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Effects of combined strength and endurance training on exercise capacity in kidney transplant cyclists and runners

Valentina Totti[1], Rocco Di Michele[2], Giulio Sergio Roi[3], Sandro Bartolomei[2], Giovanni Mosconi[4], Gianluigi Sella[5], Alessandro Nanni Costa[6], Gabriela Sangiorgi[7], Manuela Trerotola[1], Lia Bellis[1], Franco Merni[2] and Massimo Cardillo[1]

[1]*Centro Nazionale Trapianti, Istituto Superiore di Sanità, Rome, Italy*
[2]*Dipartimento di Scienze per la Qualità della Vita, Università di Bologna, Bologna, Italy*
[3]*Scuola di Specializzazione in Medicina dello Sport e dell'Esercizio Fisico, Università di Bologna, Bologna, Italy*
[4]*Unità Operativa di Nefrologia e Dialisi, Ospedale Morgagni-Pierantoni, AUSL Romagna, Forlì, Italy*
[5]*Unità Operativa di Medicina dello Sport, CMP Centro di Medicina e Prevenzione, AUSL della Romagna, Ravenna, Italy*
[6]*IRCCS Azienda Ospedaliero Universitaria di Bologna, Policlinico di Sant'Orsola, Bologna, Italy*
[7]*Centro Riferimento Trapianti della Regione Emilia-Romagna, Bologna, Italy*

Abstract
Introduction. After transplantation, engaging in regular physical activity (PA) or sport is recommended for health. Participation to competitive sports is increasingly common among kidney transplant recipients while little is known on how training affects the physical performance in transplanted athletes.
Aim. The purpose of this case study was to assess the effects of a tailored training program on exercise parameters in kidney transplant cyclists (CKTRs) and runners (RKTRs).
Methods. Twelve male transplanted athletes were enrolled. The workload at aerobic and anaerobic thresholds, the submaximal aerobic power ($V'O_2$ stage) and rate of perceived exertion (RPE) during an incremental cycling or running test, and the peak instantaneous force (PIF) during a countermovement jump were assessed at baseline (T_0) and after 6 months of tailored training (T_6) consisting in strength and aerobic exercises. Exercise adherence, blood lipid profile and renal function were also investigated.
Results. Eight CKTRs and 4 RKTRs completed the 6-month training period, with a significant increase of training volume (minutes/week). The exercise adherence was met by 90% in both groups. At T_6, there were significant ($p<0.05$) improvements of maximum workload attained, the workload corresponding to the aerobic threshold and PIF, while workloads at anaerobic threshold, $V'O_2$ stage and RPE were unchanged. Blood cholesterol significantly decreased ($p<0.01$), while the other blood parameters were unchanged.
Conclusions. These findings indicate that the combined strength and endurance training is well tolerated and may improve exercise performance in this selected population of KTRs.

Key words
- exercise
- training
- kidney transplant recipients
- sport
- fatigue

INTRODUCTION

Kidney transplantation is the standard treatment for end-stage renal disease and can offer a new independence from the disease process. After transplantation, engaging in regular physical activity is recommended to counteract the effects side of the immunosuppressive therapy as weight gain and represents in all respects a therapeutic intervention for improving health [1]. Contrary to what is commonly thought, sport can also be practiced after a solid organ transplantation. Indeed, participation to recreational and competitive sports activities is increasingly common among kidney trans-

Address for correspondence: Valentina Totti, Centro Nazionale Trapianti, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: valentina.totti@iss.it.

plant recipients (KTRs). Totti *et al.* showed that transplant recipients practicing football are able to attain energy expenditure levels and quality of life similar to healthy controls [2]. Moreover, it was shown that well-trained KTRs can safely participate to a long-distance road cycling race without acute signs of kidney damage and can benefit from physical activity, even at a competitive level [2-4].

The increasing interest on the benefits of physical activity in transplant recipients has led to a number of studies showing the effects of different exercise training programs on health and exercise capacity in this population [5]. Nevertheless, most studies focused on sedentary or moderately active transplant recipients, while still little is known on how training affects the physical performance in transplanted competitive athletes.

