# Exercise after Heart Transplantation: Typical Alterations, Diagnostics and Interventions

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**ABSTRACT**

For the treatment of terminal heart failure, heart transplantation is considered to be the gold standard, leading to significantly improved quality of life and long-time survival. For heart transplant recipients, the development and maintenance of good functional performance and adequate exercise capacity is crucial for renewed participation and integration in self-determined live. In this respect, typical transplant-related alterations must be noted that play a significant role, leading to restrictions both centrally and peripherally. Before patients begin intensive and structured exercise training, a comprehensive diagnosis of their exercise capacity should take place in order to stratify the risks involved and to plan the training units accordingly. Particularly endurance sports and resistance exercises are recommended to counter the effects of the underlying disease and the immunosuppressive medication. The performance level achieved can vary considerably depending on their individual condition, from gentle activity through a non-competitive-level to intensive competitive sports. This paper includes an overview of the current literature on heart transplant recipients, their specific characteristics, as well as typical cardiovascular and musculoskeletal alterations. It also discusses suitable tools for measuring exercise capacity, recommendations for exercise training, required precautions and the performance level usually achieved.



## Introduction

Heart failure (HF) has a prevalence of 1–2 %, making it one of the most widespread adult diseases in Europe. Between 6 and 25 % of HF patients are currently in the advanced stages of this disease. This tendency is on the increase, with the incidence of HF rising as patients live longer due to improved and innovative treatment options [1–3].

The gold standard for treating terminal HF is still heart transplantation (HTX), even in this age of donor shortages [4]. Compared with conventional treatment or treatment using a left ventricular assist device (LVAD), HTX improves survival rates, exercise tolerance and quality of life [5]. The survival rates after one, five, and ten years are currently approx. 85, 75, and 60 %, respectively [6, 7]. With these survival times, the optimum build-up of exercise capacity and functional performance is therefore crucial.

With reference to the latest literature, this overview describes common patient characteristics, typical transplant-related alterations to the musculoskeletal and cardiovascular system, as well as general requirements and precautions with regard to sports activities after HTX. It also discusses suitable tools for measuring exercise capacity, recommendations for exercise training and the performance level usually achieved after transplantation.

### Patient characteristics

Currently, about 5000 HTXs per year are performed worldwide, with a slightly increasing overall tendency. Median survival after HTX in adults is now 12.5 years and extends to 15 years to 1-year survivors [7]. About 75 % of all recipients are male with a mean age at transplantation of 55 years. However, the age range for recipients is quite large, with 30 % of patients younger than 40 years and 30 % of patients older than 60 years, leading to different physical overall prerequisites [7].

The main indications for HTX in adults are usually non-ischaemic dilated cardiomyopathy (51 %) (e. g. due to doxorubicin, alcoholism, familial condition, myocarditis, post-partum cardiomyopathy) or ischaemic cardiomyopathy (32 %) [6–9]. About half of all patients are bridged with mechanical circulatory support (MCS) prior to transplantation, mainly by the use of LVADs [7]. In these patients, LVAD-related complications are often the reason for high-urgency listing and transplantation (mostly anticoagulation complications, driveline infections or device failure) [10].

Prior to HTX, many patients already suffer from concomitant diseases, such as hypertension (51 %), diabetes mellitus (27 %) or hyperlipidaemia, which also remain after surgery. In addition, the following transplant-related complications can occur and influence prognosis and clinical condition significantly: early graft failure, rejection, cardiac allograft vasculopathy (CAV), late graft failure, severe renal dysfunction, malignancy (mostly skin cancers), or infections [7–9].

