Physical Activity in Daily Life 1 Year After Lung Transplantation

Daniel Langer, PT, MSc, a,b Rik Gosselink, PT, PhD, a,b Fabio Pitta, PT, PhD, c Chris Burtin, PT, MSc, a,b Geert Verleden, MD, PhD, b Lieven Dupont, MD, PhD, b Marc Decramer, MD, PhD, b and Thierry Troosters, PT, PhD a,b

Background: Reduced physical fitness has been reported to occur after lung transplantation. Pre- and post-transplant factors, including an inactive lifestyle, have been proposed as possible causes. However, daily physical activity has not been objectively assessed so far in lung recipients. The purpose of this study was to objectively measure daily physical activity in lung recipients.

Methods: Twenty-two clinically stable patients with single (n = 7) and bilateral lung grafts (n = 15) underwent measurements of physical activity with activity monitors at least 12 months after surgery. Results were compared with findings from 22 healthy, age- and gender-matched control subjects.

Results: Substantial and statistically significant differences in daily activity were observed. Steps, standing time and moderate-intensity activity of lung recipients were reduced by 42%, 29% and 66%, respectively, relative to controls. Daily sedentary time was increased by 30%. Daily steps correlated with self-reported physical functioning (r = 0.81), 6-minute walk distance (r = 0.68), quadriceps force (r = 0.66) and maximum workload (r = 0.63).

Conclusions: This study has shown for the first time that daily activity is substantially reduced after lung transplantation and related to measures of physical fitness and health-related quality of life. Future studies need to examine whether physical activity can be modified to improve functional recovery after lung transplantation. J Heart Lung Transplant 2009;28:572–8. Copyright © 2009 by the International Society for Heart and Lung Transplantation.

Lung transplantation (LTx) has gained widespread acceptance as a therapeutic option for end-stage lung disease.1 Survival rates have improved in successive years with a current worldwide survival half-life of about 5 years.2 Patients have continued to report limitations in physical functioning despite substantial improvements in general quality of life.3,4 Persisting limitations in exercise capacity and skeletal muscle weakness have also been reported.5–11 Inactivity prior to transplantation12 and resulting pre-transplant deconditioning6,13 are likely to influence functional recovery after surgery. Repeated episodes of infection and rejection, use of anti-inflammatory and immunosuppressive drugs and a sedentary lifestyle are possible post-transplant contributors to limitations in physical fitness.5,6,9

Daily physical activity (PA) has been studied in heart and liver recipients, but with ambiguous results. Heart recipients were classified as either “moderately active” (1,100 kcal/week spent in recreational activities), based on self-report,14 or very sedentary, based on accelerometer measurements.15 No statistically significant differences between liver recipients and healthy controls were reported for accelerometer measurements of daily PA.16 To our knowledge, no data on daily PA after lung transplantation have been published. Given this absence of data and the contradictory findings in other study populations after transplantation, the purpose of the present investigation was to objectively measure daily PA in lung recipients.

The main research questions were: (1) Do stable lung recipients reach levels of daily PA comparable to those of healthy, age-matched control subjects 1 year after LTx? (2) Is daily PA in lung recipients related to measures of exercise capacity, muscle force and health-related quality of life?

METHODS

Subjects
Our experimental protocol was approved by the ethics review board of the University Hospital Leuven. Criteria for participation in our study were: (1) age >40 years;
(2) status ≥12 months post-transplantation; and (3) no
infection or acute allograft rejection requiring hospital
admission within the preceding 30 days. Exclusion
criteria were: (1) retransplantation; (2) heart–lung or
multiple-organ transplantation; and (3) signs of bronchi-
olitis obliterans syndrome (Stage ≥1), as defined by the
initial diagnostic criteria from the International Society
for Heart and Lung Transplantation (ISHLT).17 Age-
and gender-matched volunteers were included as control
subjects. Healthy individuals were all relatives of stu-
dents from the Department of Rehabilitation Sciences at
the Katholieke Universiteit Leuven.

Assessment of Daily Physical Activity

Daily PA was assessed with two activity monitors. Both
activity monitors were worn simultaneously on 4 con-
secutive days during 12 waking hours. Subjects were
instructed not to change their daily routine while
wearing the devices.