Conditioning programs including a combination of strength and endurance training are known to impact performance-related parameters such as running or cycling economy and the power output associated to the maximum oxygen uptake in healthy competitive cyclists and runners [6]. While this kind of training may be used also by competitive KTRs, some aspects specific of that population might lead to a sub-optimal training stimulus and adaptation. Indeed, reduced muscle mass and strength are common conditions during dialysis and muscle wasting is major clinical problem due to the dialysis [7]. As a consequence, perceived muscular fatigue may be increased with possible inability to maintain a given force or power output [8]. Furthermore, immunosuppressive therapy as cyclosporine reduces oxidative activity and capillarity of some muscles, possibly contributing to reduce exercise tolerance [9]. The long-term systematic combination of immunosuppressive drug and glucocorticoid therapy may also induce muscle atrophy and bone loss [10].

To investigate the impact of combined strength and endurance training in competitive KTRs athletes, the purpose of the present case study was to assess the effects of a tailored training program on a selection of performance parameters on kidney transplant cyclists and runners.

MATERIALS AND METHODS

Patients' information

CKTRs and RKTRs were recruited from a national association who organize sport events for transplant recipients (ANED Sport, Associazione Nazionale Emodializzati, Dialisi e Trapianto). All participants regularly practiced sports before enrolment in the study and were declared eligible by the Sport Physicians. The following inclusion criteria were used: age 18-60 years, at least 6 months after organ transplantation and regularly trained. Exclusion criteria were orthopaedic limitations, psychiatric or neurological disorders, proteinuria within nephrotic range, sedentary lifestyle and any cardiovascular contraindication to exercise testing and training. Twelve KTRs – 8 male cyclists (CKTRs), 4 male runners (RKTRs) – provided informed consent before inclusion according to the procedures approved by the local Ethics Committee and following all the guidelines for experimental investigation required by the institutions. The study conformed to the policy statement with respect of Declaration of Helsinki. Subjects were informed about the nature of the research and the assurances of anonymity.

Diagnostic assessment

Information on medical illness, pathologies leading to renal disease, dialysis vintage and medications were collected using structured questionnaires.

Renal function and blood lipid profile were recorded from the last medical check from each participant. Fat mass percentage (FM%) was determined by the Jackson & Pollock equation using seven skinfolds (abdominal, thigh, triceps, bicep, subscapular, suprailiac, chest) measured with a Harpenden calliper [11].

In relation to the practiced sport, an incremental cycling or treadmill exercise protocol were used to determine the aerobic and anaerobic thresholds. For cyclists, the cycling exercise protocol started with a workload of 25 W and increased by 50 W every 3 minutes, while, for runners, the treadmill exercise protocol started with a speed of 10 km/h and was increased by 1 km/h every 4 minutes. At every stage, a capillary blood sample from the earlobe was taken to measure blood lactate concentration (YSI Model 1500 Sport Lactate Analyser; Yellow Springs Instrument Co, Yellow Springs, Ohio, USA) to estimate the workload associated to the aerobic and anaerobic thresholds, corresponding to 2 and 4 mmol of lactate, respectively. The test was ended when lactate was >4mmol/L. The rate of perceived exertion (RPE) was recorded at each step using 0-10 visual analogue scale. The oxygen consumption ($V'O_2$) was measured using an open-circuit spirometry system (Sensor Medics Corp., Anaheim, CA, USA), which was carefully calibrated before each test. Respiratory gases were analysed for volume and fractions of oxygen and carbon dioxide, and the steady state $V'O_2$ expressed in terms relative to body mass (mLO_2/kg/min) averaged over the final two minutes of the first stage of the incremental test, was used to calculate the $V'O_2$ stage.

Finally, countermovement jumps (CMJ) were performed on a dual-force platform system (Kistler Instruments Ltd., Farnborough, United Kingdom). The peak instantaneous force (PIF) of the lower limbs was considered as the outcome measure over three attempts. Training volume was recorded by direct interviews before the tests. Adherence to the exercise program and eventual adverse events were also recorded.

