Physical Activity in Solid Organ Transplant Recipients: Organizational Aspects and Preliminary Results of the Italian Project


ABSTRACT

Most of the difficulties when trying to realize the proposal to prescribe physical activity for transplantation patients come from patient attitudes and cultural beliefs that ignore the benefits of exercise, but there also are organizational aspects arising from the difficulties that these patients face in accessing supervised exercise facilities. To address these difficulties, the Italian study project “Transplant … and Now Sport” was developed based on a model of cooperation among transplantation specialists, sports physicians, and exercise specialists organized as a team combining their specific skills to effectively actuate the physical exercise programs. This preliminary report is based on 26 patients (16 male, 10 female; 47.8 ± 10.0 years old; 21 kidney and 5 liver transplantations; time from transplantation 2.3 ± 1.4 years) who performed prescribed and supervised exercises consisting of 3 sessions per week of aerobic and strengthening exercises for 1 year. Preliminary results show a significant decrease in body mass index ($t = 1.966; P < .05$) and a significant increase in peak aerobic power ($t = 4.535; P < .01$) and maximum workload ($t = 4.665; P < .01$) on the incremental cycling test. Also maximum strength of knee extensors ($t = 2.933; P < .05$) and elbow flexors ($t = 2.450; P < .05$) and countermovement jump performance ($t = 2.303; P < .05$) significantly increased. Creatinine and proteinuria tended to decrease, but the differences were not significant. In health-related quality of life assessed by the SF-36 questionnaire, the Bodily Pain, General Health, Vitality, Social Functioning, and Role Emotional scale scores showed a significant improvement ($P < .05$). Preliminary results of the study protocol “Transplant… and Now Sport” show the positive effects of the model based on cooperation among transplantation centers, sports medicine centers, and gyms in the administration of a supervised exercise prescription. These data should be considered a contribution to developing...
It is well known that cardiovascular and metabolic diseases (hypertension, diabetes, hyperlipidemia, obesity) affect mortality and morbidity in solid organ transplant recipients [1]. It is also well established that immunosuppressive therapy often results in numerous adverse effects, including osteoporosis, sarcopenia, and weight gain [2,3]. Furthermore, most of the patients presenting for transplantation are physically inactive or have very low levels of exercise capacity [4]. On the other hand, there is wide agreement that regular physical activity is protective and can counteract cardiovascular and metabolic diseases, osteoporosis, sarcopenia, and most of the risk factors derived from physical inactivity and a sedentary lifestyle [5].

Notwithstanding this knowledge, until now the role of exercise after transplantation has not been emphasized enough. As pointed out by Gordon et al. [6], there is no uniform agreement among transplant professionals about the need for or recommended extent of exercise after transplantation. There are also many practical difficulties when trying to realize the proposal to prescribe physical activity for transplantation patients. Probably, most of these difficulties come from patient attitudes (ie, lack of motivation and interest, fear of injury) and cultural beliefs that ignore the benefits of exercise, which may derive in part from the silence of transplant professionals about the benefits of exercise and in part from the common belief that other medical issues are more important than exercise [6].

Another organizational aspect that usually is not taken into account arises from the difficulties that transplantation patients have in accessing supervised exercise facilities; this also is a common problem for patients with many other illness [7,8]. Transplantation patients are usually involved in a rehabilitation period before discharge after surgery, and they usually receive only general suggestions to increase their level of physical activity after discharge, without considering the organizational aspects of these suggestions. As a consequence, the preventive role of physical activity is largely underutilized because health care professionals do not rigorously promote exercise to transplantation patients and do not incorporate the promotion of exercise into routine patient management [6]. In other words, after discharge, the main questions should be not only “Which activity is better?” but also “How can patients easily access physical activity?”

To answer these questions, the Italian National Transplant Centre in 2008 set up the “Transplant…and Now Sport” project as a unique proposal aimed at studying the outcomes of a personalized prescription of organized and supervised physical activity for solid organ transplantation patients performed in certified gyms, and at sensitizing physicians to promoting exercise to transplant recipients. In this article, we present the rationale of the project with some preliminary results of the study, with the aim of contributing to the debate regarding the needs and the effects of physical exercise on transplantation patients, mainly focusing on organizational aspects.