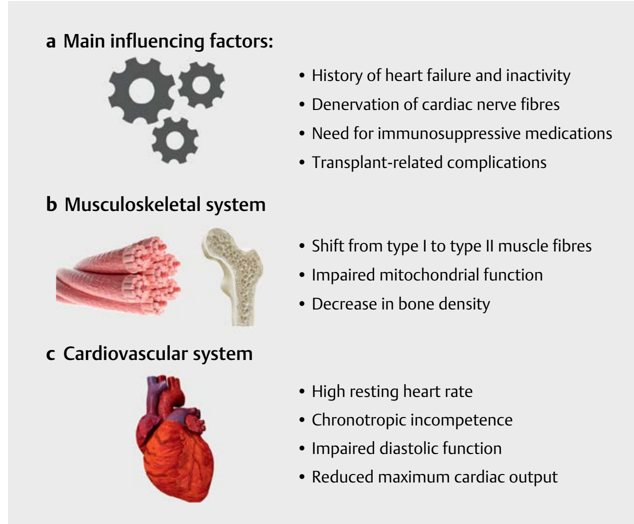
Participation in a cardiac rehabilitation programme after discharge from acute hospital care varies amongst the different countries and also depends on the patient's degree of debility [11]. The overall readmission rate after HTX is highest in the first year (40 % of patients) and decreases clearly in the long term (25 % are readmitted in the time between 2 and 5 years) [7]. Specific outpatient checkups at the individual transplant centre are initially performed frequently and can later be reduced to once a year.

With regard to exercise, the following musculoskeletal and cardiovascular alterations must also be considered after HTX (▶**Fig. 1**):

## Alterations to the musculoskeletal system

Clinical condition following HTX is determined not only by the individual anamnesis, by the altered haemodynamics of the transplanted heart, and the sequelae of life-long immunosuppression, but also and especially by damage incurred prior to HTX [12]. The period before HTX is usually characterised by long phases of disease, so that patients usually display significant deconditioning of the peripheral muscles due to inactivity [13–15]. Muscle fibre composition changes from type I to types IIa and IIb. Following HTX, the muscle cross-sectional area does usually grow in size again, but the proportion of type I muscle fibres remains reduced, even in the long term [16–18].

A prolonged obstacle to effective muscle training is the required immunosuppressive therapy (calcineurin inhibitors, corticosteroids). This is partly due to the resulting chemical impairment of muscular structures (mitochondria) but also to the changed supply of energetic substances within the muscles, leading to impaired oxidative function [19]. Consequently, an HTX patient has to complete significantly more training units than a non-immunosuppressed person in order to achieve the same increase in muscle mass. Because this is not possible during the early stages owing to very restricted exercise tolerance, transplant recipients require considerable time to make up their deficits. In addition, the intake of corticosteroids in conjunction with physical inactivity leads to a decrease in bone density [20] and possible osteoporotic fractures [15].




▶**Fig. 1** Typical alterations after heart transplantation: main influencing factors (a) that lead to changed prerequisites for both the musculoskeletal (b) and cardiovascular system (c). Regular structured exercise can counteract most of these changes and improve functional performance significantly.

## Alterations to the cardiovascular system

Following HTX, the cardiovascular system changes significantly [12]. Transplantation leads to a denervation of the sympathetic and parasympathetic nerve fibres. This denervation is responsible for numerous physiological phenomena usually observed in HTX patients, e. g. a high resting heart rate (HR) (approx. 95 bpm), a delayed increase in HR during exercise (chronotropic incompetence), delayed achievement of resting HR during the recovery phase following exercise, and significantly restricted HR variability [21–23].

Denervation gradually leads to an emptying of the catecholamine storage in the myocardium, meaning that the transplanted heart is then reliant on the stimulation of circulating catecholamines [21, 23]. Overall, the catecholamine receptors display an increased sensitivity. In an unfavourable case, this can lead to an increased incidence of arrhythmia, whereby therapy with beta blockers is not a viable option because it significantly reduces exercise tolerance.

