



PLANO DE ATIVIDADES

2024

**GRUPO DESPORTIVO
DE TRANSPLANTADOS DE PORTUGAL**



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TÍTULO

PLANO DE ATIVIDADES 2024

EDIÇÃO

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1. INTRODUÇÃO

O Grupo Desportivo de Transplantados de Portugal (GDTP) é uma organização sem fins lucrativos, reconhecida pelo Instituto do Desporto e da Juventude como Associação Promotora do Desporto. O GDTP foi fundado em 2003 e é desde então membro da Federação Internacional de Jogos para Transplantados (WTGF – *World Transplant Games Federation*). Atualmente, o GDTP é igualmente membro da Federação Europeia de Jogos para Transplantados e Dialisados (ETDSF - *European Transplant and Dialysis Sports Federation*).

O GDTP tem como missão contribuir para a melhoria da qualidade de vida da sua população alvo, nomeadamente transplantados e candidatos a transplante, através da promoção de atividades desportivas com vista à melhoria da saúde, da autoestima, da autossuficiência e do bem-estar pessoal e interpessoal de todos os que se identificam com a causa do GDTP.

A atuação do GDTP tem portanto como base dois pilares fundamentais, a saúde e o exercício físico. O GDTP dá igualmente ênfase ao aspeto psicossocial, de extremo importância para a nossa população alvo e para populações semelhantes à nossa, sendo que as atividades contribuem para a melhoria do bem-estar do doente e permitem igualmente a partilha de experiências de vida.

Além da adversidade da doença acredita que podemos ser campeões na Vida, mais do que no Desporto, associando todo o espírito de confraternização, de união e de excelência desportiva presente, bem como os valores da igualdade e da inclusão social.

Pelo exposto, o GDTP compromete-se a dinamizar a prática desportiva no seio da sua população alvo, visando assim a promoção da saúde e de estilos de vida saudáveis.

2. OBJETIVOS GERAIS

Os objetivos gerais dos GDTP são:

- Sensibilizar e motivar os transplantados e candidatos a transplante à prática de exercício físico, mostrando-lhes os seus benefícios;
- Organizar ações de formação e projetos de investigação no âmbito da promoção do exercício físico na população alvo;
- Organizar eventos desportivos a nível nacional;
- Selecionar, preparar e apoiar atletas portugueses em competições Internacionais.

Os objetivos apresentados visam promover e orientar a generalização da atividade desportiva como fator educativo, mas também cultural, sendo indispensável na formação plena da pessoa humana e indo ao encontro com o preconizado na Lei de bases do Desporto.

3. POPULAÇÃO ALVO / DESTINATÁRIOS

A população alvo do GDTP é constituído essencialmente por:

- Transplantados (nomeadamente transplantados de órgãos tais como rim, fígado, pâncreas, coração, pulmão e medula óssea);
- Candidatos a transplante.

Para complementar o nosso trabalho, pretendemos ter o apoio e chegar também a toda a população que se identifica com o GDTP:

- Amigos e familiares de doentes;
- Qualquer cidadão com interesse na nossa causa.

4. DADOS ESTATÍSTICOS

O Instituto Português do Sangue e da Transplantação (IPST, IP) tem por missão garantir e regular, a nível nacional, a atividade da medicina transfusional e da transplantação e garantir a dádiva, colheita, análise, processamento, preservação, armazenamento e distribuição de sangue humano, de componentes sanguíneos, de órgãos, tecidos e células de origem humana.

O IPST, IP tem na solidariedade de todos o seu valor máximo pois toda a sua atividade é decorrente do gesto comum da dádiva de sangue, células, órgãos e tecidos.

É este gesto de solidariedade que o GDTP também quer transmitir à população alvo, a todos os parceiros e entidades que se encontram direta ou indiretamente ligadas à transplantação. Associada a este gesto de solidariedade e a esta causa, o GDTP pretende continuar a promover os hábitos saudáveis de vida cooperando com outros organismos que tenham igualmente esta missão.

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Todas as oportunidades de doação têm que ser consideradas para que os doentes que necessitam não percam nenhuma possibilidade de ter melhor qualidade de vida ou mesmo de sobreviver.

Os dados estatísticos reportados IPST, IP. relativos à Doação e Transplantação de Órgãos em Portugal são apresentados no Anexo 1.

5. FUNDAMENTAÇÃO CIENTÍFICA

Como introduzido no ponto anterior, o exercício físico ajuda na prevenção e melhoria das doenças e sintomas secundários adjacentes ao transplante, tais como o excesso de peso, a diabetes, as doenças ósseas, a hipertensão arterial, entre outras complicações associadas à doença e à componente terapêutica.