MATERIALS AND METHODS
Organizational Aspects

The project is based on a model of cooperation between transplantation specialists, sports physicians, and exercise specialists (graduates and postgraduates in physical education and/or physiotherapy). In Italy, they are working in transplantation centers, sports medicine centers, and gyms, respectively, and can be organized as a team combining their specific skills to effectively actuate the physical exercise programs. The physicians in the transplantation centers have the duty of selecting patients suitable for physical activity, considering exclusion criteria. The sports physicians are charged to prescribe a personalized program of physical activity based on the results of functional assessments performed at the sports medicine centers. In the gyms, the patients carry out the prescribed program and train under the supervision of certified personnel. This organization aims to check the patients from clinical (transplant center) and functional (sports medicine center) points of view, but also to identify facilities in their home districts where patients can easily perform their training programs.

Study Protocol

This is a multicenter, controlled, prospective, nonrandomized study that considered the enrollment of 120 patients (range 18 to 70 years), 6 months to 8 years after solid organ transplantation (kidney, liver, heart), with clinical and functional stabilities checked by the transplant centers. Exclusion criteria were orthopedic limitations, psychiatric or neurological disorders, and any other cardiovascular contraindication to exercise testing and training [9].

Patients recruited from different transplantation centers were divided into 2 groups: the cases group (A), in which personalized physical activity was prescribed by the sports physicians, and the control group (B), in which some generic lifestyle indications were given without specific prescription and supervision. All subjects (groups A and B) received individualized counselling about the protocol “Transplant…and Now Sports” by the transplantation center. Written informed consent was obtained from the patients before inclusion, according to the procedures approved by the ethical committees of the transplant centers involved in the study.

Blood chemistry, urinalysis, and cardiovascular assessments were performed by the transplantation center to assess the exclusion criteria and to check the function of the transplanted organ. After the administration of the SF-36 questionnaire to evaluate health-related quality of life (HRQoL), the patients who matched the inclusion criteria were sent to the sports medicine center to carry out the functional assessment tests for exercise capacity, muscle strength, and body composition. Based on the results of these tests, the sports physicians prescribed the individual program of exercise only for patients in group A. For the patients in group B, the physicians recommended generic exercises for physical fitness without prescription as routine patient management. Then, patients
in group A were sent to a certified gym to start the prescribed physical activity under the supervision of a suitably trained physiotherapist or a graduate in physical education. 

Patients in both groups were checked at baseline (T0) and 12 months (T12) from the time of enrollment, coming back to the transplantation and to the sports medicine centers at T12 to repeat both the clinical and the functional assessment tests performed at T0. All physicians and exercise specialists involved in the study were required to participate in a 1-day course to implement and to share their knowledge on the clinical aspects of transplant recipients, on the effects of physical exercise, and on the protocol of the study.

Exercise Capacity

Incremental exercise testing was performed on a cycle ergometer starting from 20 W, with increments of 20 W every 4 minutes until voluntary exhaustion or until the appearance of electrocardiographic signs of pathology or inappropriate blood pressure response. A 12-lead electrocardiogram was monitored continuously throughout the test. At each step, blood pressure was measured and a capillary blood sample from the earlobe was taken to measure blood lactate concentration in order to estimate the workload corresponding to aerobic and anaerobic thresholds, conventionally declared at 2 and 4 mM of lactate, respectively [10,11].

Oxygen uptake (Vo2) was determined continuously using an open circuit method (Sensor Medics Corp., Anaheim, CA) calibrated against known gas mixtures before each test. Oxygen uptake at the aerobic and anaerobic thresholds in relation to the workload and heart rate were then calculated. Oxygen uptake at the highest tolerated level of exercise also was determined (Vo2peak).

