



CASE REPORT

High Level Cycling Performance 10 Years after Cardiac Transplantation

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Abstract

Purpose: To describe cycling performance in a well-trained male a decade after Cardiac Transplantation (CTX).

Case report: The patient was diagnosed with arrhythmogenic right ventricular cardiomyopathy at 14 years of age and underwent CTX at 35 years. Exercise training began 3 weeks after CTX, and progressively increased in volume and intensity. Ten years after CTX he participated in twelve one-day cycling races over an eight-month period. Maximal cardiopulmonary exercise test was performed before the study. One race was monitored using a power meter.

Results: VO_{2peak} (47.2 mL/kg/min), maximal HR (161 bpm), and oxygen pulse (18.8 mL/bpm) were 113%, 92%, and 118% of age-predicted values respectively. HR, W, and relative VO_2 at the ventilatory threshold and at the respiratory compensation point were 128 bpm, 120 W, and 75% VO_{2peak} , and 142 bpm, 155 W, and 86% VO_{2peak} respectively. Cycling economy was ~80 W per liters per O_2 /min. The race was completed in 7 hours and 56 minutes, at an average of 141 bpm and 162 W, remaining between moderate-to-high intensity (4 h 2 min), and above high-to-severe intensity (2 h 19 min).

Conclusion: Long-term aerobic training may result in a remarkable cycling performance a decade after CTX, likely because of cardiovascular adaptations.

Keywords

Aerobic capacity, Exercise training, Exercise tolerance, Heart transplant recipients, Cycling, Sport performance

Abbreviations

ANED: Associazione Nazionale Emodializzati, Dialisi E Trapianto; ARVC: Arrhythmogenic Right Ventricular Cardiomyopathy; ATP: Adenosine Triphosphate; NT-pro-BNP: N-Terminal prohormone of Brain Natriuretic Peptide; CTX: Cardiac Transplantation; ECG: Electrocardiography; HR: Heart Rate; HTR: Heart Transplant Recipients; ICD: Implantable Cardioverter Defibrillator; RCP: Respiratory Compensation Point; RPE: Rating Of Perceived Exertion; VCO_2 : Carbon dioxide output; VO_2 : Oxygen uptake; VO_{2peak} : Peak oxygen uptake; VT: Ventilatory Threshold; W: power output

Introduction

Cardiac Transplantation (CTX) is a treatment option for selected individuals with end-stage heart failure. However, long-term outcomes are limited by the development of cardiovascular complications, and coronary allograft artery disease is the main cause of death in Heart Transplant Recipients (HTR) five years after intervention [1,2]. Training programs among HTR are

recommended in the early post-operative period as well as in the long term [3] and cardiorespiratory fitness has been demonstrated to improve after exercise training [4,5]. Previous studies on the effects of exercise training in HTR have been performed early after CTX and have applied moderate exercise intensities [6,7]. The results of these studies are not entirely consistent, and how training late after CTX affects endurance capacity has not been well defined. Even less is known regarding the effects of strenuous and prolonged exercise training in long-term HTR.

Previous studies have analyzed performance by the assessment of physiological parameters such as peak oxygen uptake ($\text{VO}_{2\text{peak}}$), which is generally considered the most important measure of cardiorespiratory fitness and endurance capacity. In cycling, analysis of power output in training and racing conditions has been shown to be a more valuable method for quantifying training intensity and cycling performance than $\text{VO}_{2\text{peak}}$ [8]. In the current report, we describe laboratory and field data of a cyclist HTR who participated in 12 one-day cycling races over an eight-month period 10 years after CTX.