O desporto para transplantados fomenta a competição saudável, objetivando a boa condição física, psicológica, social e cultural, tão importantes na conservação do transplante como na qualidade de vida do transplantado.

A prática de exercício regular neste grupo específico da população alvo é fundamental para combater o sedentarismo associado ao tratamento em si, bem como à cessação de atividade laboral de um número significativo de ativos, bem como para prevenir problemas de saúde secundários.

A atividade física regular realizada em intensidades moderadas, já provou ter efeitos benéficos na melhoria da saúde (composição corporal, capacidade aeróbia, força e resistência muscular e flexibilidade) (Pederson e Saltin 2006), muitas vezes traduzidas na redução dos sintomas e incapacidade para atividades de vida diária (Kujala, 2006).

Após o transplante, os tempos de internamento hospitalar e especificamente também em cuidados intensivos, o aumento do tempo de sedentarismo, a medicação imunossupressora e episódios de rejeição podem afetar negativamente a tolerância ao exercício e a qualidade de vida dos indivíduos transplantados.

A medicação imunossupressora especificamente é causadora da perda de massa óssea e massa muscular que importa limitar através de programas de exercício físico. Especificamente os indivíduos submetidos a transplante de órgãos sólidos apresentam grandes limitações da capacidade física funcional e um risco aumentado de doença cardiovascular e o exercício físico tem o potencial de, tanto a curto como longo prazo, conduzir a benefícios nesta população. No entanto, existem ainda lacunas no conhecimento especialmente através da condução de estudos randomizados e controlados e resultados de follow-up de longo prazo (Mathur, 2014).

O exercício e a atividade física são intervenções importantes que possuem o potencial de melhorar os *outcomes* de candidatos a transplante e de indivíduos transplantados. À data, existe pesquisa ainda limitada que suporta os benefícios do treino, particularmente benefícios de longo prazo e outros benefícios para além da capacidade funcional e da qualidade de vida. Torna-se absolutamente necessário produzir evidência científica de qualidade nesta área de conhecimento e intervenção (Mathur, 2014).

No sentido de complementar o projeto, constam do Anexo 2 alguns artigos científicos cujo principal objetivo é o estudo da atividade física na nossa população alvo.

6. IMPACTO

O retorno à atividade e particularmente à atividade física devem fazer parte da reabilitação do transplantado. A prática desportiva após a realização de um transplante é recomendada mas com alguns cuidados. As indicações dependem do tipo de transplante e do tipo de desporto praticado. A prática do exercício físico visa a prevenção e melhoria das doenças e sintomas secundários apresentados anteriormente, tais como o excesso de peso, a hipertensão, entre outros.

Qualquer recetor de órgãos ou candidato poderá praticar exercício físico atendendo sempre ao quadro clínico do mesmo e à frequência e intensidade do exercício físico.

As atividades do GDTP visam sobretudo demonstrar que o exercício não só não é proibido a quem recupera de um transplante, mas que pode contribuir para um melhor estado de saúde e para uma maior longevidade do enxerto.

As atividades promovem igualmente o convívio entre elementos de uma população muito específica, permitindo uma troca de experiência enriquecedora e saudável, contribuição assim de forma positiva em termos de impacto social.