The DynaPort activity monitor (DynaPort) quantifies
time spent in different postures (i.e., standing, sitting
and lying), time spent walking and daily steps. A
detailed description of the device can be found else-
where.18 In previous validation studies the device was
able to accurately detect postures and movements in
slowly moving subjects.12,19 Daily walking time, daily
steps (computed from walking time and average walk-
ing frequency), standing time and sedentary time (time
spent lying and sitting) were the parameters from the
DynaPort that were chosen to characterize daily PA of
study subjects.

The SenseWear Pro activity monitor (Armband) was
used to estimate energy expenditure during daily activ-
ities. The Armband integrates monitoring of body move-
ment by a biaxial accelerometer with non-invasive sensors
measuring the following physical parameters: changes in
body temperature; near-body ambient temperature; heat
flux; and galvanic skin resistance. The provided software
(SENSWEAR Professional, version 6.0.2.1444) uses pro-
prietary algorithms to provide minute-by-minute esti-
mates of energy expenditure, expressed in metabolic
equivalents (METs). Time spent in activities of at least
moderate intensity was used as main outcome. These
were defined as activities requiring at least 3 METs.
Thirty minutes of moderately intense PA are known to
result in health benefits when performed on a daily
basis.20 Energy estimates of the Armband were previ-
ously validated in patients with chronic obstructive
pulmonary disease (COPD).21

Health-related Quality of Life

The Medical Outcomes Study Short Form (SF-36) ques-
tionnaire was used to evaluate self-reported domains of
the health-related quality of life (HRQoL) measure in
lung recipients.22 The SF-36 questionnaire was not
administered in healthy control subjects. Instead, stan-
dard reference scores25 and population norms from the
general Dutch population were used as reference val-
ues.24 The SF-36 was previously validated in COPD
patients25 and has been used in patients before and
after LTx.3,4,26,27

Other Measurements

Pulmonary function, maximal inspiratory and expira-
tory pressures, quadriceps force, handgrip force, max-
imal exercise capacity and 6-minute walking distance
(6MWD) were assessed in our laboratory according to
protocols described previously in more detail.12

Statistical Methods

Group means were compared using unpaired t-tests.
SF-36 domain scores were compared with Dutch pop-
ulation norms,24 derived from a sample with similar age
and gender distribution. Physical and mental SF-36
summary scores were calculated for comparison with
standard reference values with a mean of 50 and a
standard deviation (SD) of 10.23 Pearson product-mo-
moment correlation coefficients were calculated between
parameters of PA, physical fitness and HRQoL.

RESULTS

Subjects

Eighty-nine patients underwent surgery at the Univer-
sity Hospital Leuven between March 2005 and Decem-
ber 2006. Seventy-seven of these patients were still alive
during the inclusion period between January 2007 and
February 2008. Forty-seven of them met the age criteria.
Five additional patients were excluded because of not
meeting other inclusion criteria. Pre-transplant diag-
noses of the 42 eligible patients were lung emphysema
(n = 30), interstitial lung disease (n = 7), pulmonary
hypertension (n = 3) and bronchiectasis (n = 2).
Twenty patients were not included in our sample
because they either refused to participate (n = 7) or
lived far away from our center (n = 13).

Twenty-two patients agreed to participate and under-
went measurements at an average of 15.5 months
(range 12 to 24 months) after surgery. Pre-operative
diagnoses of included patients were emphysema
(n = 18), interstitial lung disease (n = 2), pulmonary
hypertension (n = 1) and bronchiectasis (n = 1). Seven
patients received single-lung and 15 received bilateral
lung grafts. All lung recipients were clinically stable.
Three of 22 patients followed a structured rehabilita-
tion program at the University Hospital Leuven after
transplantation. All patients received a daily dose of
steroids (methylprednisolone) ranging between 0.2 and
0.4 mg/kg/day during the first year after transplantation.
None had returned to work by the time of their
measurements. Twenty-two healthy, age- and gender-
matched control subjects were included. All were retired by the time of their measurements. Anthropometric data of study subjects are shown in Table 1.

