



DEPARTMENT OF BIOLOGICAL STANDARDISATION, OMCL NETWORK & HEALTHCARE (DBO)

MLF/as

Working document, with no legally binding status, intended exclusively for the addressees and their associates, under the responsibility of the addressees (listed opposite). Level 1

English / Anglais

PA/PH/TO (14) 33 3 R

Strasbourg, July 2015

EUROPEAN COMMITTEE (PARTIAL AGREEMENT) ON ORGAN TRANSPLANTATION (CD-P-TO)

TO066 - Position paper on Transplantation and physical activity

Document submitted by: Claudia Carella

EDQM Responsible Scientific Officer: Marta Lopez Fraga

Distribution		
For action:		
For information:		

Position Paper on Transplantation and Physical Activity

Carella C, Fattinger B, Avsec D, Simeonova M, Mosconi G, Roi GS, Totti V, Trerotola M, Nanni Costa A

on behalf of the European Committee on Organ Transplantation (CD-P-TO)

INTRODUCTION

Physical inactivity is an important risk factor for cardiovascular disease, which has recently been defined both as a pandemic threat with repercussions on health care, and as the fourth leading risk factor for global mortality⁽¹⁾. According to WHO, physical inactivity levels are rising in many countries⁽²⁾. This not only has major implications for the prevalence of non-communicable diseases (NCDs) and the general health of the population worldwide, but it also adds to the burden on Healthcare Systems which now have to cope with the additional cost of treating NCDs. Several studies report the positive impact of regular physical activity in the prevention of primary and secondary cardiovascular disease as well as stroke, diabetes, hypertension, colon cancer, breast cancer and depression.

It has been demonstrated that transplant patients may develop medical complications such as metabolic syndrome, susceptibility to infection and chronic diseases which may compromise the outcome of transplantation and graft survival in the long-term. Immunosuppressive therapy may play a role in the development of such complications, but the psychological response to post-transplant treatments must also be taken into consideration when dealing with this type of complication.

The solid organ transplant population is characterised by an increased risk of developing cardiovascular disease after receiving a transplant, and the analysis of available post-transplant data shows a high number of complications including an increased incidence of diabetes, weight gain possibly leading to obesity, and dyslipidaemia. It is now known that the key factors affecting weight gain in transplant recipients are the post-transplant treatment itself, which alters metabolic function, and the hunger induced by the improvement patients experience in their physical condition after the transplant. Quality of life is known to have a major influence on the success of a transplant, and is evaluated by various social indicators including returning to work or resuming studies, becoming a parent, participating in social activities in general, and social reintegration. Physical activity and exercise are meaningful indicators for social reintegration since they help organ transplant patients adjust to the changes in their lives brought about by a transplant, develop their body awareness and enhance their physical and mental condition.

From a public health standpoint, it is important to recognise that cardiovascular disorders are currently the leading cause of death in the transplant population and that, in order to reverse this trend, appropriate medical and behavioural counter measures are urgently required. Exercise capacity is a more powerful predictor of mortality among men than other established risk factors for cardiovascular disease⁽³⁾, with each 1MET (metabolic equivalent) increase in exercise capacity

conferring a 12 percent improvement in survival (*Table1*). Another aspect to be taken into account is that regular exercise reduces the risk of chronic metabolic and cardiorespiratory diseases, in part because exercise exerts anti-inflammatory effects. The anti-inflammatory effects of regular exercise may be mediated via both a reduction in visceral fat mass (with a subsequent decrease in adipokine release) and the introduction of an anti-inflammatory environment with each bout of exercise (4,5).

PRESENT SITUATION IN EUROPE

A survey was conducted among the Council of Europe member states to check for similar projects or programs on the quality of life of transplanted patients focusing on physical activity. Although follow-up data for transplanted patients are registered and monitored in all the countries surveyed there are no general national rules on how and what to measure apart from standard clinical parameters, blood values, immunosuppression levels, and general health status, etc.

Physical activity has been recognised as an added value but is not regularly included in most of the programmes. Physiotherapy is prescribed by National Health Systems when needed, with some countries providing a few weeks of rehabilitation after liver, heart and lung transplantation. However, no funding is provided for further physical activity as a means of improving quality of life.

While the importance of physical activity is widely recognised, the majority of National Health Systems have not yet been able to develop a system for promoting physical activity in general and for transplanted patients in particular.

The survey found that, in one member state, the national health insurance scheme covers the cost of physical activities prescribed by a follow-up physician, but that patients were required to pay for physiotherapy themselves. It also found that in many member states, rehabilitation with physiotherapy is provided after heart, liver and lung transplantation and, in most cases, is covered by national health insurance bodies.

OUR RECOMMENDATIONS

National Authorities should educate, advise and heighten the awareness of physicians performing transplants and caring for transplanted patients about the importance of prescribing regular physical activity after transplantation, depending on individual needs and health status. Such activities may be started very soon after surgery and should continue under supervision after the patient is discharged from hospital.

