factors may influence exercise performance after transplantation. Some of these antedate the procedure, such as age of onset and duration of the pretransplant illness, as well as physical deconditioning and psychological factors associated with long-term debilitation [4–6]. Further postoperative negative influences on recovery could arise from cardiac denervation [7], the short- and long-term complications of allograft transplantation, and the adverse reactions of long-term immunosuppression [34]. Reduction in exercise capacity has been related to acute and chronic anaemia. This may be induced by most of the drugs used, as in our patients, for immunosuppression such as azathioprine or cyclosporin, with different mechanisms [35, 36]. However, although at admission our patients showed a reduction in haemoglobin concentration, anaemia was progressively corrected over time, whilst exercise capacity did not improve further after the 6th month, clearly indicating that other factors may have contributed to the observed reduction.

We have found no report on 6-MWD in HLT. In patients with end-stage pulmonary fibrosis submitted to single-lung transplantation, GROSSMAN *et al.* [37] found values of 6-MWD quite similar to ours. Interestingly, 6-MWD was the one parameter improving at 18th month in comparison to admission, behaving differently from the $V'_{O_2,peak}$. The improvements in 6-MWD in our patients may be, at least in part, related to a learning effect. The 6-MWD is dependent on the physical capacity of patients and may be used as an index of their ability to cope with daily activities [19].

Respiratory muscle function

Inspiratory and expiratory muscles were similarly affected at admission. Improvements in inspiratory and expiratory muscle strength as assessed by MIP and MEP were similar. The rehabilitation programme included both specific inspiratory and abdominal muscle training, but at discharge increases in MIP and MEP were 11 and 21% of the admission value, respectively. Many factors may influence the results of respiratory muscle strength assessment. Motivation and learning may affect measurements [38], distortion of rib cage due to surgery, anaemia, and steroid-induced myopathy [39] may reduce respiratory muscle strength. Our data are in keeping with those of SCIURBA *et al*. [13] and SANDERS *et al*. [16] in HLT patients. The MIP of our patients measured after 6 months are also in agreement with the findings of WILLIAMS *et al*. [40], who performed MIP assessments in single and double transplant recipients 3 months after surgery. In contrast to our results, KIMOFF *et al*. [15] found mean values of MIP greater in four HLT patients than in their control population 3–9 months after surgery. We found no reports on MEP assessment in HLT. Comparison with other studies is difficult, due to different times of evaluation, different methods of measurement, different rehabilitation programmes, if any, prevalence of surgery-induced phrenic nerve lesions and prevalence of infectious and rejection episodes.

Skeletal muscle function

General muscle performance was evaluated by means of the assessment of the peak torque of flexor and extensor leg muscle during isokinetic exercise [22]. Isokinetic exercise is a dynamic type of resistive exercise. Existing studies identify, but do not adequately define, a correlation between torque values and age, sex and conditioning state [22, 41, 42]. Postoperative reduction in IEX and IFX was similar and increases over time were parallel. Chronic preoperative inactivity, psychological factors, steroid myopathy and drug effects may reduce skeletal muscle function in HLT patients [34].

Although preoperative rehabilitation is considered important to achieve good lung function and good exercise performance after lung transplantation [25], our patients did not perform such programmes before surgery due to the fact that they were referred to us only after transplantation. With regard to respiratory muscle strength, $V'_{O_2,peak}$, quadriceps and hamstring torque values as percentage of predicted (or control) (fig. 1) all the considered parameters showed a postoperative reduction ranging 40–60% compared to normal subjects. The greatest improvements were observed in respiratory muscle strength. This result might be related to the rehabilitation programme. Although, for ethical reasons, we did not study a control population, we feel that a rehabilitation programme might be useful in the postoperative treatment of HLT patients. Due to unavoidable complications of HLT, such as thoracic wound, opportunistic infections and acute lung rejection episodes, patients with HLT are often not able to perform a continuous rehabilitation programme. In this regard, our patients performed a rehabilitation programme over a very wide range of periods (20–70 days).

To our knowledge, there is no report on the effects of the single components of a rehabilitation programme in lung transplant recipients. Furthermore, in the one study reporting MIP increase with time, single and double transplant recipients performed postoperative rehabilitation programmes consisting only of aerobic exercise, without any specific inspiratory muscle training [40]. For these reasons, although the clinical benefits of exercise training [43], inspiratory muscle training [44] and weight-lifting training [45] are well-documented both in normal and in pathological conditions, conclusions on the possible effects of rehabilitation in HLT can only be speculative.

In conclusion, in recipients of heart-lung transplantation, skeletal and respiratory muscle function and exercise performances are reduced after surgery, may improve with time but are still below normal values after 18 months. The benefits of rehabilitation programmes should be evaluated with controlled studies.

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