**Daily Physical Activity**

Number of steps, standing time, sedentary time and time spent in moderately intense PA of study subjects are shown in Figure 1. Data of transplant recipients in these plots are expressed as a percentage of the average value of healthy controls. Only a few lung recipients exceeded average levels of PA in healthy control subjects. Average daily step count was 4,977 (SD 2,332) in the transplant group as compared with 8,645 (SD 3,491) in healthy controls (difference between means: −2,668 steps [−29%]; 95% confidence interval: −5,475 to −1,861; p = 0.000). Daily walking time averaged 55 minutes (SD 25) in the transplant group and 81 minutes (SD 26) in healthy controls (difference between means: −26 minutes [−32%]; 95% confidence interval: −10 to −10; p = 0.002). Daily standing time averaged 201 minutes (SD 76) in the transplant group and 283 minutes (SD 99) in healthy controls (difference between means: −82 minutes [−29%]; 95% confidence interval: −135 to −29; p = 0.004). Daily sedentary time (lying or sitting averaged 447 minutes [SD 76] in the transplant group and 358 minutes [SD 112] in healthy controls; difference between means: 104 minutes [32%; 95% confidence interval: 40 to 168; p = 0.002). Daily time spent in moderately intense activity (≥3 METs) averaged 104 minutes (SD 26) in healthy controls (difference between means: 92 minutes [32%; 95% confidence interval: 40 to 168; p = 0.002). Number of steps, standing time, sedentary time and time spent in moderately intense PA of study subjects are shown in Figure 1. Data of transplant recipients in these plots are expressed as a percentage of the average value (100%) in healthy controls (Healthy). Abbreviations: DynaPort = DynaPort activity monitor; Armband = SenseWear armband; (A) Step Count = daily step count; (B) Standing = daily standing time; (C) Sedentary = daily sitting and lying time; (D) MIPA = moderately intense physical activity (≥3 METs). *Statistically significant difference between groups (p < 0.01).

**Muscle Force and Exercise Capacity**

Data on muscle force and exercise capacity of study subjects are presented in Table 3. These indicators of physical fitness were all reduced in lung recipients compared with healthy controls. Differences between groups were not statistically significant for handgrip force (−10%), maximal inspiratory pressure (−16%)

**Table 2. HRQoL Scores From the SF-36 for Lung Recipients**

| SF-36 scales | Lung recipients | Reference value
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Physical function</td>
<td>64.0 ± 19.8</td>
<td>83.0</td>
</tr>
<tr>
<td>Role—physical</td>
<td>68.8 ± 33.5</td>
<td>76.4</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>69.2 ± 22.5</td>
<td>74.9</td>
</tr>
<tr>
<td>General health</td>
<td>59.3 ± 23.9</td>
<td>70.7</td>
</tr>
<tr>
<td>Vitality</td>
<td>64.4 ± 17.5</td>
<td>68.6</td>
</tr>
<tr>
<td>Social function</td>
<td>83.6 ± 20.3</td>
<td>84.0</td>
</tr>
<tr>
<td>Role—emotional</td>
<td>91.7 ± 19.2</td>
<td>82.3</td>
</tr>
<tr>
<td>Mental health</td>
<td>76.5 ± 18.8</td>
<td>76.8</td>
</tr>
<tr>
<td>SF-36 summary scales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical component (PCS)</td>
<td>42.8 ± 11.2</td>
<td></td>
</tr>
<tr>
<td>Mental component (MCS)</td>
<td>53.8 ± 10.9</td>
<td></td>
</tr>
</tbody>
</table>

Data expressed as mean ± SD.