In conjunction with chronotropic incompetence, the donor heart must increase its stroke volume (SV) during physical exercise via the Frank–Starling mechanism so that cardiac output (CO) can be adapted at least partially to the degree of exertion. In many patients, however (especially during the initial phase), insufficient relaxation/compliance of the left ventricle can be observed (diastolic dysfunction) [24, 25]. The consequence is an increased end-diastolic pressure in the left ventricle despite reduced end-diastolic volume. This in turn impinges the Frank–Starling mechanism, accompanied by non-optimal adaptation of SV during physical activity [26]. Overall, CO remains reduced both at rest and during exercise, and often only a low rise in systolic blood pressure can be generated [27–29].

Partial reinnervation is fundamentally possible after HTX and has a clinical impact on exercise capacity. In total, 40 – 70 % of patients display cardiac reinnervation over the long term. Corresponding changes can be observed very early (approx. 6 months) in the sympathetic nerve fibres, and later (after 1–3 years) in the parasympathetic nerve fibres [22]. Despite long-term compensation mechanisms, however, the result still remains reduced in comparison to persons with healthy hearts [22].

In addition to these cardiac changes, persisting lung damage can also be observed in the pulmonary capillary beds of many patients due to their long-term HF.

## Efficacy and benefits of exercise-based interventions

In stable HTX patients exercised-based interventions are recommended [12, 30–32]. Results from a smaller retrospective study provide first indications of a protective effect of exercise-based rehabilitation immediately after HTX [33]. They show a significant association between the number of completed rehabilitation units in the first 90 days after HTX and survival rates (hazard ratio, 0.90, 95 % CI, 0.82–0.97, p = 0.007) [33]. In the meantime, the efficacy of exercise-based rehabilitation on peak oxygen consumption (peak $VO_2$) has been confirmed (MD 2.49 ml/kg/ min, 95 % CI, 1.63–3.36) by a meta-analysis of 9 studies including 284 patients [34]. Only one of the studies evaluated documented adverse events.

The ability of moderate intensity continuous training (MICT) (e. g. at 60–70 % peak $VO_2$) to improve exercise capacity in HTX patients has been confirmed by meta-analyses and systematic reviews including a few smaller studies [35–37]. Other documented positive effects of MICT are increase in peak HR, improvement in the oxidative capacity of skeletal muscle [38], improvement in blood pressure [39], improvement in endothelial function [40–42], and improvement in quality of life [43–46].

Randomised controlled trials have also confirmed the feasibility and efficacy of high intensity interval training (HIIT) in HTX patients. These studies show that interval training can be considered in long-term care (> 1 year after HTX) but also earlier (11 weeks after HTX [47]), with positive improvements in peak $VO_2$ [47–51], muscular exercise capacity [47, 48], endothelial function [52], and quality of life [53], with reduced anxiety and depression [53].

The results of a randomised crossover study show low superiority of HIIT vs. MICT (> 80 % peak $VO_2$ vs. 60–70 % peak $VO_2$) in terms of improvement in exercise capacity and quality of life [54, 55]. Regarding compliance aspects (attendance or dropouts), another randomised controlled study [47] revealed no differences between HIIT and MICT (each 58/72 or 82 % of sessions were performed), indicating that both exercise modalities are well tolerated and accepted. However, experiences with HIIT in other cardiovascular patient populations [56–58] showed that a larger proportion of patients were unable to maintain high intensities over longer periods (e. g. 4-min intervals).

Moderate resistance training (50–60 % of 1 repetition maximum [1RM]) improves muscle strength [36] and counteracts the negative effects of immunosuppressive therapy on muscle and bone metabolism [15, 59–61]. Studies have also demonstrated that resistance training programmes successfully restore bone mineral density and increase lean mass to levels greater than pre-transplantation, as well as reduce body fat [19].

In addition to the positive physical effects described, structured exercise training can also achieve significant mental benefits. Particularly during the initial phase after HTX, many patients suffer from bouts of depression [62]. Increasing exercise capacity and/or training within a social group has the potential to significantly improve the moods and quality of life of these patients. Assuming that they meet the necessary physical criteria, participation in sports competitions (e. g. The World Transplant Games) can also be beneficial, accompanied by a reinforcement of self-confidence and expected self-efficacy.