National Authorities should encourage research to develop a reliable and simple "rehabilitation after transplant" model programme for use by transplant recipients under the supervision of Sports Medicine doctors.

National Authorities should start specific campaigns for transplanted patients, through patient organisations, scientific societies and health foundations in both the public and private sectors, to promote regular physical activity as part of the social reintegration of transplanted patients.

Physicians should recommend regular physical activity for transplant recipients, even those with chronic disease, as a healthy habit that will improve their quality of life.

Health institutions, National Authorities and specialists should create common rehabilitation guidelines for post-transplant patients.

National Health Systems should recognise the importance of prescribing physical activity as an adjunct to immunosuppressive therapy for transplanted patients and provide appropriate funding.

Health institutions, National Authorities and specialists should raise awareness on an international level of the importance and benefits of introducing prescribed physical activity in conjunction with immunosuppressive therapy for transplanted patients. This would be of benefit not only to the patients, whose quality of life would improve, but also to member states themselves since it would reduce the cost of post-transplant follow-up (economic impact), expedite patients' return to the workplace (socio-economic impact), improve their quality of life, confirm the efficacy of transplantation as a life-saving therapy, increase confidence in the transplant system and raise awareness of donation culture (public and social impact), all of which are aspects that Governments should take into account.

THE ITALIAN EXPERIENCE

In 2008, the Italian National Transplant Centre (*Centro Nazionale Trapianti, CNT*) began a study on a group of transplant athletes taking part in national and international sports competitions in order to verify the effects of sporting activity on solid-organ transplant recipients⁽⁶⁾. The results for physiological response, energy expenditure, kidney function and endurance of physical strain in the group were comparable to those obtained for non-transplant athletes. On the basis of these results for athletes, a research protocol was established in 2010 to measure exercise effectiveness in transplant patients as post-transplant therapy for use alongside pharmacological treatments. This provided a unique opportunity to study the outcomes of a personalised prescription of organised and supervised physical activity for solid-organ transplant patients.

During the Italian Winter Transplant Games organised by the Italian Association of Dialysis and Transplant Patients (ANED sport) in 2009⁽⁷⁾, solid-organ transplant recipients' abilities during physical activity and their perception of their physical and mental state were studied. A team of experts in sports medicine and transplants performed specific tests on 16 transplanted skiers to measure body mass index, body fat percentage (plicometer), explosive power in the lower limbs (the Bosco test), energy expenditure (armband) and the perception of personal state of health (SF-36).

Another study, the "NoveColli Life" study, involved transplanted cyclists and aimed to check certain aspects of renal function in transplant recipients during a 130-kilometre cycling-race, and to compare the data obtained with those of non-transplant cyclists competing in the same event. Twenty transplanted athletes covered the 130 km in an average of six hours and 37 minutes versus six hours and 15 minutes for the 44 non-transplanted subjects. All the athletes gave venous blood and urine samples the day before the race (Pre), immediately after the race (Post) and 24 hours after competing (24h). Urea, creatinine, micro albuminuria, urinary proteins and urine specific gravity were measured to assess renal function. A significant increase was found between Pre and Post values and a significant decrease between Post and Post 24h values in both groups.

The results indicate a significant difference in renal function between transplanted cyclists and the non-transplant subjects at these three times (before, during and 24hrs after the race). Non-transplanted cyclist values remained within the normal range. A similar trend was observed in the transplant recipient cyclists and the variations were comparable to those measured in the non-transplanted group, although the values of the transplanted group were higher, slightly above the normal range.

CLINICAL TRIAL

To support scientific research and information on physical activity and transplants, the Italian National Transplant Centre and the University of Bologna, in collaboration with the Isokinetic Education & Research Department, sponsored the Research Protocol "A transplant...and now it's time for sport", the first scientific study designed to measure the effects of exercise in patients after solid organ transplantation. The primary endpoint of this study was to demonstrate, through scientific measurements, that physical activity is essential for all transplant recipients. Promoting the prescription of regular physical activity as supportive therapy for patients with chronic conditions would not only help prevent many diseases, but would also alleviate the financial burden of disease on public healthcare systems. In particular, supervised exercise can help control the overall physical (and mental) well-being of transplant recipients, leading to significant improvements in post-transplant quality of life⁽⁸⁾.

Preliminary data indicate that, twelve months after recruitment, transplanted patients who performed physical activity showed an improvement in body composition (decrease in the percentage of adipose tissue) and an increase in work capacity (+15% increase in muscle strength and +17% in cardio-respiratory endurance)⁽⁹⁾. These effects are accompanied by an improvement in the self-perception of physical health (+8%) and overall health (+10%). The preliminary results of the study are therefore very encouraging and confirm the hypothesis that exercise has drug-like effects.

The "A transplant...and now it's time for sport" protocol was established in 2010 by a team of transplant experts and sport physicians employed by different Italian Local Health Authorities. The premise of this study was that cardiovascular disorders are the leading cause of death in transplant recipients and that physical exercise is essential not only for "transplant athletes" but for all transplant recipients receiving anti-rejection treatments (cortisone and immunosuppressive drugs) which encourage changes in lipid metabolism and can cause serious heart disorders.