Case Report: Materials and Methods

The subject was enrolled with the support of ANED Sport (Associazione Nazionale Emodializzati, Dialisi e Trapianto), an association involved in promoting physical activity after solid organ transplantation. The study was approved by the institutional review board at the CEAV Romagna (Health Service of the Emilia-Romagna region, protocol number 2194/2011/I.5/481), and the subject gave written informed consent. The subject is a 45-yr-old-male, affected by Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) diagnosed in 1984, characterized by recurrent episodes of ventricular tachycardia treated with amiodarone and an Implantable Cardioverter Defibrillator (ICD) over time. At 35 years, because of the rapid progression to heart failure with biventricular dysfunction, he was placed on a cardiac transplant waiting list, and underwent CTX in 2004, receiving a donor heart from a 16-yr-old male (78-kg, 185-cm). The post-operative course was normal. The post-CTX period was uneventful, leading rapidly to a complete recovery. Regular follow-up assessments, including coronary angiograms and endo-myocardial biopsies were performed to ensure that there were no tissue rejection episodes. After one year of cardiac rehabilitation, he started gradually to train for cycling. After 2 years post-CTX he began cycling outdoors, 4-5 sessions/week of 3-4 hours duration (10,000-12,000 km/year) using a heart rate monitor, training in the range of 125-135 beats per minute (bpm).

Between February and October 2015 he completed 12 long course competitive races for a total of 1594 racing km (mean 132), and 30642 altitude gain (mean 2533). Medications and dosage at the time of testing,

training, and racing included Ciclosporine, 150 mg/day; Prednisone 2.5 mg every second day; Verapamil 240 mg/day; Indobufene 200 mg/day; Pravastatin 40 mg/day; Lansoprazole 15 mg/day. The medical therapy was unchanged from 2006. No significant side effects have been reported.

Before to start the study the participant underwent a maximal Cardiopulmonary Exercise Test (CPX) on a wind-load cycle ergometer equipped with an SRM Powermeter [9]. Bicycle gearing was individualized according to the functional capacity and habits of the subject [10,11]. Integrated 12-lead electrocardiographic tracings were continuously monitored and recorded during the test. Gas-exchange measurements were performed using a metabolic cart (CPET, Cosmed, Rome, Italy). Calibration of the system was performed immediately before the test by using a 3-liter syringe to calibrate the turbine, and a two-point calibration of the gas analyzers was performed using gases of known oxygen, carbon dioxide and nitrogen concentrations. Oxygen uptake (VO_2) and carbon dioxide output (VCO_2) were acquired breath-by-breath, and subsequently averaged over 15 seconds.

According to current recommendations, three exercise intensity zones were defined considering the first Ventilatory Threshold (VT) using the V-slope method, and a second ventilatory threshold or Respiratory Compensation Point (RCP) determined by the inversion of the VE/VCO_2 ratio as the nadir of the VE/VCO_2 versus work rate relationship [12]. Heart Rate Deflection Point (HRDP) was also determined [10]. Exercise intensity was considered light to moderate (below VT), moderate to high (between VT and RCP), and high to severe (above RCP). CPX test results are presented in Table 1.

Echocardiography, cardiac magnetic resonance, coronary angiography, N-terminal prohormone of brain natriuretic peptide (NT-pro-BNP) and monthly 24-hour ECG Holter monitoring, with a typical long training session included, were analyzed.

The subject performed one of these competitions (Maratona dles Dolomites) with a mobile powermeter mounted on his bike (SRM Professional Training system, Schoberer Rad Messtechnik, Julich, Germany). In order to take into account the climatic conditions and the residual torque applied on the SRM system, the zero off set frequency procedure was performed by the cyclists before the race. Data were recorded every 1 second, and transferred after the race from the SRM powercontrol for analysis.

The *Maratona dles Dolomites* was completed in 7 hours and 56 minutes, with the individual finishing 2841st of 4449 finishing competitors, and 662nd of 1061 in the age-group category (45 to 49 years). The Heart Rate (HR) versus time and altitude relationships are presented in Figure 1. Lowest, mean, and highest HR values

Table 1: Cardiopulmonary exercise test results.