However, the general impact of exercise on the progression of CAV (regardless of specific training modalities) needs further investigation [35, 63].

## Assessment of functional and cardiopulmonary exercise capacity

Before the onset of exercise training, adequate diagnostics should be performed [12]. With the help of a substantiated assessment of functional and cardiopulmonary exercise capacity, the cardiopulmonary, metabolic, and muscular exercise tolerance of HF patients can be objectively determined [64]. In HTX patients, these results can facilitate evaluation of patient condition and individual risk stratification, as well as provide indications about the long-term prognosis [66–69]. A substantiated assessment is a prerequisite for planning the content of effective exercise training units, for individual exercise control, and also for monitoring recovery. These diagnostic measures are especially crucial for patients who would like to pursue sports activities unsupervised.

▶ **Table 1** provides a summary of potential assessment procedures for testing functional and cardiopulmonary exercise capacity in HTX patients, whereby modifications are necessary to suit the current health status of the individual patient [64, 65, 70–79]. In addition, performance-limiting comorbidities, especially internal, neurological or orthopaedic, should be collected, documented and considered.

Besides objective parameters, the rated perception of exertion (RPE) of patients should definitely also be recorded in order to train adequate self-perception and to prepare for the challenges of everyday life. In addition to the assessment procedures suggested in ▶ **Table 1**, specific sports diagnostics are also possible and recommended in patients with sporting ambitions.

## Precautions before and during physical exercise training

Before starting intensive exercise training, as well as at regular intervals thereafter, an ischaemia diagnosis is recommended due to the possibility of CAV and related sudden cardiac death because a denervated heart gives no warning symptoms (silent ischaemia) [80]. The results from a cardiopulmonary exercise test (CPET) are of no use here owing to its insufficient sensitivity [81]. Therefore, CAV diagnostics will be performed usually annually during the outpatient checkups at the transplant centre. Depending on renal function and previous findings, either dobutamine stress echocardiography (DSE) and/or invasive coronary angiography are commonly used. If the results are unclear, further investigations (e. g. intravascular ultrasound (IVUS) or coronary flow reserve (CFR)) are needed to obtain safe sport release [82, 83].

In general, planning and execution of exercise training after HTX must always be adapted to the current clinical condition, the individual comorbidities and possible transplant-related complications.

▶ **Table 1** Possible assessments for testing of functional and cardiopulmonary exercise capacity in heart transplant recipients [64, 65, 70–79].

| | **Test** | **Test protocol** | **Measurement parameters** |
|---|---|---|---|
| Functional assessment | 6-min walking test | ATS standard with/without aids | Distance, RPE, usage of aids, number/duration of recovery periods, reason for stopping |
| | Timed up and go test * | Standard with/without aids | Time, usage of aids, certainty of movement, mobility classification |
| Ergometry | CPET on bicycle | 1. Ramp (5–15 watts/min)<br>2. WHO Step (25 watts/2 min)<br>3. In patients with good exercise tolerance, higher increases/steps are also conceivable | ECG, HR, watts, RPE, exercise duration, reason for stopping, $VO_2$, $VE/VCO_2$ slope, RER, lactate, oxygen saturation, values at VAT, periodic breathing |
| | CPET on treadmill * * | 1. Select protocol with constant low speed and increase load by increasing elevation<br>2. In patients with good exercise tolerance, increasing speed is also conceivable | ECG, HR, elevation, speed, RPE, exercise duration, reason for stopping, $VO_2$, $VE/VCO_2$ slope, RER, lactate, oxygen saturation, values at VAT, periodic breathing |
| | IGR on bicycle | 4-min step protocol at different exercise levels | ECG, HR, watts, RPE, $VO_2$, CO, $avDO_2$, RER, lactate, oxygen saturation, systolic blood pressure, cardiac index |
| Strength assessment | Handgrip strength test | Standard one-arm for both right and left hand | Newtons, kg, lbs |
| | Strength training with machines or barbells | 1. Submaximal test to predict 1RM<br>2. In patients with high strength training experience, 1RM test is also conceivable | Newton, kg, lbs, repetitions |