*Statistically significant difference between groups (p < 0.01).
Peripheral and Respiratory Muscle Force and Exercise Capacity of Study Subjects

<table>
<thead>
<tr>
<th></th>
<th>Lung recipients</th>
<th>Controls</th>
<th>Δ</th>
<th>95% CI of Δ</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Handgrip (kgF)</td>
<td>36 ± 16</td>
<td>40 ± 9</td>
<td>-4</td>
<td>-12 to 4</td>
<td>0.35</td>
</tr>
<tr>
<td>MIP (cmH₂O)</td>
<td>-76 ± 48</td>
<td>-91 ± 59</td>
<td>15</td>
<td>51 to -21</td>
<td>0.41</td>
</tr>
<tr>
<td>MEP (cmH₂O)</td>
<td>159 ± 44</td>
<td>186 ± 42</td>
<td>-27</td>
<td>-55 to 1</td>
<td>0.06</td>
</tr>
<tr>
<td>Quadriceps (Nm)</td>
<td>102 ± 36*</td>
<td>155 ± 35</td>
<td>-53</td>
<td>-76 to -30</td>
<td>0.00</td>
</tr>
<tr>
<td>6MWD (m)</td>
<td>483 ± 66*</td>
<td>696 ± 77</td>
<td>-213</td>
<td>-257 to -169</td>
<td>0.00</td>
</tr>
<tr>
<td>Wmax (Watt)</td>
<td>74 ± 23*</td>
<td>182 ± 56</td>
<td>-108</td>
<td>-136 to -80</td>
<td>0.00</td>
</tr>
<tr>
<td>VO₂max (L)</td>
<td>1.2 ± 0.3*</td>
<td>2.4 ± 0.6</td>
<td>-1.2</td>
<td>-1.5 to -0.9</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± Standard Deviation. Δ, mean difference between groups; 95% CI, 95% confidence interval; p, probability of difference when the null hypothesis is true (no difference between groups); Handgrip; Handgrip Force; MIP, Maximal Inspiratory Pressure; MEP, Maximal Expiratory Pressure; Quadriceps, Maximal Isometric Quadriceps Force; 6MWD, Six-minute walking distance; Wmax and VO₂,max, maximum workload and maximal oxygen consumption achieved during a maximal incremental cycle ergometer test.

*Statistically significant difference between groups.

and maximal expiratory pressure (−15%). Statistically significant differences were observed in quadriceps force (−34%), 6-minute walk distance (−31%), maximum workload (−59%) and maximal oxygen consumption (−50%).

**Differences Between Single- and Bilateral lung Recipients**

Bilateral lung recipients had a higher forced expiratory volume in 1 second (FEV₁; 85 [SD 13] percent of predicted values [%pred] vs 72 [SD 14] %pred in single-lung recipients; p = 0.05), whereas diffusing capacity for carbon monoxide was comparable between groups (60%pred in both groups). In tests of maximal exercise capacity none of the lung recipients reached measured maximum minute ventilation (average: 69% of maximum ventilation, range 63% to 79%) or had oxygen desaturation, according to transcutaneous measurement. All patients reported high scores for leg fatigue (average score 8 out of 10) and low scores for dyspnea (average score 3 out of 10) on a modified Borg scale at maximal exercise. Despite better lung function in double-lung recipients, we observed trends toward better leg muscle force, exercise capacity and daily PA in single-lung recipients. Quadriceps force in single-lung recipients was 90 (SD 26) %pred compared with 75 (SD 13) %pred in bilateral lung recipients (p = 0.09). Peak workload in single-lung recipients was 63 (SD 29) %pred, whereas bilateral lung recipients achieved 52 (SD 12) %pred (p = 0.21). Peak oxygen consumption was comparable between groups. Single-lung recipients took 5,990 (SD 2,995) steps per day compared with 4,275 (SD 1,495) steps in bilateral lung recipients (p = 0.08).

**Relation of Daily PA to Physical Fitness and HRQoL**

Correlations between measures of daily PA, muscle force, exercise capacity and HRQoL are presented in Table 4. Moderate to good (r = 0.49 to 0.72), statistically significant correlations were observed between measures of PA and physical fitness. Moderate, statistically significant inverse relationships (r = −0.51 to

