



# Physical rehabilitation in heart transplantation\*

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## ABSTRACT

After heart transplantation patients improve their quality of life. However, they frequently have clinical problems in the post operative period, as physical deconditioning, muscular atrophy, weakness and lower maximal aerobic capacity, in part due to the inactivity in the preoperative period and to factors as the difference in donor/receptor body surface, heart denervation, among others. Regular physical activity plays an important role in heart transplanted patients follow-up and should be recommended as soon as possible, may be in pre-discharge phase, going on after discharge, which could help patients to have a satisfactory life-style, similar to what they had before the disease, returning to active and productive life.

## INTRODUCTION

The heart transplantation is the last therapy for patients with final-stage heart failure, resulting in hemodynamic normalization in rest and during exercise, improving tissue perfusion and the neurohormonal harmful effects that follow heart failure<sup>(1)</sup>.

After heart transplantation, patients present physical exercise intolerance due to disturbance on hemodynamic performance as result of cardiac, neurohormonal, vascular, muscle-skeletal and pulmonary abnormalities. This could be partially explained by the pre-transplant heart failure, the surgical act itself, the in-hospital period, the use of immunosuppressive agents, the number of rejection events and the transplantation time<sup>(2,3)</sup>.

Physical activity has demonstrated to be of great relevance in the post-transplantation rehabilitation, improving the exercise capacity, thus facilitating the return to regular daily activities after long pre- and post-transplantation deconditioning period, also reducing some frequent complications such as: hypertension, obesity, body alteration, libido reduction, osteoporosis, anxiety, depression, euphoria and lower physical capacity<sup>(3)</sup>.

## PHYSIOLOGICAL RESPONSE OF THE TRANSPLANTED HEART

Among the surgical techniques for heart transplantation, the most employed are the standard and the bicaval. The standard technique involves the neural cut at the atrioventricular connection level, thus preserving more parasympathetic than sympathetic fibers. The bicaval technique involves the full removal of the cardiac junction, the upper and lower vena cava, resulting in complete heart denervation<sup>(4,5)</sup>.

Thus, the stimulus required for the beginning of the nervous fibers reinnervation process presents higher probability to occur when the neural cut occurs in full. This may explain why the standard surgical technique shows evidences of regeneration only of

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sympathetic fibers, while the bicaval technique shows reinnervation evidences of both the sympathetic and parasympathetic fibers<sup>(6)</sup>, fact that may have clinical relevance, once the complete reinnervation increases the control of the blood pressure due to the higher reflex in the heart rate change, leading to a better adaptation during physical exercise.

The post-transplantation rest heart rate is high when compared to healthy individuals of same gender and age. However, a progressive delay both to reach maximal heart rate and to its reduction in the recovery period is observed during the exercise. In heart rate variability analysis, where the measurement of the maximal and minimal spectral bands in the variability indicates parasympathetic and sympathetic activation, respectively, a decline on the maximal variability at the exercise initial phase was observed, what probably would be indicating parasympathetic reinnervation in transplanted individuals through the bicaval technique, what was not observed through the standard technique<sup>(6)</sup>.

The peak oxygen intake presents reduced value in transplanted individuals, what may be related to the surgical technique employed, among other factors such as: systolic and diastolic dysfunction, muscular atrophy, metabolic abnormalities as result of the heart failure (that remain after transplant), use of medicine that reduce the exercise capacity and sympathetic stimulation as result of the use of immunosuppressive agents. However, the regular physical activity may improve the oxygen intake<sup>(7)</sup>.

The systemic effects of nitric oxide influence from the denervated sinus node and the modifications of the cardiac wall tension up to the serum catecholamine concentration. In transplanted individuals, the nitric oxide improves the heart rate regulation through the sinus node stimulation, through the reflex response to vasodilatation and through the neuromodulation influences on the autonomic heart control<sup>(8,9)</sup>.

The ciclosporine associated to hypertension may be partly mediated through the sodium retention and the body plasma volume<sup>(10)</sup>. Both are described as stimulators of the atrial natriuretic peptides (ANP) secretion for the protection against the blood pressure elevation. Thus, it has been demonstrated that the ANP is increased after heart transplantation. However, no difference in the ANP level between the bicaval and standard techniques was observed<sup>(2)</sup>.