**Abbreviations:** * , only in patients with 6-min walking distance below 200 m and using aids; * * , only for patients without balance disorders; 1RM, one repetition maximum; ATS, American Thoracic Society; $avDO_2$, arteriovenous oxygen difference; CO, cardiac output; CPET, cardiopulmonary exercise test; CR, cardiac rehabilitation; ECG; electrocardiogram; HR, heart rate; IGR, inert gas rebreathing; RER, respiratory exchange ratio; RPE, rated perceived exertion; VAT, ventilator anaerobic threshold; $VE/VCO_2$ slope, relation between ventilation and carbon dioxide production; $VO_2$, oxygen uptake; WHO, World Health Organization.

A potential negative influence of the individual medication regime on exercise therapy must also be considered. Thus, statins are usually prescribed to prevent the progression of CAV, but their use is often accompanied by side effects such as muscle pain, tensions, stiffness, cramps, or muscle weakness [84].

Indications of possible rejection episodes should be heeded (e. g. low stress tolerance, shortness of breath, oedemas, cardiac dysrhythmia, raised or high temperature). In order to recognise these episodes early on, it makes sense to measure and document body temperature, blood pressure, fluid balance, and weight every day, at least in the first few weeks or months. During rejection episodes, the intensity of exercise training must be clearly reduced. In case of cortisone bolus therapy, it must be stopped completely [31].

A must for all patients: fluid balance must be regulated due to the volume dependence of cardiac performance after cardiac denervation. Due to the delayed circulatory reactions, warm-ups prior to exercise training should be fundamentally slower and longer than for e. g. other coronary groups. Exercise training should not be started or stopped abruptly.

Attention should also be paid during exercise training to appropriate environmental conditions with low risks of injury or germ contamination (e. g. patients should avoid exposure to bird droppings due to possible risk of cryptococcosis infection) [85]. Fortunately, patients are usually well educated regarding these important issues.

## Recommendations for endurance training

After HTX, haemodynamically stable patients should participate in medically supervised exercise-based measures, and all training measures should be continued in the long term [12, 30–32, 86]. Patients should be introduced as early as possible (2nd to 3rd week postoperatively) to monitored endurance training [30–32]. The International Society for Heart and Lung Transplantation (ISHLT) therefore suggests the routine use of a cardiac rehabilitation programme after HTX with a class Ib recommendation. Regular endurance training is especially valuable in heart transplant recipients with internal comorbidities (e. g. hypertension or diabetes mellitus) [30].

In general, different exercise modalities are established and recommended, including MICT, intensive interval training with short intervals or HIIT. Their individual use depends on the clinical status and later on the patient's preferences.

Shortly after transplantation, endurance training should be started with MICT at low intensity (< 50 % of the peak $VO_2$ or 10 % below the first ventilatory threshold) [32]. Exercise intensity should be determined using the Borg scale (RPE 11–14) and/or the respiratory rate ("speech rule"), which means that the respiratory rate should permit conversation [31, 32]. Intensity of MICT can also be defined as up to 50 % of the maximum load (watt) achieved during CPET [31, 32]. In very weak patients, intensive interval training with short intervals (20–30 s) could also be an option to induce first exercise tolerance.

In the further course, clinically stable patients with good exercise tolerance can gradually be brought up to more intensive endurance training (e. g. MICT at 60–80 % of peak $VO_2$), possibly also in the form of HIIT, if tolerated [35, 47]. In addition, combined methods are also thinkable (e. g. 1 day HIIT and 3 days MICT), whereby MICT is suggested as the basic exercise mode. The summarized exercise recommendations and selected control parameters are shown in ▶ **Table 2**, [12, 58, 86].