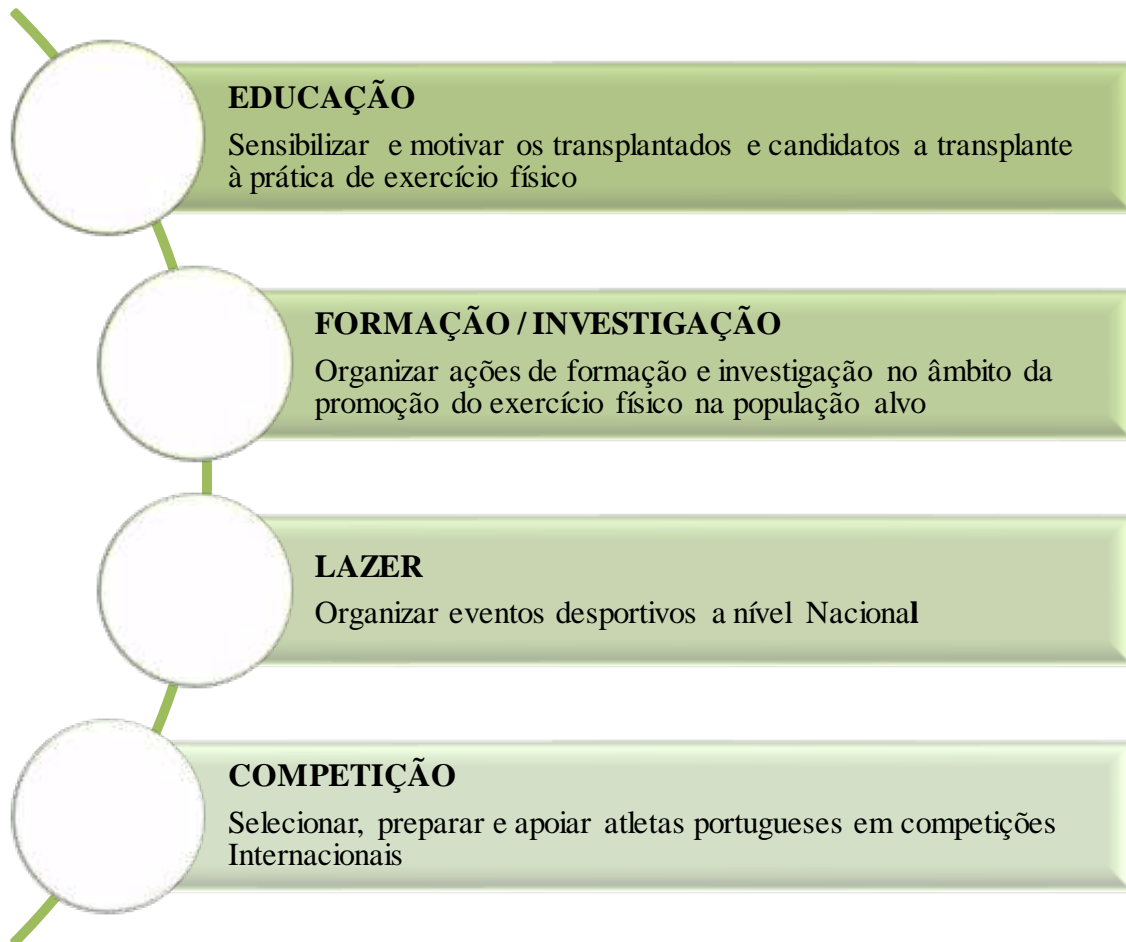
Acreditamos que o GDTP tem um forte potencial no apoio à comunidade transplantada e candidata a transplante em diferentes áreas, como seja o apoio psicossocial referido anteriormente.

7. PLANO DE ATIVIDADES

O Plano de Atividades do GDTP para o ano de 2024 apresenta os objetivos do GDTP, as respetivas atividades planeadas nas diferentes áreas de atuação, bem como os prazos de implementação e os recursos estimados para as respetivas atividades, conforme anexo 3.



Por sua vez, as áreas referidas estão associadas aos objetivos anteriormente apresentados.



7.1. CONSIDERAÇÕES AO ORÇAMENTO

Ao longo do ano, poderão ser realizadas outras atividades, sugeridas pela Direção ou por qualquer elemento da Associação. Qualquer atividade poderá ser integrada no plano sempre que se enquadre no âmbito dos objetivos e da missão da Associação.

As despesas diversas visam assegurar o funcionamento da Associação.

De reportar ainda as seguintes ATIVIDADES DIRETIVAS:

- Assembleias Gerais** - Planeamento de duas Assembleias Gerais, para março de 2024 (para apresentação de aprovação do Relatório de Atividades e do Relatório de Contas 2023) e novembro de 2024 (para apresentação do Plano de Atividades para 2025 e respetivo orçamento).
- Reuniões de Direção** - Planeamento de reuniões mensais e consoante necessidade, com aviso prévio mínimo através de convocatória.
- Reuniões Extraordinárias** - Planeamento de reuniões extra para o tratamento de ocorrências e exceções não programadas.

8. IDENTIFICAÇÃO DA CAPACIDADE FINANCEIRA

A única fonte de receitas do GDTP são as quotas dos associados, cujo montante anual é de 12€por associado.

O GDTP tem igualmente parcerias com sociedades científicas, outras associações de doentes, instituições académicas, entre outros, mas que não consubstanciam apoio financeiro para as suas atividades.

O apoio do Programa Nacional Desporto para Todos do Instituto Português do Desporto e Juventude tem uma importância vital para o desenvolvimento das atividades.

9. CONCLUSÕES

O Plano de Atividades de 2024 encontra-se estruturado, à semelhança dos anos anteriores, em diferentes áreas de atuação relevantes para a prossecução da missão do GDTP.