	Start*	VT	RCP	HRDP	Maximum Achieved	%PRED
Power output						
Exercise time (min:sec)	0:00	7:45	14:40	15:35	18:30	-
Workload (W)	80	120	155	160	259**	-
Cadence (RPM)	60	73	86	89	104**	-
Metabolic						
VO ₂ (mL/kg/min)	22.9	34.4	39.3	39.7	47.2	113
VO ₂ (METs)	6.5	9.8	11.2	11.3	13.5	124
VO ₂ (L/min)	1395	2.100	2.400	2.420	2.789	110
VCO ₂ (L/min)	998	1.900	2.350	2.430	3.800	-
RER (VCO ₂ /VO ₂)	0.72	0.92	0.98	1.00	1.26	-
Cardiovascular						
Heart rate (bpm)	108	128	142	144	161	92
Heart rate recovery (bpm at 1 min)	-	-	-	-	138	-
Oxygen pulse (VO ₂ /HR, mL/bpm)	11.8	15.1	16.9	16.8	18.8	130
Ventilatory						
VE (L·min ⁻¹)	26	48	59	63	135	96
Respiratory rate (br/min)	15	18	24	26	52	104
VE/VO ₂ (L·min ⁻¹ /L·min ⁻¹)	19	22	24	26	43	-
VE/VCO ₂ (L·min ⁻¹ /L·min ⁻¹)	26	23	25	25	33	-
VE/VCO ₂ slope	-	21	21	21	29	-
PetCO ₂ (mmHg)	39	43	43	44	36	-

*After warm-up. **mean values of the last minute of the CPX.