With regard to exercise control, the use of HR to determine exercise intensity after HTX is problematic due to chronotropic incompetence. For experienced athletes, however, HR can at least be viewed as complementary to the Borg scale. HR ranges must then be determined individually, depending on the HR pattern, and only make sense for MICT (not intensive interval training with short intervals or HIIT).

## Recommendations for resistance training

Moderate and individually dosed resistance training (30–60 % of 1RM) should be integrated into the exercise regime postoperatively as soon as possible [12, 30–32, 86]. In particular, resistance training is suitable for counteracting the catabolic side-effects of immunosuppressive therapy and the loss of muscle mass, muscle strength and bone density caused preoperatively by HF and inactivity [19]. Therefore, the guidelines of the ISHLT suggest regular resistance training with class 1b recommendation, especially to reduce the risk of falls and fractures [30]. Muscles of the lower extremities should be given priority because they are important for activities of daily living (e. g. walking, climbing stairs) and are an essential prerequisite for improved participation. In general, all measures performed shortly after HTX should be gentle on the patient's sternum due to surgery. A gradual increase in upper-extremity extent of motion and resistance training should be considered up to 3 months after transplantation [11].

In the further course, the intensity can be gradually increased (up to 60–80 % of 1RM) in experienced patients with good exercise tolerance **(▶Table 2).**

## Exercise capacity and sports activities

Despite the described pathomorphological changes to the heart and motor apparatus, functional performance increases significantly after HTX. The mean six-minute walking distance (6MWD) achieved is usually 500 metres or more (> 85 % of predicted), and the ability

▶**Table 2** Recommended exercise modalities for patients after heart transplantation: (a) Moderate intensity continuous training (MICT) is suggested as basic exercise mode. (c) High intensity interval training (HIIT) should be introduced only in the further course of clinically stable patients [12, 58, 86].

| | | |
|---|---|---|
| **a) Moderate intensity continuous training (MICT)** | | |
| | Low to moderate intensity | Moderate to high intensity |
| % of peak $VO_2$ (ml/kg/min) | 40–60 % | 60–80 % |
| % of peak load (watts) | 40–60 % | 60–80 % |
| Borg Scale | RPE 11–14 | RPE ≥ 15 |
| Respiratory rate | Respiratory rate should permit conversation (speech rule) | |
| Duration | From 5 up to ≥ 60 min | |
| Frequency | 3–5 (7) days per week/most days of the week | |
| **b) Intensive interval training with short intervals** | | |
| | High intensity phase | Recovery phase |
| % of peak $VO_2$ (ml/kg/min) | ≥ 80 % | very low |
| % of peak load (watts) | ≥ 80 % | very low |
| Borg Scale | RPE > 15 | RPE ≤ 11 |
| Duration | 20–30 s high intensity vs. 40–60 s recovery; 10 to ≥ 20 intervals | |
| Frequency | 3–5 (7) days per week/most days of the week | |
| **c) High intensity interval training (HIIT)** | | |
| | High intensity phase | Recovery phase |
| % of peak $VO_2$ (ml/kg/min) | ≥ 80 % | 40–60 % |
| % of peak load (watts) | ≥ 80 % | 40–60 % |
| Borg Scale | RPE > 15 | RPE 11–13 |
| Duration | ≤ 4 min high intensity vs. 3 min recovery; ≤ 4 intervals | |
| Frequency | 2 days per week with at least 1 resting day in between | |
| **d) Resistance training** | | |
| | Low to moderate intensity | Moderate to high intensity |
| % of 1RM | 30–60 % | 60–80 % |
| Repetitions | 10–15 | 8–10 |
| Borg Scale | RPE 11–14 | RPE ≥ 15 |
| Sets | 1–(3) | 1–3 |
| Resting time between sets | > 1 min | |
| Progression | Gradual increase | |
| Number of exercises | 4–8 | |
| Frequency | 2–3 days per week – with resting day in between | |

**Abbreviations:** 1RM, one repetition maximum; RPE, rated perceived exertion; $VO_2$, oxygen uptake.

to master everyday tasks is very good [70, 87, 88]. With regard to their symptoms, 90 % of patients return to New York Heart Association (NYHA) class I or II after HTX, i. e. no longer or just slightly restricted [89].