The type B natriuretic peptide (BNP) also presents elevated plasma concentration. It deals about a natural antagonist of the renin-angiotensin-aldosterone system and its secretion is sensible to the plasma volume expansion and to the ventricular wall distension. The findings of higher BNP levels in patients submitted to standard surgical technique if compared to patients submitted to bicaval technique may be a result of the increase on the right ventricle post-load, presenting higher transpulmonary gradient and the incidence of the mitral incompetence, what may contribute to the increase in the pulmonary capillary pressure, without leading to ventricular dysfunction<sup>(2)</sup>.

The reduction in the blood compliance observed in transplanted individuals might be a reflex of the hypertension induced by ciclosporine by means of a decline in the peripheral vasodilatation

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or alterations in the vascular mechanisms. Furthermore, the higher sympathetic activity in the blood vessels outlet may lead to an increase in the tonus of the arteries smooth musculature with consequent increase in the vessels stiffness.

The cardiac output in rest and in the beginning of the exercise in denervated heart is basically mediated through the increase in the pre-load, in other words, increase in the final diastolic volume and increase in the systolic volume through Frank-Starling mechanism. However, during progressive exercise, the inadequate increase in the heart rate through the release of the surrounding catecholamines leads to the increase in the cardiac output, however, not sufficient for maximal exercise<sup>(11,12)</sup>.

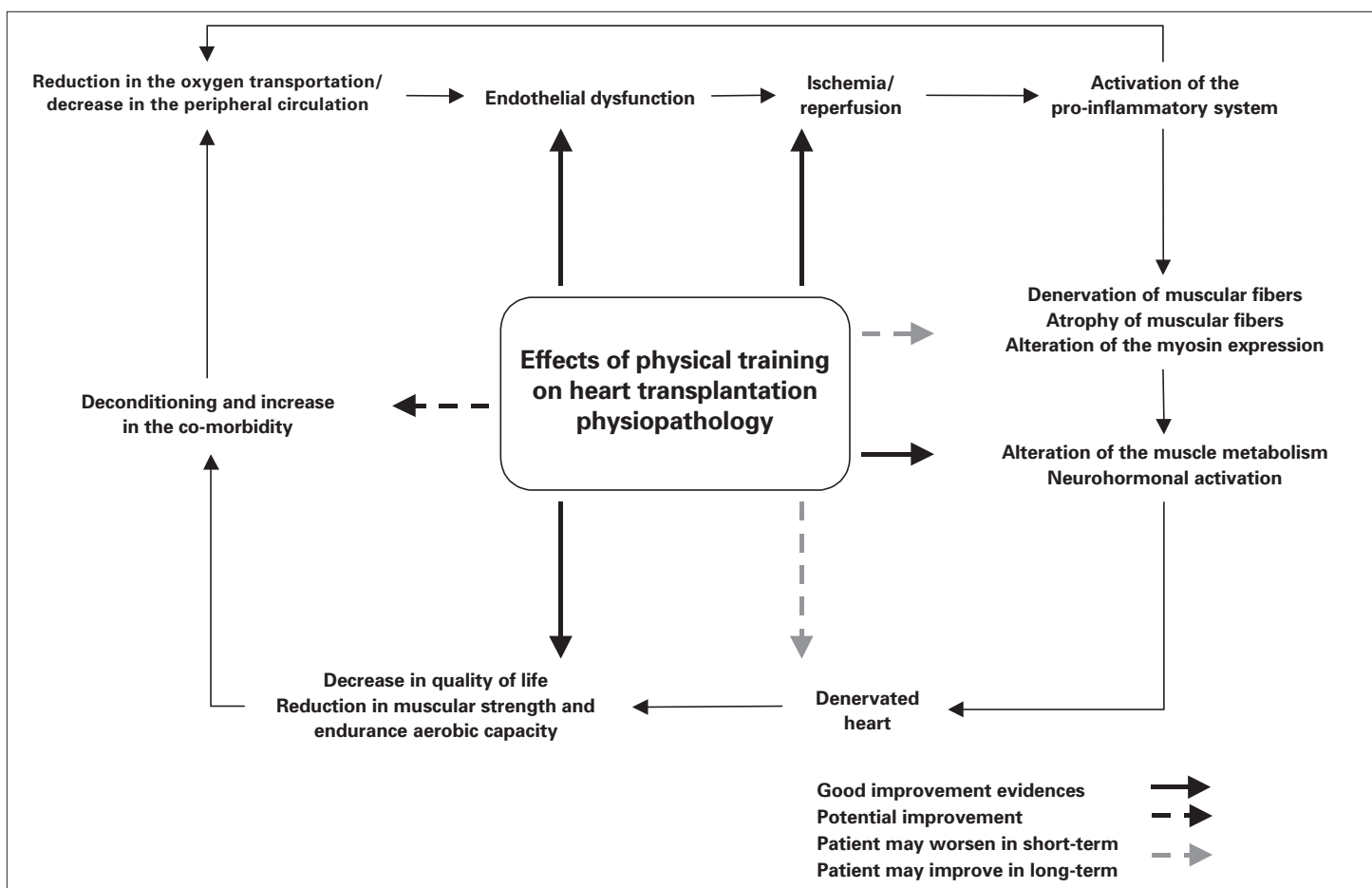
In studies where the standard and bicaval techniques are compared, the cardiac output presented similar values between groups in the first six months and higher after one year with the standard technique. Besides, the standard technique also presented lower