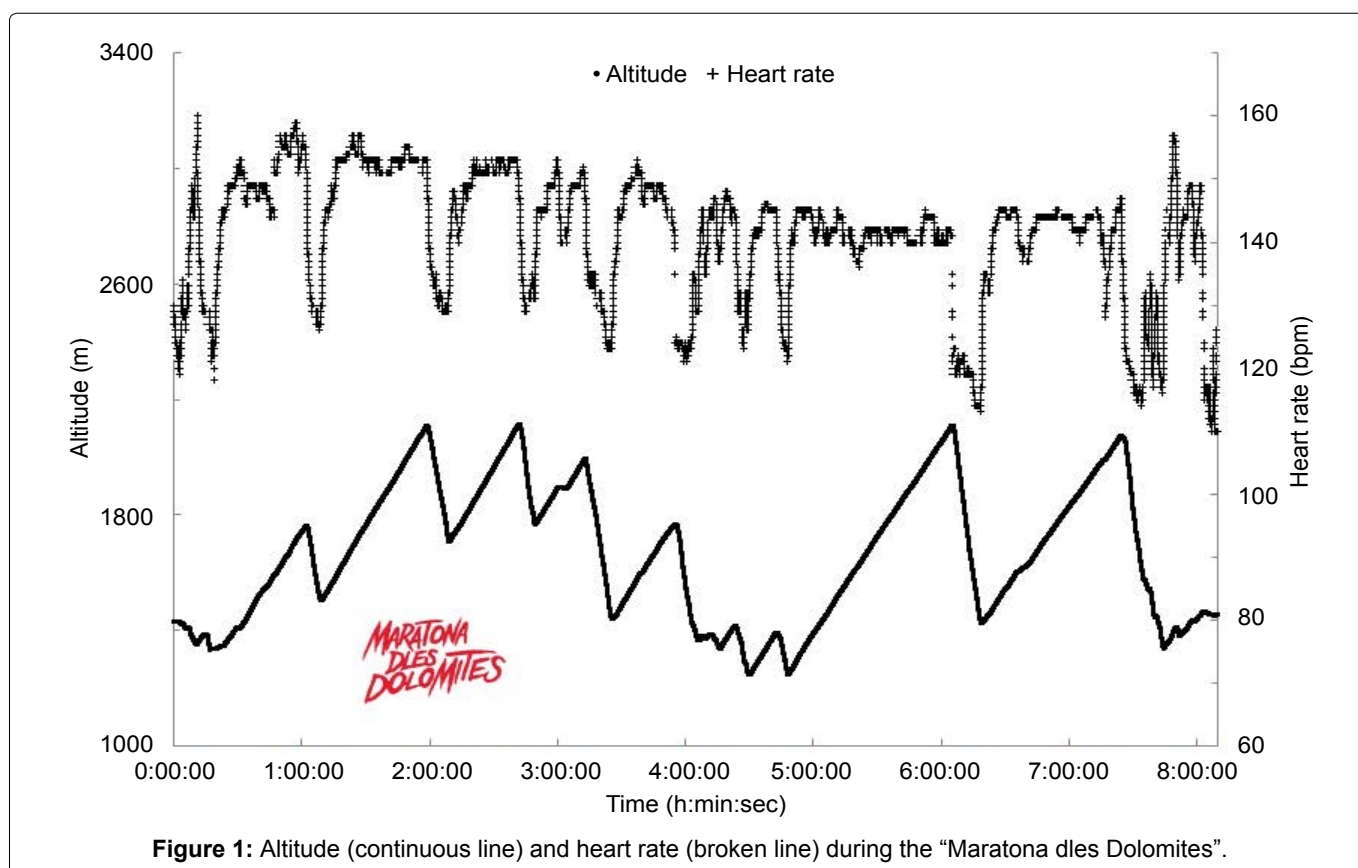


Figure 1: Altitude (continuous line) and heart rate (broken line) during the “Maratona dles Dolomites”.

during the entire race were 73, 141, and 161 bpm respectively. Lowest, mean, and highest WR values during the whole race were 54, 166, and 596 watts respectively. He remained 1 hour and 31 minutes below VT (light-to-moderate intensity, HR 115 ± 17 bpm); 4 hours and 6 minutes between VT and RCP (moderate-to-high intensity, HR 141 ± 4 bpm); and 2 hours and 19 minutes

above RCP (high-to-severe intensity, HR 151 ± 3 bpm). The maximal power outputs per kg of body mass for various time durations during the whole race are presented in [Figure 2](#).

Details of the physiological variables registered during the eight mountain ascents completed during the *Maratona dles Dolomites* are presented in [Table 2](#).