However, the recorded peak values remain below those of an age-matched group with healthy hearts [90]. In the CPET, a peak $VO_2$ of approx. 16–20 ml/kg/min is usually measured, corresponding to around 60–70 % of predicted values [35]. Of course this is considerably better than in the phase directly before HTX [90] and also better than results after LVAD implantation [91, 92], but it still remains reduced compared to healthy patients. Significantly better values can be achieved only in individual patients, sometimes even at the level of high-performance sports activity [93]. These are usually patients who participated intensively in top-level sport prior to their heart transplant and who also exercised regularly and intensively after HTX. In our experience, these patients do not generate an exaggerated maximum CO after transplantation (as one would assume) but profit considerably from optimal peripheral structures and processes (improved oxygen extraction during peak exercise, optimised inter- and intramuscular coordination). To provoke such adaptations, regular exercise interventions are needed.

Many different sports activities are thus not only possible after HTX but also recommended. Endurance sports, such as running, jogging, walking, cycling, hiking, cross-country skiing, gymnastics, and yoga, are suitable. Swimming and aquafit are also options, provided that certain hygienic criteria (e. g. a microbiologically controlled swimming pool) are met. In contrast, all sports activities with an increased risk of injury and/or infection (e. g. contact sports, swimming in microbiologically contaminated water) are not recommended.

With regard to organised sport, there are some options for structured exercise training and competitions already available. Patients with other transplanted organs (e. g. kidney or liver) or patients requiring dialysis treatment are often also included in such clubs and events. The current exercise possibilities for transplant recipients include: related sports clubs, national championships, European championships and also world championships. Mostly summer sports are offered, but winter games also sometimes take place. The current leading international associations include the European Heart and Lung Transplant Federation (EHLTF), the European Transplant and Dialysis Sports Federation (ETDSF), and the World Transplant Games Federation (WTGF).

However, there are also HTX patients who participate in "normal" sport programmes and competitions (for healthy hearts) or sporting challenges, in individual cases with impressive results, such as finishing the Hawaii Ironman or the summit ascent of high mountains [93]. Thus, the performance level after HTX can vary considerably depending on the individual (age, concomitant diseases, previous experience, training frequency, and grade of reinnervation), from low intensity (e. g. heart groups) to a non-competitive level, and up to intensive competitive sports.

# Conclusion and Outlook

HTX improves quality of life considerably, with a crucial role being played by the increase in exercise capacity. After transplantation, patients usually achieve a peak $VO_2$ which is approx. 60–70 % of predicted values. This is considerably better than in the phase directly before HTX [90] and also better than results after LVAD implantation [91]. But in comparison to age-matched healthy test persons, the values are still reduced. However, the reached exercise capacity permits patients to master everyday tasks very well as well as to participate in many different sports activities. In exceptional cases, with appropriate conditioning and structured exercise training, even intensive competitive sports activities are possible.

In the future, innovative developments are conceivable in immunosuppressive medication, concomitant with impacts on the described transplant-related alterations, the clinical condition, and survival times. Likewise, the increased use of rate-responsive pacemakers is conceivable in order to minimise the consequences of chronotropic incompetence [28].

However, despite all conceivable improvements to HTX therapy, regular endurance and resistance training will continue to be the basis for adequate exercise capacity and can also contribute to mental stabilisation. Therefore, specific exercise programs should be offered to HTX recipients routinely and on a long-term basis beyond inpatient cardiac rehabilitation periods.

## Conflict of Interest

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose. The authors confirm that this manuscript adheres to the ethical standards in sports and exercise science research [94].

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