Muscle Strength and Power

Muscle strength was measured by the 1-repetition maximum strength tests, calculated using an indirect method (consisting of 7 to 12 repetitions with submaximal workload) [12]. Leg press and free weights were used to evaluate the maximum strength of some muscular groups in the lower (knee extensors, plantar flexors) and upper (elbow flexors, elbow extensors, and shoulder abductors) limbs. The power of the lower limbs was measured indirectly from the fly time of a countermovement jump and is expressed as maximum displacement of the center of mass during fly (Optojump, Microgate, Italy) [13].

Body Composition, Urinalysis

Body mass index was calculated using the formula kg/m2. Creatinine and proteinuria at rest were assessed by standard laboratory methods to check renal function [14].

HRQoL

The Medical Outcomes Study Short Form Questionnaire (SF-36) was used to evaluate self-reported domains of health status. The SF-36 is a 36-item questionnaire that includes 8 scales of HRQoL: Physical Functioning (PF), Role Limitation due to Physical Health (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Limitations due to Emotional Health (RE), and Mental Health (MH). These scales are scored from 0 to 100, with a higher score being more positive [15]. Questionnaires were completed by the patients at T0 and T12, before the clinical check-up.

Exercise Prescription

The exercise prescription included cardiovascular and strengthening exercises. The cardiovascular exercise was performed on a stationary bicycle, with heart rate corresponding to the aerobic threshold, previously determined by the incremental cycling test. The right intensity was continuously monitored by heart rate monitors (Polar, Finland), so the heart rate of the patient was maintained at a constant during the aerobic exercise with slight adjustments of the mechanical power of the stationary bicycle. The duration of this exercise was 30 minutes, with a frequency of 3 times per week. Strengthening exercises consisted of 2 sets of 20 repetitions at 35% of the previously determined 1-repetition maximum for each of the selected muscle groups of the upper and lower limbs.

Statistical Methods

Descriptive statistics (means ± standard deviations) were calculated for all continuous variables. A paired t test was used to evaluate the differences between T0 and T12 for each variable, applying post-hoc Bonferroni analysis (SPSS statistical program). Statistical significance was set at P < .05.
PRELIMINARY RESULTS

A total of 150 transplant recipients were considered between September 2010 and September 2013; 38 recipients were excluded from recruitment due to living too far from the gyms, medical complications, death, or loss to clinical follow-up. At present, 112 patients are enrolled, but only 26 have reached T12 since the enrollment date. Therefore, this preliminary analysis is based on 26 patients of the cases group (16 male, 10 female, mean age 47.8 ± 10.0 years old, 21 kidney and 5 liver transplant recipients, mean time from transplantation 2.3 ± 1.4 years), from 5 transplantation centers, who have completed the functional assessment tests for physical capacity in 6 sports medicine centers and have already reached T12, performing the supervised exercise programs in 8 certified gyms (Fig 1). The main preliminary results of the study regarding the urinalysis, the functional assessment tests, and the HRQoL questionnaires at T0 and T12 are shown in Tables 1, 2, and 3. Creatinine and proteinuria tend to decrease at T12, but the differences between T0 and T12 are not significant. All of the physiological variables significantly increase at T12, whereas only 5 of 8 scales of the SF-36 questionnaire significantly increase at T12.

DISCUSSION

The preliminary results of this study support the effectiveness of the proposed model involving transplantation centers, sports medicine centers, and gyms. This model is based on good cooperation among transplantation specialists, sports medicine physicians, and exercise specialists, who act as a unique team specifically trained to prescribe and administer personalized programs of physical activity, consisting of both aerobic and strengthening exercises. The collaboration of these 3 different health care professionals is effective to provide a continuous active network on a local scale, not only suggesting but managing the physical activity needs of the transplantation patients.

The multidisciplinary collaboration model proposed in this study led to significant improvements of many physiological variables related to physical fitness after 12 months of supervised exercise, achieving positive effects on the cardiovascular and musculoskeletal systems, and also on some psychological aspects of HRQoL, indicating that a biopsychosocial approach is suitable to face the many difficulties in proposing exercise as a treatment for transplantation patients, and probably for many other patients. The preliminary results of the urinalysis indicate that performing a supervised protocol of aerobic and strengthening exercises 3 times per week for 1 year does not involve any changes in renal function; therefore, such a physical activity protocol does not interfere negatively on allograft function in the kidney transplantation patients and can be considered a safe part of therapy. The relatively low percentage of dropouts at T12 in the cases group (5 of 74; 7%) were all because these transplantation patients resumed their normal work schedules (thus having less time to devote to exercise), suggesting that motivation and supervision of the physical activity play an important role in adherence to the treatment.