values of pulmonary resistance and higher values of right atrium pressure in the same period<sup>(4)</sup>. However, no alterations in the performance between techniques during the exercise were observed.

Studies are controversial with regard to the rest ejection fraction of the left ventricle after heart transplantation when presenting similarity in relation to the reference value. However, there is an agreement that the ejection fraction of the left ventricle increases along the exercise in the same proportion as for a healthy individual<sup>(13,14)</sup>.

## PHYSICAL REHABILITATION OF THE TRANSPLANTED HEART

The regular physical activity has played important role in the improvement of quality of life both in healthy individuals and in people suffering from heart disease, either in the primary phase or in the second phase of the heart disease (figure 1).



**Fig. 1** – Association between physical capacity and heart transplantation and the potential role of physical training on the systemic improvement, on the physiopathological effect, on quality of life and on functional capacity

Post-heart transplantation patients present improvement in the quality of life. However, they frequently present physical deconditioning, muscular atrophy, muscle weakness and lower aerobic capacity as result in part of the pre-surgical inactivity and factors as the difference in the donor/receptor body surface and heart denervation<sup>(15)</sup>. The immunosuppressive therapy that aids receptor to tolerate the donor's heart limits the physical capacity such as the rejection episodes or symptoms that suggested the reduction in the cardiocirculatory performance<sup>(16)</sup>.

Regular physical activity plays important post-transplantation role and should be recommended as soon as possible for the reestablishment of the physical capacity, enabling transplanted individuals to take over their daily and recreative activities<sup>(17)</sup>.

During the in-hospital phase, we initiate the physical conditioning program in the Heart failure and transplantation Unit-InCor-HCFMUSP as soon as the hemodynamic reestablishment and the weaning from post-transplant intravenous drugs occur. The physical rehabilitation program used in this phase is the one proposed by the University of Stanford, which consists of aerobic exercises in cycle-ergometer or walking with progressive increase on duration and intensity with monitoring of the heart rate, blood pressure and subjective fatigue (Borg Scale (figure 2) from slightly tiring and tiring)<sup>(18)</sup>. Besides the proposed program, we also initiate training of articular mobility, flexibility and resistance of the large muscular groups<sup>(19)</sup>. At the discharge phase, we orient patients to walk on the plane level for a period of 40 to 60 minutes in speed of 80 to

100 meters/minute, 4 to 5 times a week in home regimen. Six months after discharge the hemodynamically stable patients perform cardiopulmonary exercise test for cardiopulmonary evaluation, being later allowed to regular physical conditioning programs, with ventilatory thresholds being used for the physical activity prescription.

6.
7. Very easy
8.
9. Easy
10.
11. Relatively easy
12.
13. Slightly tiring
14.
15. Tiring
16.
17. Very tiring
18.
19. Exhaustive
20.