As atividades são planeadas atendendo à constante vontade e necessidade de melhoria contínua e de cooperação com outras entidades, parceiras ou cuja missão se enquadra no âmbito do GDTP.

Pretende-se continuar a apostar na sensibilização de transplantados e candidatos a transplantes, em prol do bem-estar físico e psíquico da população alvo e, sequeamente, da sua qualidade de vida.

ANEXO 1

DADOS ESTATÍSTICOS

REPÚBLICA PORTUGUESA SAUDE

SNS SERVIÇO NACIONAL DE SAÚDE

Doação e Transplantação de Órgãos, Tecidos e Células

Atividade Nacional Anual 2022

IPST

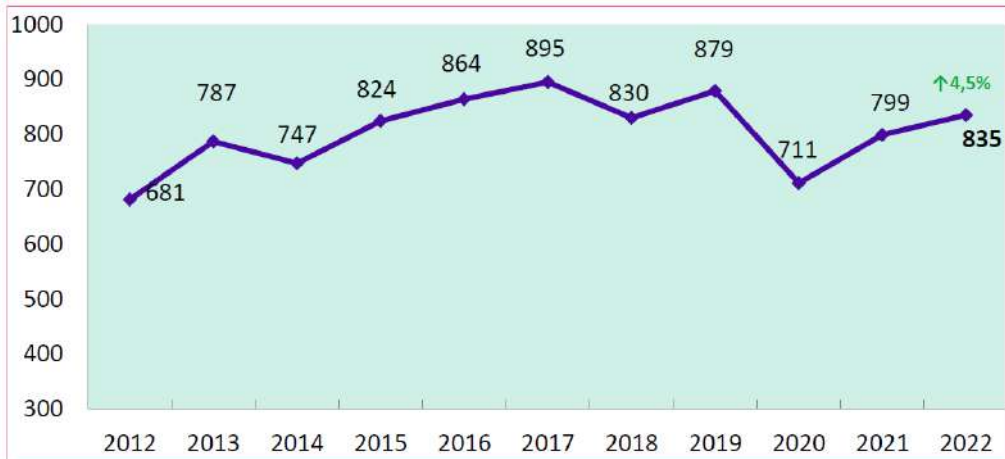
Margarida Ivo da Silva

Coordenação Nacional da Transplantação

20 de abril 2023

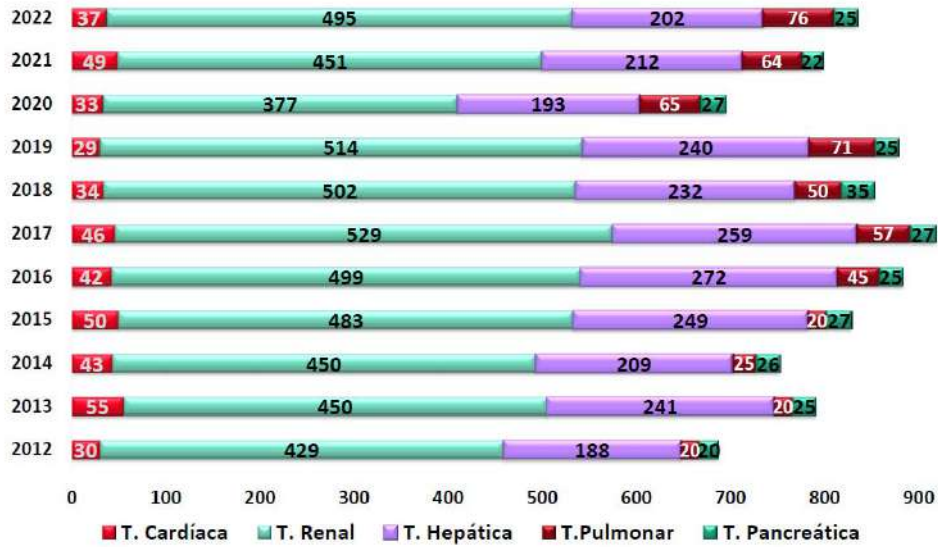
Transplantação de Órgãos¹ 2012 a 2022

835 órgãos transplantados em 2022, mais 36 que em 2021 (TC 4,5%)