There are some limitations in this preliminary report. Firstly we do not present and discuss the results of the control group. Those patients did not obtain significant improvements in the studied physiological and psychological parameters, but thus far the number of control patients enrolled is too small to make a good comparison. The question of whether supervised controlled exercise could be more effective than generic lifestyle indications will be answered and discussed at the end of the study.

A second limitation is the nonrandomized design, which is dependent on the adopted model in order to allow the selected patients to practice physical activity in gyms close to their homes. The accessibility of the facilities where patients can easily carry out the personalized programs of exercise seems to be crucial in every proposal of exercise as a therapy, and according to our project, a solution can be found in organizing a network of certified gyms closely connected with the physicians charged to prescribe exercise.

Finally, we present the results obtained only by kidney and liver transplantation patients who completed the

| Table 1. Preliminary Urinalysis Obtained on 26 Transplantation Patients Who Performed 12 Months of Prescribed Exercises With Supervision |
|----------------------|-----------------|-----------------|
|                      | Creatinine mg/dL| Proteinuria g/dL |
| T0                   | 1.4 ± 0.5       | 0.10 ± 0.14     |
| T12                  | 1.3 ± 0.4       | 0.08 ± 0.08     |
| t                    | 1.272           | 0.262           |
| p                    | >.05            | >.05            |
| Δ                    | −7%             | −20%            |

| Table 2. Preliminary Results Obtained on 26 Transplantation Patients Who Performed 12 Months of Prescribed Exercises With Supervision |
|----------------------|------------------|------------------|------------------|------------------|------------------|------------------|
|                      | Body Mass Index, kg/m² | Wmax | V̇O₂peak, mL/kg/min | HRmax, beats/min | Fmax KE, N | CMJ, m | FmaxEF, N |
| T0                   | 24.2 ± 3.6        | 92 ± 33 | 22.0 ± 6.9 | 135 ± 23 | 912 ± 332 | 0.229 ± 0.115 | 87 ± 26 |
| T12                  | 23.9 ± 3.9        | 109 ± 41 | 25.3 ± 7.3 | 142 ± 26 | 1050 ± 432 | 0.257 ± 0.100 | 102 ± 33 |
| t                    | 1.966             | 4.665 | 4.535 | 3.101 | 2.933 | 2.303 | 2.450 |
| p                    | <.05              | <.01 | <.01 | <.01 | <.05 | <.05 | <.05 |
| Δ                    | −1%               | +18% | +15% | +5% | +15% | +12% | +17% |

Wmax: maximum workload at the end of the incremental cycling test; V̇O₂peak: higher value of oxygen consumption in the incremental cycling test; HRmax: maximum heart rate attained at the end of the incremental cycling test; Fmax KE: maximum force of knee extendors; CMJ: maximum vertical displacement during counter-movement jump; FmaxEF: maximum force of the elbow flexors.
CONCLUSIONS

Preliminary results of the study protocol “Transplant…and Now Sport” including patients who up to now have completed the protocol highlight the positive effects of the model based on the cooperation among transplantation centers, sports medicine centers, and gyms in the administration of a supervised exercise prescription. Despite some limitations, this report can be considered an impetus to discuss, develop, and promote other detailed exercise protocols for transplant recipients and to foster improved posttransplantation health and survival. Furthermore, we think that the preliminary data of our study can assist transplant professionals in counselling transplant recipients, think that the preliminary data of our study can assist transplant professionals in counselling transplant recipients, and to foster improved posttransplantation health and survival. Furthermore, we think that the preliminary data of our study can assist transplant professionals in counselling transplant recipients, thus helping to ensure that physical activity becomes a safe routine medical treatment plan for patient management, as advocated by Gordon et al. [6].

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REFERENCES