Fig. 2 – Borg scale of subjective fatigue

The physical training adequate intensity for transplanted individuals is not yet well established. However, some methods for the prescription of physical activity have been suggested such as the maximal heart rate percentile, the peak oxygen intake and the ventilatory thresholds<sup>(15,16)</sup>. Regardless the post-transplantation physical activity prescription method, patients have obtained beneficial results (table 1).

**TABLE 1**  
**Benefits of post-heart transplantation physical conditioning**

Reduction in the rest heart rate and submaximal exercise heart rate
Increase in maximal heart rate
Increase in oxygen intake
Improvement of respiratory efficiency
Reestablishment of bone mineral density
Increase in muscular strength
Reduction in neurohormonal activity
Decrease in systolic and diastolic blood pressure
Improvement of endothelial function
Reduction of body fat
Improvement of quality of life

Studies have demonstrated that the regular physical activity may revert or diminish the physiological alterations in transplanted patients<sup>(15,16)</sup>. Transplanted individuals submitted to cardiac rehabilitation programs in exercise sessions of four times a week with moderate intensity present improvement in the aerobic capacity between 20 and 50%. The possible mechanisms for this improvement are the increase in the peripheral metabolism, especially through the better oxygen extraction and hemodynamic changes including the increase in the heart rate, the cardiac output<sup>(20)</sup>, the endothelial function<sup>(16)</sup> and the reduction in the neurohormonal activity<sup>(21)</sup>. Besides, the respiratory efficiency is also improved during exercise<sup>(15)</sup>.

Physical activity with resistance exercises has been used in the post-transplant period to increase muscular mass and bone density<sup>(22,23)</sup>. This activity is particularly important because a loss of free fat and bone mass occurs in this group of patients as result of the heart failure and the use of post-transplant medicine. Thus, it was demonstrated in transplanted patients submitted to resistance-exercise training that the bone density was reestablished at the pre-transplant level while in the control group the bone density decreased in 6%<sup>(22)</sup>.

Home physical training programs with aerobic and resistance exercises have been proposed for transplanted patients<sup>(15)</sup>. How-

ever, an increase of 49% of the  $\dot{V}O_2$  peak was observed in supervised training against 18% in home exercises as well as a higher exercise tolerance and lower ventilatory response after 6 months of training.

However, the effect of physical activity and post-transplant arteriosclerosis as secondary prevention that theoretically could delay or prevent the coronary arterial disease is not yet elucidated. Just as physical activity and immunologic system in transplanted patients, it is known that in healthy individuals the moderate intensity exercise may increase the resistance to infection by activating the release of immunostimulative factors such as growth hormone, prolactin and cytokines. Paradoxically, the intense exercise may reduce this beneficial effect by elevating immunosuppressive factors such as glucocorticoids and opioids<sup>(24)</sup>.

Thus, the treatment of post-heart transplantation patients must include a physical activity program. Just as the clinical therapeutics deals about maintaining the function of organs, the physical activity further favors physiological adaptations resulting in improvements on quality of life.

## POST-HEART TRANSPLANTATION REHABILITATION AND PHYSICAL CONDITIONING HANDBOOK

**Class I** – Conditions in which there are evidences and/or agreement that some procedure is effective or useful:

- 1) early physical rehabilitation;
- 2) aerobic physical activity;
- 3) resistance-exercise physical activity;
- 4) supervised physical activity program;
- 5) exercise test, preferably cardiopulmonary exercise test.

**Class II** – Condition in which there are conflicting evidences and/or divergence of opinion with regard to the usefulness and effectiveness of some procedure or treatment:

- a) Evidence or opinion that favors the utilization of the treatment:
  - 1) non-supervised physical activity program;
  - 2) physical activity in heated swimming pool;
  - 3) recreative activities.
- b) Evidence of less established opinion:
  - 1) participation in competitive games without supervision;
  - 2) high-intensity sporadic physical activity.

**Class III** – Condition in which there are evidences and/or agreement that the procedure/treatment is not useful and in some cases, it may even be harmful:

- 1) hemodynamic instability;
- 2) light or severe rejection episodes;
- 3) infection process;
- 4) clinical, orthopedic or neurological limitation that disables physical activity.

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