"Therapeutic" intervention

After testing, a tailored training program was given to each participant. Each training program included 3 sessions/week of aerobic exercise (cycling or running) and 2 sessions/week of strength exercises that included isometric squats (4 sets of 10 seconds), lunges (3 sets of 10 repetitions) and plantar flexors (3 sets of 10 repetitions). Warm-up, cool-down and stretching exercises were included in each training sessions. All training sessions were not directly supervised, anyway all KTRs were contacted after 3 and 6 months by phone to assess progress and adherence to the program. The same testing protocol was repeated after 6 months of training.

Data were analyzed with descriptive statistics. Differences between T_0 and T_6 were assessed by paired t-tests, assuming as significant a value of $p<0.05$.

RESULTS

Follow-up and outcomes

The demographic and clinic characteristics of the participants are shown in *Table 1*. All KTRs were assuming regular immunosuppressive therapy. The exercise program adherence, defined as compliance in executing the assigned exercise program (total number of session n=72) during the 6-month period was met by 7 out of 8 CKTRs and 3 out of 4 RKTRs, i.e., 83% of the subjects. The training volume showed increases of 77±40% at T_6 (*Table 2*; $p<0.01$), without reporting adverse events.

No changes were observed for FM% that remained stable in both groups at T_6 ($p>0.05$; *Table 2*). The workloads associated to the aerobic and anaerobic thresholds showed improvements in CKTRs of 22±32% and 11±26% respectively and in RKTRs of 5±5% and 0±6% respectively at T_6 ($p>0.05$; *Figure 1*). RPE measured at the end of the last stages of the tests non significantly increased in both groups. Furthermore, in both groups, a higher workload at the end of the tests was observed at T_6 (+13±15%; $p<0.05$).

PIF showed improvements of 6±11% ($p<0.05$). $V'O_2$ stage remained unchanged at T_6 (*Figure 2*).

Blood cholesterol showed a significant decrease (-8±9%, $p<0.01$) while the other blood parameters remained unchanged (*Table 2*).

DISCUSSION

This case series showed that competitive KTRs were able to complete a 6-month training including 3 sessions/week of aerobic exercise and 2 sessions/week of strength exercises without any evident adverse effects. Moreover, the majority of athletes showed overall improvements in the workload associated to the aerobic thresholds and the maximum sustained workload, with a slightly increased exercise tolerance. The wide range of performances of this small group of subjects affected the standard deviation around the mean (i.e., the coefficient of variation) and also the presence of opposite trends in some subjects confirmed the physiological variability present even in healthy subjects, as reported by the literature [12]. Regarding the PIF, the study group showed a significant improvement at T_6, as a possible effect of strength exercises on the muscles of the lower limbs also in KTRs. Chan *et al.* showed that KTRs were mostly capable of generating muscular power similar to healthy subjects, corroborating that fatigue is not only explained by deficits in the muscular and cardiovascular systems [13]. The same mechanisms were showed in elite healthy cyclists, where adding strengthening to endurance training can increase strength and rate of force development as appear in CKTRs [14]. In the present study, the $V'O_2$ stage, which can be roughly considered an indicator of economy of cycling or running, did not show significant improvements. However, considering the three subjects who achieved more than 1,500 minutes/week of training volume, we found a significant decrease of the $V'O_2$ stage ($p<0.05$), indicating that the effects of an adequate volume of combined endurance and strength training tends to improve the economy of locomotion, as already reported in healthy cyclists [14]. Furthermore, Montero *et al.* showed that exercise programs including strength training improve the energy cost of cycling and shows a superior effect compared with endurance training alone [15]. The present findings confirm that, despite the intake of immunosuppressive therapies often associated with glucocorticoid, KTRs may improve the exercise performance by combined endurance and strength trainings, counteracting the side effects of the pharmacological therapies, and may reduce the muscle atrophy and weakness. Moreover, immunosuppressive therapy alone seems to have no inhibitory effect on the physiological factors related to the aerobic and muscular metabolism and regular training could be considered as a therapy that counteract the side effects of other drugs on aerobic capacity and muscle strength. Future studies are needed to more deeply investigate this aspect in larger samples of subjects. The limitations of the study are represented by the lack of data on renal function (e.g., creatinine), hydration status and training volume at the time of enrolment in the study. Another limitation is the small sample of subjects and the absence of a specific questionnaire to assess the exercise program adherence, as we used self-reported interviews.