The Italian National Transplant Centre and the FITOT foundation jointly trained 250 doctors and graduates in physical education and recruited 45 transplant clinicians in ten Italian regions to the study. A total of 148 Italian transplant patients were enrolled in the study, 83 in the clinical group and 54 in the control group. Twelve-month results were obtained from two pilot regions (Emilia Romagna and Veneto) where respectively 21 and 33 recipients were taking part in the study.

The parameters of the patients improved with physical activity, the percentage of body fat tended to decrease (-1% as a trend), lower and upper limbs strength increased by 3% up to 25% and aerobic capacity increased by an average 14%.

Over the one year period, the *improvement* in self-perception of health status was as follows: physical health status +8%, general health status +10%, psychological well-being +6%.

CONCLUSION

The Italian protocol "A transplant...and now it's time for sport" shows that, in transplanted patients, regular physical activity and supervised physical exercise are largely positive in terms of patient safety and have beneficial effects on quality of life.

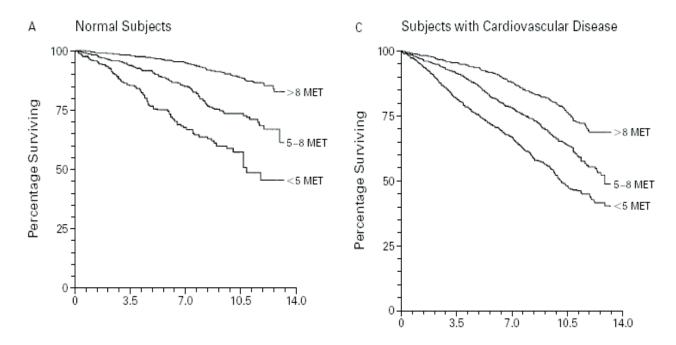
Regular physical activity of moderate intensity, such as walking, cycling, or any kind of bodily movement produced by skeletal muscles that requires energy expenditure, has significant benefits for health ⁽¹⁰⁾.

Furthermore the *Action Plan for the Global Strategy for the prevention and control of non-communicable diseases* (issued by WHO through Resolution WHA61.14) urges Member States to implement national guidelines on physical activity for health and encourages them to develop and put into practice policies and interventions targeting the importance of physical activity for health.

The CD-P-TO (European Committee – partial agreement – on organ transplantation) recommends that all Council of Europe countries promote specific physical activity programs as a complementary treatment for transplanted patients and a means of improving quality of life, and encourages Governments to act on this suggestion to improve the general health of their national population.

TABLE

Table 1: Myers et al., NEJM 2002, 346:793-801



REFERENCES

- 1. Kohl HW3, Craig CL, Lambert EV et al: "The pandemic of physical inactivity: global action for public health". Lancet 2012;380:294-305.
- 2. World Health Organisation: "Global recommendations on physical activity for health". WHO Library Cataloguing-in-Publication Data, WHO 2010.
- 3. Myers J Prakash et al: "Exercise capacity and mortality among men referred for exercise testing". N Engl J Med 2002:346:793-801.
- 4. Gleeson M et al: "The anti-inflammatory effects of exercise: mechanism and implications for the prevention and treatment of disease". Nat rev Immunol 2011;11:607-615.
- 5. Kwon H et al: "Adipokines mediate inflammation and insulin resistance". Front Endocrinol (Lusanne) 2013;4:71.
- 6. Trerotola M, Grasso E, Storani D, Totti V, Roi GS, Mosconi G, Nanni Costa A: "A Transplant... and Now It's Time for Sport: The Importance of Physical Activity for Transplant Recipients". Organs Tissues & Cells 2013; 16(3):175-182.
- 7. Mosconi G, Cuna V, Tonioli M, Totti V, Roi GS, Sarto P, Stefoni S, Trerotola M, Nanni Costa A: "Physical activity in solid organ transplant recipient: preliminary results of the Italian Project". Kidney Blood Press Res 2014; 39:0-0; published on line: May 31, 2014.
- 8. Didsbury M, McGee RG, Tong A, Craig JC, Chapman JR, Chadban S, Wong G: "Exercise Training in Solid Organ Transplant Recipients: A Systematic Review and Meta-Analysis". Transplantation 2013;95: 679-687.
- 9. Roi GS, Stefoni S, Mosconi G, Burra P, Granito M, Macini P, Mastrosimone S, Nacchia F, Brugin E, Rigotti P, Sarto P, Sella G, Tamè M R, Sgarzi S, Totti V, Trerotola M, Tripi F, Ermolao A, Nanni Costa A: "Physical Activity in Solid Organ Transplant Recipients: Organisational Aspects and Preliminary Results of the Italian Project. Transplantation Proceedings, in press.
- 10. Heiwe S, Jacobson SH: "Exercise training for adults with chronic kidney disease" (Review). The Cochrane Library 2011, Issue 10