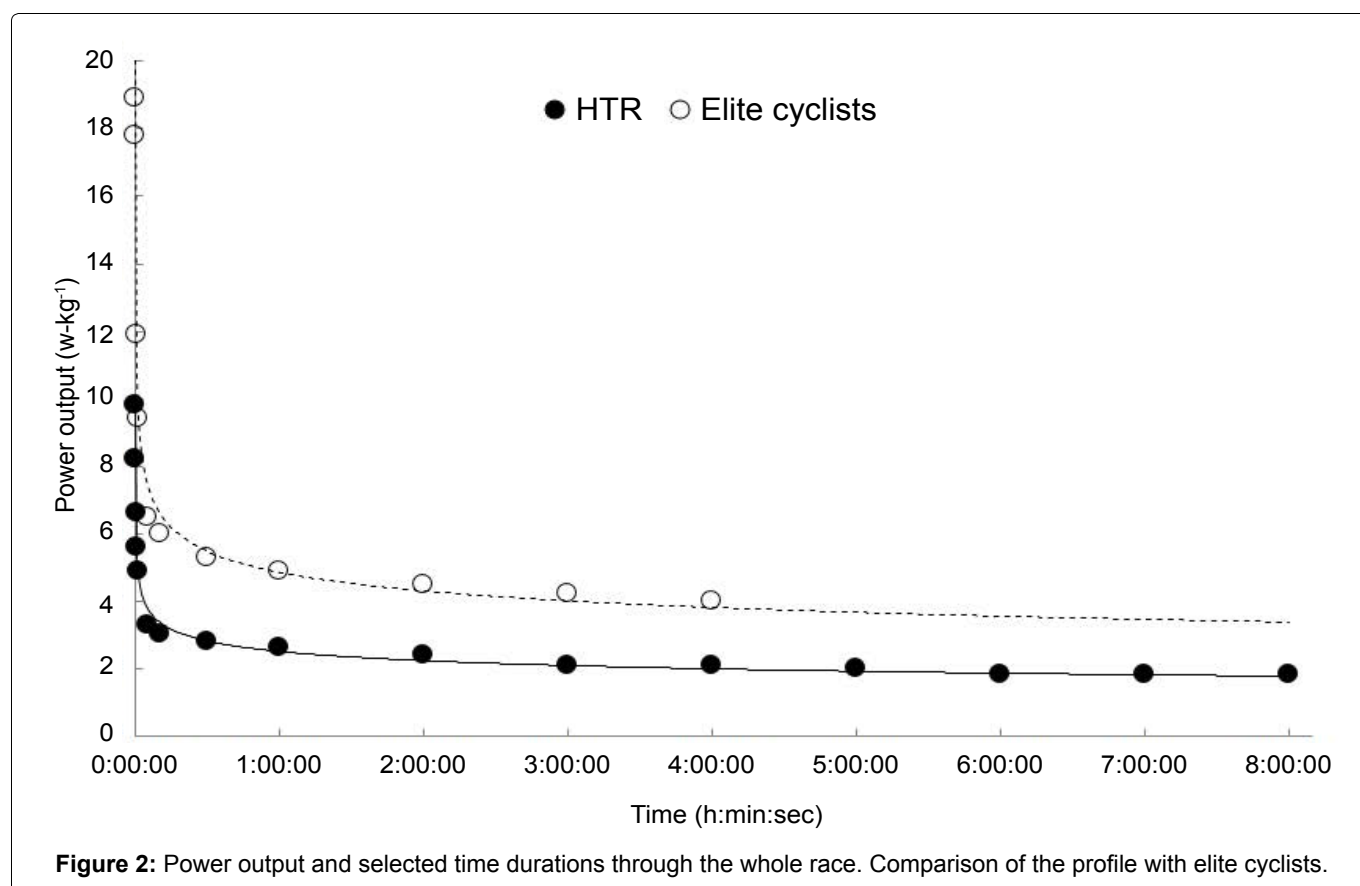


Table 2: Results of eight high mountain ascents in one race (Maratona dles Dolomites). n.a.: not applicable because of transient heart rate monitor dysfunction.

Variable	Campolongo 1 st	Pordoi	Sella	Gardena	Campolongo 2 nd	Giau	Falzarego	Gatto
Distance (km)	6.44	9.29	5.52	5.67	6.44	9.66	12.4	0.92
Temperature (°C)	15.5	20.7	18.5	21.4	30.9	35.8	35.2	38.6
Time (h:min:sec)	0:30:28	0:49:48	0:32:56	0:23:28	0:29:39	1:16:33	1:05:01	0:04:39
Altitude (start-summit, m)	1413-1763	1503-2109	1709-2113	1770-2005	1413-1763	1254-2110	1429-2074	1340-1393
Upgrade (mean-max, %)	6.1-11.0	6.9-10.0	7.9-12.0	4.3-10.0	6.1-11.0	9.3-15.0	5.8-15.0	7.2-19.0
Power output (mean-max, w)	159-259	177-293	176-242	161-261	161-254	158-246	149-291	197-596
Cadence (mean-max, rpm)	63-112	62-87	60-102	65-106	65-101	52-80	57-100	60-79
Speed (mean-max, km/h)	12.7-34.6	11.2-15.6	10.6-17.2	14.5-33.4	13.1-25.3	7.6-12.1	11.5-27.0	11.9-14.8
Heart rate								
Start of the ascent (bpm)	137	127	129	131	123	123	114	120
Mean-max (bpm)	n.a.-n.a	152-157	150-153	147-151	146-153	142-145	142-145	142-157
descent, 1-min recovery (bpm)	134	140	142	137	138	n.a.	132	130
descent, 2-min recovery (bpm)	130	134	134	134	123	n.a.	123	118

The eight-month study period was uneventful. There were no occurrences of arrhythmias, myocardial damage or ischemia.

Results and Discussion

This patient's history shows that long-term aerobic training resulted in remarkably high exercise capacity ten years after CTX. The high VO_2 peak value observed (47.2 mL/kg/min) is similar to that obtained by Haykowsky, et al.

in a HTR who completed a half-ironman triathlon [13], and corresponds to excellent exercise capacity relative to age-matched healthy subjects [5]. The hemoglobin values have been determined monthly during the 6 months before the cycling event, and ranged from 13.0 to 13.8 g/dL.

One contributing factor to his performance is the heart rate response to increasing exercise intensity during CPX. From rest to peak exercise we observed a

change in heart rate of 90 bpm. The difference observed between laboratory testing and the races at higher perceived exercise intensity can be explained by the fact that racing conditions allow higher absolute and relative exercise intensities, in turn affecting the patient's metabolic requirements [14]. Higher HR max values during racing may reflect the quantity of activated muscle mass when pedaling in climbing conditions at higher absolute and relative exercise intensities [15]. Heart rate recovery showed a normal response as documented by the 23-bpm decrease one minute after the end of the CPX. This response is similar to that of HTR who exhibit functional evidence of cardiac reinnervation [16]. This adaptation is likely only partial since it has been demonstrated that complete reinnervation in HTR requires 15 years [17].