CONCLUSIONS

The outcomes of this case study demonstrate that combined endurance and strength training is overall well tolerated in this sample and may improve sport

Table 1
Demographic and clinical characteristics of cyclists (CKTRs) and runners (RKTRs) kidney transplant recipients

	CKTRs								RKTRs				Mean±SD
Patient (n)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**1**	**2**	**3**	**4**	**n=12**
Dialysis vintage (months)	126	72	0	66	96	24	13	48	48	24	6	7	44.2±39.6
Age (years)	54	45	44	40	49	51	50	61	33	50	45	60	48.5±7.9
Time from transplant (years)	15	3	6	5	17	4	12	22	4	10	7	17	10.2±6.3
Body Mass Index (kg/m^2)	24.7	26.5	23.1	24.1	22.4	22.3	22.4	30.5	23.7	20.6	22.6	22.7	23.8±2.6
Pathologies leading to renal disease	G	P	G	G	G	G	N	P	G	P	G	G	--

G: glomerulonephritis; P: polycystic kidney disease; N: nephropathy.

Table 2

Fat mass, training volume, performance parameters, rate of perceived exertion (RPE), blood lipid profile and renal function in cyclists (CKTRs) and runners (RKTRs) kidney transplant recipients at baseline (t0) and after 6 months of training (t6)

		CKTRs								RKTRs				Mean±SD
Patient (n)		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**1**	**2**	**3**	**4**	**n=12**
Fat mass (%)	T_0	11.9	17.5	8.6	20.6	11.2	15.0	8.5	23.3	18.0	7.6	21.8	11.2	14.6±5.5
	T_6	12.5	22.9	9.7	17.3	13.1	13.7	8.8	23.8	20.2	8.5	19.4	10.0	15.0±5.5
Training volume (min/week)	T_0	120	240	720	1620	540	234	552	720	240	150	180	480	483±419
	T_6	180	480	480	2,880	1,620	720	600	1,620	240	100	270	600	816±822**
V'O_2 stage (mL/min/kg)	T_0	19.79	22.18	23.66	23.99	24.53	24.93	25.83	18.10	30.72	35.01	35.89	38.31	26.9±6.5
	T_6	19.66	19.41	25.08	22.01	22.07	27.87	25.67	17.56	31.59	33.45	36.76	39.30	26.7±7.2
S2 - Workload (W)	T_0	171	100	143	100	165	93	168	58	--	--	--	--	125±43
S2 - Workload (W)	T_6	167	108	158	136	172	150	145	102	--	--	--	--	142±26
S2 - Workload (km/h)	T_0	--	--	--	--	--	--	--	--	9.7	9.3	12.0	10.7	10.4±1.2
S2 - Workload (km/h)	T_6	--	--	--	--	--	--	--	--	10.0	10.0	12.0	11.8	11.0±1.1
S4 - Workload (W)	T_0	247	215	231	176	211	132	215	97	--	--	--	--	191±52
S4 - Workload (W)	T_6	239	163	238	203	226	208	203	136	--	--	--	--	202±36
S4 - Workload (km/h)	T_0	--	--	--	--	--	--	--	--	12.1	12.7	13.7	15.4	13.5±1.4
S4 - Workload (km/h)	T_6	--	--	--	--	--	--	--	--	13.0	12.0	14.3	14.7	13.5±1.2
Max workload (W)	T_0	250	250	250	200	250	200	250	125	--	--	--	--	222±45
Max workload (W)	T_6	250	250	300	200	300	250	250	150	--	--	--	--	256±50*
Max workload (km/h)	T_0	--	--	--	--	--	--	--	--	12.0	13.0	14.0	15.0	13.5±1.3
Max workload (km/h)	T_6	--	--	--	--	--	--	--	--	13.0	13.0	14.5	16.0	14.1±1.4
RPE (0-10 scale)	T_0	5	5	4	5	6	6	4	4	5	5	3	4	4.7±0.9
	T_6	5	5	5	5	7	7	5	7	4	5	2	5	5.2±1.4
Peak instantaneous force (N)	T_0	1,598	1,841	1,574	1,659	1,504	1,509	1,285	1,427	1,330	1,351	1,692	1,326	1,508±172
	T_6	1,698	2,006	1,437	1,810	1,759	1,710	1,209	1,489	1,385	1,314	2,178	1,239	1,602±308*
Total Cholesterol (mg/dL)	T_0	178	220	237	261	195	211	230	217	173	174	168	171	203±31
	T_6	161	222	200	244	170	193	160	210	164	165	164	172	185±28**
Triglycerides (mg/dL)	T_0	87	280	99	199	55	249	115	93	126	145	61	145	138±71
	T_6	87	282	98	157	37	250	105	90	166	122	60	144	133±73
Creatinine (mg/dL)	T_0	1.58	1.68	1.84	1.10	1.34	1.82	1.70	1.05	0.92	1.30	1.00	1.31	1.39±0.33
	T_6	1.54	1.56	1.88	1.07	1.47	1.89	1.48	1.05	0.89	1.43	1.00	1.23	1.37±0.33
eGFR (mL/ min/1.73mq)	T_0	49	47	43	79	60	42	46	76	101	62	86	59	62.5±19.1
	T_6	50	51	42	81	54	40	50	76	104	55	86	64	62.8±19.8
Glucose (mg/dL)	T_0	65	85	85	114	101	100	99	91	79	84	90	79	89.3±12.9
	T_6	71	76	87	116	92	107	102	85	81	77	79	83	88.0±13.7