### Table 4. Correlations Between Parameters of Physical Activity, Physical Fitness and Health-related Quality of Life

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<tbody>
<tr>
<td>Physical fitness</td>
<td></td>
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<tr>
<td>Handgrip (%pred)</td>
<td>−0.23</td>
<td>−0.17</td>
<td>0.03</td>
<td>0.02</td>
<td>−0.03</td>
</tr>
<tr>
<td>MIP (%pred)</td>
<td>−0.22</td>
<td>−0.08</td>
<td>−0.25</td>
<td>0.22</td>
<td>−0.06</td>
</tr>
<tr>
<td>MEP (%pred)</td>
<td>0.01</td>
<td>0.13</td>
<td>−0.10</td>
<td>0.06</td>
<td>0.31</td>
</tr>
<tr>
<td>Quadriceps (%pred)</td>
<td>0.62*</td>
<td>0.66*</td>
<td>0.45</td>
<td>−0.54*</td>
<td>0.49*</td>
</tr>
<tr>
<td>6MWD (%pred)</td>
<td>0.63*</td>
<td>0.68*</td>
<td>0.41</td>
<td>−0.51*</td>
<td>0.72*</td>
</tr>
<tr>
<td>Wmax (%pred)</td>
<td>0.54*</td>
<td>0.63*</td>
<td>0.45</td>
<td>−0.55*</td>
<td>0.67*</td>
</tr>
<tr>
<td>VO₂max (%pred)</td>
<td>0.15</td>
<td>0.18</td>
<td>0.08</td>
<td>−0.11</td>
<td>0.17</td>
</tr>
<tr>
<td>HRQoL</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>PCS (SF-36)</td>
<td>0.72*</td>
<td>0.73*</td>
<td>0.46*</td>
<td>−0.53*</td>
<td>0.59*</td>
</tr>
<tr>
<td>MCS (SF-36)</td>
<td>0.11</td>
<td>0.05</td>
<td>−0.14</td>
<td>0.05</td>
<td>−0.14</td>
</tr>
</tbody>
</table>

Dyna, DynaPort Activity Monitor; Armband, SenseWear Armband; Walk, daily walking time; Steps, daily step count; Stand, daily standing time; Sedentary, daily sitting and lying time; MIPA, moderately intense physical activity; Handgrip, handgrip force; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; Quadriceps, maximal isometric quadriceps force; 6MWD, 6-minute walk distance; Wmax and VO₂max, maximum workload and maximal oxygen consumption achieved during a maximal incremental cycle ergometer test; %pred, percentage of predicted reference values; HRQoL, health-related quality of life; PCS, physical component summary scale; MCS, mental component summary scale.

*Statistically significant correlation (p < 0.01).
were found between parameters of physical fitness and daily time spent sedentary (sitting or lying).

Domains of the SF-36 reflecting physical health components were most closely related to parameters of PA. This resulted in moderate to good (r = 0.46 to 0.73), statistically significant relations between PA and the PCS of the SF-36 (Table 4). A moderate inverse relationship (r = -0.53) between this domain of HRQoL and a parameter of inactivity (daily time spent sedentary) was observed. No statistically significant correlations were found between the MCS and indicators of PA.

Representative scatterplots of statistically significant relations (all p < 0.01) between daily steps and physical functioning subscale of the SF-36 (r = 0.81), functional exercise capacity (r = 0.68), quadriceps force (r = 0.66) and maximum workload (Wmax) (r = 0.63) are shown in Figure 2.

**DISCUSSION**

This study is the first controlled trial to investigate physical inactivity in patients after lung transplantation. Our data show a significant reduction in the amount of daily activities and a major reduction in moderately intense activities in stable lung allograft recipients studied 1 year after transplantation. Higher levels of daily activity were related to better preserved muscle strength, higher exercise capacity and fewer self-reported limitations in physical functioning.

**Physical Activity in Organ Recipients**

To our knowledge, no previous studies have assessed daily PA in lung allograft recipients. We found substantial (−29% to −66%), statistically significant reductions compared with healthy controls for all parameters of daily PA.

Objective measured data on daily PA in other transplant populations have been presented in liver and heart allograft recipients. Evangelista et al. reported very low levels of daily activity in women from a comparable age cohort after heart transplantation. In addition, only 15% of patients reported to engage in activities of at least moderate intensity. However, PA levels in this study were not compared with a control group.

In their study, van den Berg-Emons et al. objectively measured daily PA with accelerometry-based activity monitors after liver transplantation. They found no statistically significant reductions in activity levels of liver recipients in comparison with healthy, age-matched control subjects (10.2% vs 12.6% dynamic activities). They concluded that PA is not importantly reduced in liver recipients. Limitations in exercise capacity that have been reported in liver recipients are also less severe than those after lung transplantation.