Another contributing factor to the remarkable aerobic power of this individual could be a high stroke volume. We observed a normal increase in oxygen pulse in the transition from rest to exercise during CPX. The 18.8 mL/beat observed at peak effort is consistent with a 30% higher value than age-predicted. In contrast, patients who cannot increase their stroke volume show low oxygen pulse values. In addition, oxygen pulse promptly decreased during recovery, while it often transiently increases in patients with left ventricular dysfunction and exercise-induced myocardial ischemia. Since the oxygen pulse provides an approximation of stroke volume, these results suggest that this individual has not only normalized his stroke volume, but shows cardiac performance characteristics that mimic a healthy, highly trained person [14].

This patient's history also shows a unique and surprising aspect of exercise capacity: the ability to sustain high-intensity exercise for prolonged periods. To our knowledge, no scientific reports are available from HTR in similar events. The asymptote of the power versus time relationship observed (Figure 2) represents, from a mathematical standpoint, a power output theoretically sustainable for a very long or even indefinite time. The response observed in the patient ($0.97 \cdot t^{-0.17}$, $R^2 = 0.99$), was similar to that previously described in professional cyclists ($9.85 \cdot t^{-0.17}$, $R^2 = 0.99$) [8].

Aerobic endurance also depends on an individual's glycogen stores. An endurance athlete typically has about 450 g of glycogen at the race start. It is therefore likely that, similar to a healthy endurance athlete, this subject's muscles make greater use of fatty acids, thereby sparing glycogen. Although no biopsy reports or constant rate submaximal CPX data are available, the capacity to maintain a steady state work rate and heart rate after several hours of high intensity exercise support this concept. Moreover, this subject replenished glycogen reserves through adequate food intake before and during the race.

During the race, the patient remained -4 hours between VT and RCP, and more than 2 hours above RCP.

Although high VO_2 peak values are required for success in endurance sports, other physiological variables such as the anaerobic threshold and mechanical efficiency are important [18,19]. The anaerobic threshold in absolute terms or as a percentage of VO_2 peak is a predictor of prolonged aerobic performance (i.e., time that a given rate of ATP turnover can be maintained) [8]. This individual showed a high relative RCP, at 86% of VO_2 peak. Surprisingly, these values are similar to those observed in top-level professional road cyclists (85%), and close to the $\geq 90\%$ VO_2 peak exercise intensity performed by professional cyclists [13]. The ability to maintain a steady state exercise intensity above VT may seem surprising given that the VT has been traditionally considered a limit beyond which fatigue limits effort in cardiac patients [20]. These findings provide new insights in the utilization of such variable for exercise testing and training purposes in HTR.

Another characteristic shown by this subject is his high cycling economy, i.e. the extent to which power output was generated for a given level of VO_2 . The CPX report showed a power output/oxygen uptake ratio of -80 watts per L of O_2 /min, only slightly lower than the 85 watts per L of O_2 /min reported in top-10 finishers of the Tour de France [21], and higher than the average 76 watts per L of O_2 /min reported in elite cyclists [22]. The efficiency with which the chemical energy of ATP hydrolysis is converted to physical work depends greatly on the velocity of sarcomere and muscle fiber shortening, and type I (slow twitch) fibers have high mechanical efficiency. Although no biopsy reports are available, these results suggest that high values of mechanical efficiency, along with high % VO_2 peak at RCP and HRDP reflect a high density of efficient, type I fibers in the major muscles involved in cycling [23].

In this case study, a decade of progressively longer and more intense exercise training resulted in remarkably high aerobic capacity and endurance performance after CTX, likely due to a combination of central and peripheral adaptations. These results further support the concept that in selected patients, long-term adherence to training even at high exercise intensities improves cardiovascular, respiratory, metabolic, and musculoskeletal systems following CTX.

Acknowledgments

The authors thank the patient for his involvement and high motivation during the training and racing program. The authors also thank the Italian National Transplant Centre for the scientific support.

The experiments comply with the current laws of the country in which they were performed. None of the authors declare competing financial interests. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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