*p<0.05; **p<0.01.

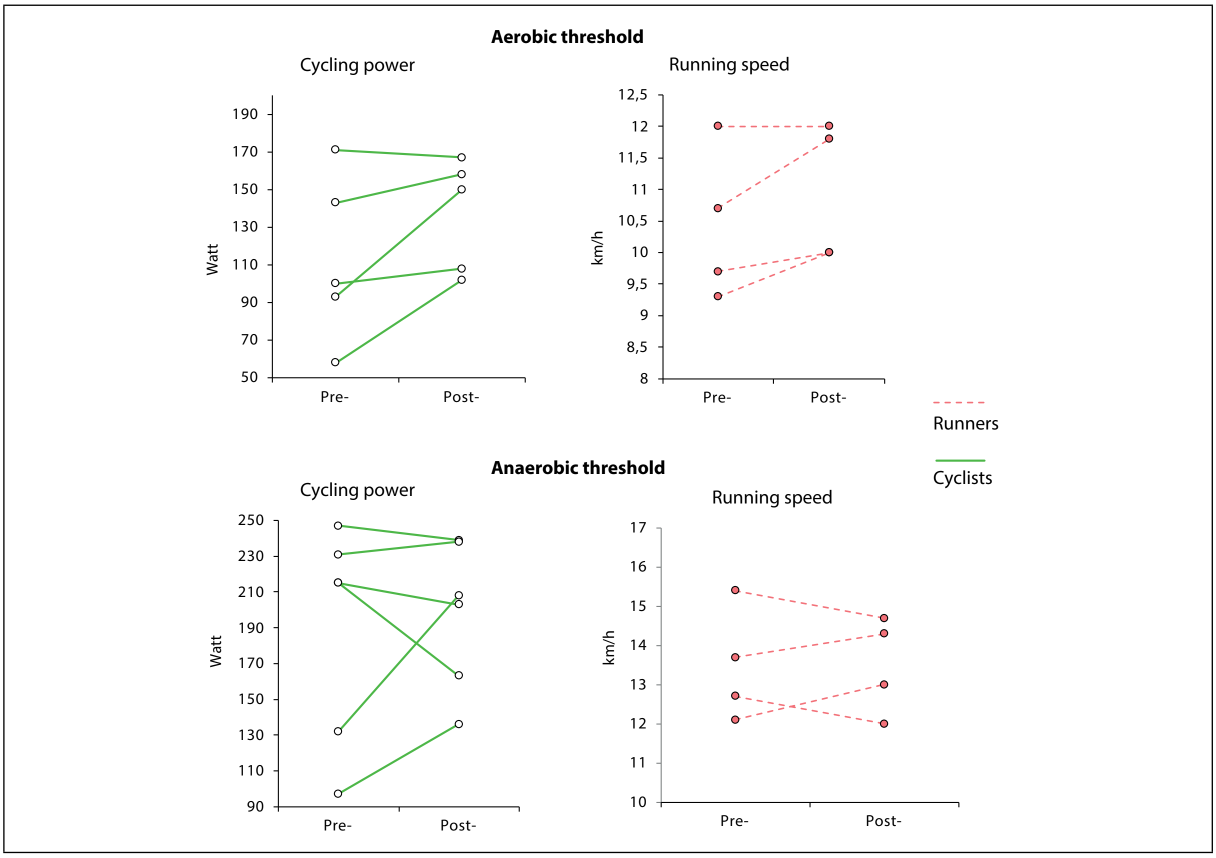

Figure 1
Scatterplot of cycling power and running speed at aerobic (95% CI diff standard: from 0.12 to 0.76, $p<0.05$) and anaerobic thresholds (95% CI diff standard: from -0.25 to 0.55, ns) pre- and post-training in kidney transplant recipients cyclists and runners respectively.

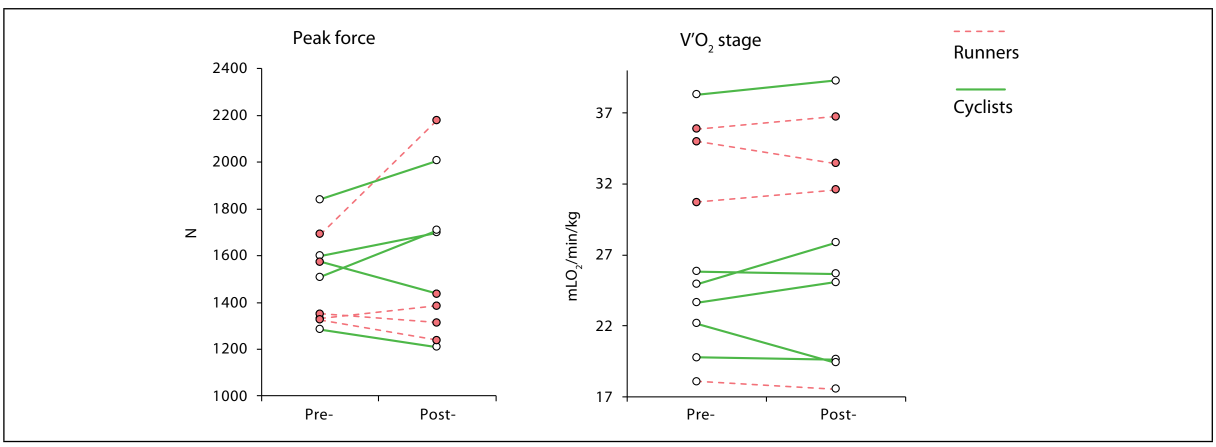

Figure 2
Scatterplot of peak force (N) (95% CI diff standard: from -0.27 to 1.03, ns) and V'O_2 stage (mLO_2/min/kg) (95% CI diff standard: from -0.14 to 0.16, ns) in kidney transplant recipients cyclists and runners pre- and post-training.

performance capacity of cyclist and runner KTRs. Referring to the scientific literature on healthy competitive athletes, physiological responses seem to appear comparable to the study group [16, 17]. Further research is needed to investigate the hydration status of transplant recipients who regularly practice sport, which is closely related to renal function. Anyway, these findings can help design future studies to determine the optimal training load to improve performance and reduce fatigue in KTRs practicing physical activity or sports.

Authors' contributions

V. Totti and R. Di Michele have participated in research design, in drafting the paper, in the performance of the research in data analysis and statistics and in critical revision of the paper; GS. Roi, S. Bartolomei, G.

Mosconi and G. Sella has participated in drafting the paper, in the performance of the research and in critical revision of the paper; A. Nanni Costa, G. Sangiorgi, M. Trerotola, L. Bellis and M. Cardillo have participated in the critical revision of the paper.

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Conflict of interest statement

The Authors declare that there is no conflict of interest. All Authors have participated in conception and design, or analysis and interpretation of the data; drafting the article or revising it critically for important intellectual content; and approval of the final version. This manuscript has not been submitted to nor is under review at another journal or other publishing venue.

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