**Relation of PA to Physical Fitness and HRQoL**

Reductions in exercise capacity in lung recipients were comparable to those noted in earlier studies. The presence of muscle weakness in our sample is also in accordance with other data after lung transplantation. Neither in single- nor bilateral lung recipients was pulmonary function a limitation to maximal exercise capacity. Pulmonary function was therefore most likely not related to the capacity of performing daily tasks. Our data are in accordance with earlier findings indicating that, even after single-lung transplantation, exercise capacity is primarily limited by peripheral muscle abnormalities rather than by ventilatory factors. Earlier studies showed that muscle groups were not uniformly affected with more pronounced leg muscle weakness. This supports the hypothesis that muscle force is not only affected by anti-inflammatory and immunosuppressive drugs, but also by differences in pre-transplant deconditioning and post-transplant PA.

Because this study was the first to objectively assess PA in addition to muscle function, exercise capacity and HRQoL, it is for the first time possible to study relationships between these parameters. Higher levels of PA were consistently related to higher (nearly normal) leg muscle strength, functional exercise capacity and self-
reported physical functioning (Figure 2). This can be taken as an indication that higher levels of daily PA could contribute to functional recovery after lung transplantation. Our cross-sectional data, however, must be interpreted with caution. Instead of causing exercise limitations and impaired quality of life, PA may also only be an intermediate variable that in turn is largely determined by various pre- and post-transplant factors. Assumptions about possible cause-effect relationships based on cross-sectional data therefore remain speculative. Our findings are in line with those of Painter et al.\(^5\) in their study of liver transplant recipients. After correction for several post-transplant confounders they observed a strong relation between (self-reported) daily PA and self-reported physical functioning. The absence of a statistically significant relation between daily PA and the MCS of the SF-36 is in support of earlier findings indicating that the physical and mental domains of HRQoL are influenced by different factors.\(^6\),\(^7\)

**Clinical Implications**

From our data it becomes clear that most patients do not return to a normally active lifestyle after LTx. We believe that more attention should be paid to this clinically relevant finding in the treatment of patients who have undergone this procedure.

Different strategies could be applied to increase PA in lung recipients. Several studies already showed positive results of structured, supervised exercise training after lung transplantation.\(^8\)–\(^4\) However, the conclusiveness of these studies was limited by the absence of a control group. Behavioral lifestyle activity counseling could be another possibility for modifying daily PA after transplantation.\(^2\)

**Limitations and External Validity**

A limitation lies within the cross-sectional nature of the collected data. It was not possible to take into account the effects of different degrees of pre-transplant PA and deconditioning because PA and physical fitness were not assessed before transplantation. Although all patients were stable at the time of inclusion we can also not exclude the possible negative effects of earlier post-transplant episodes of infection or rejection.

The present study has focused particularly on clinically stable older patients (\(>40\) years). Patients \(<40\) years of age (i.e., all patients with cystic fibrosis) were excluded due to presumably different recovery of daily activities (e.g., return to work). It is therefore likely that recorded activity profiles are only representative for lung recipients in this age cohort approximating these characteristics. Younger recipients (e.g., patients with cystic fibrosis) are probably more active, whereas patients with early development of bronchiolitis obliterans syndrome would be expected to be less active.

**Perspectives**

Longitudinal studies or interventional studies (randomized, controlled trials) are needed to study in greater detail the relationship between PA, physical fitness and HRQoL after lung transplantation.

Longitudinal studies should assess PA levels of patients before transplantation to determine how changes in PA after transplantation affect functional recovery. Modifying physical activity as an independent variable in interventional studies would provide the strongest evidence for a causal relationship between PA and functional recovery after lung transplantation.

In conclusion, this study has shown for the first time that daily physical activity is substantially reduced after lung transplantation and related to measures of exercise capacity, muscle force and health-related quality of life. Future studies are needed to determine whether physical activity can be modified to improve functional recovery after lung transplantation.

**REFERENCES**