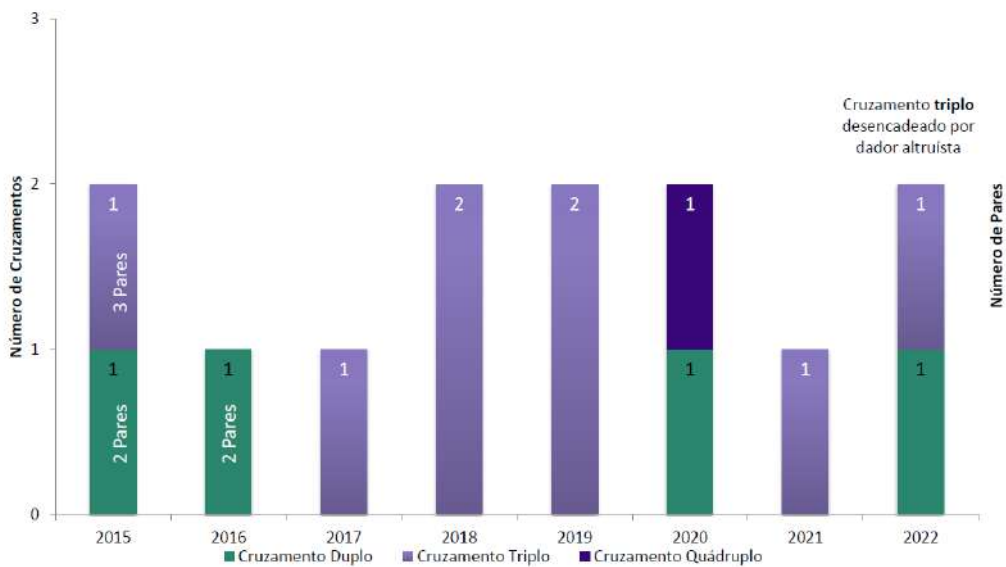
¹ Inclui órgãos provenientes de dador falecido, vivo e sequencial

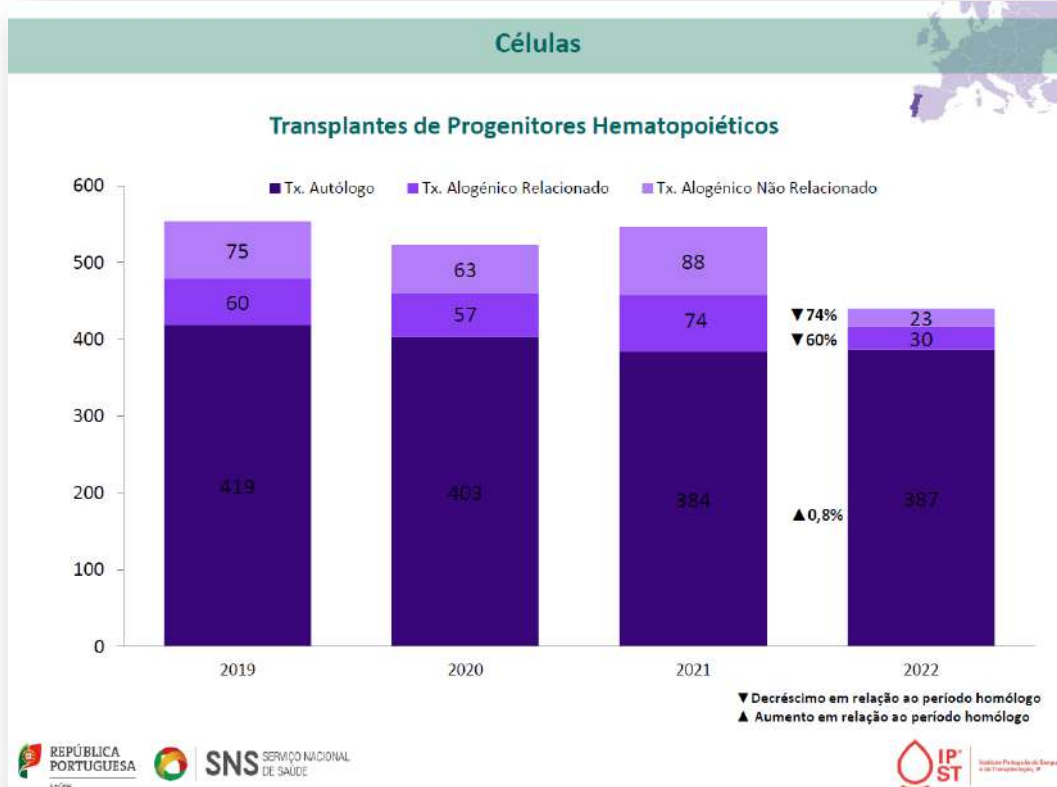
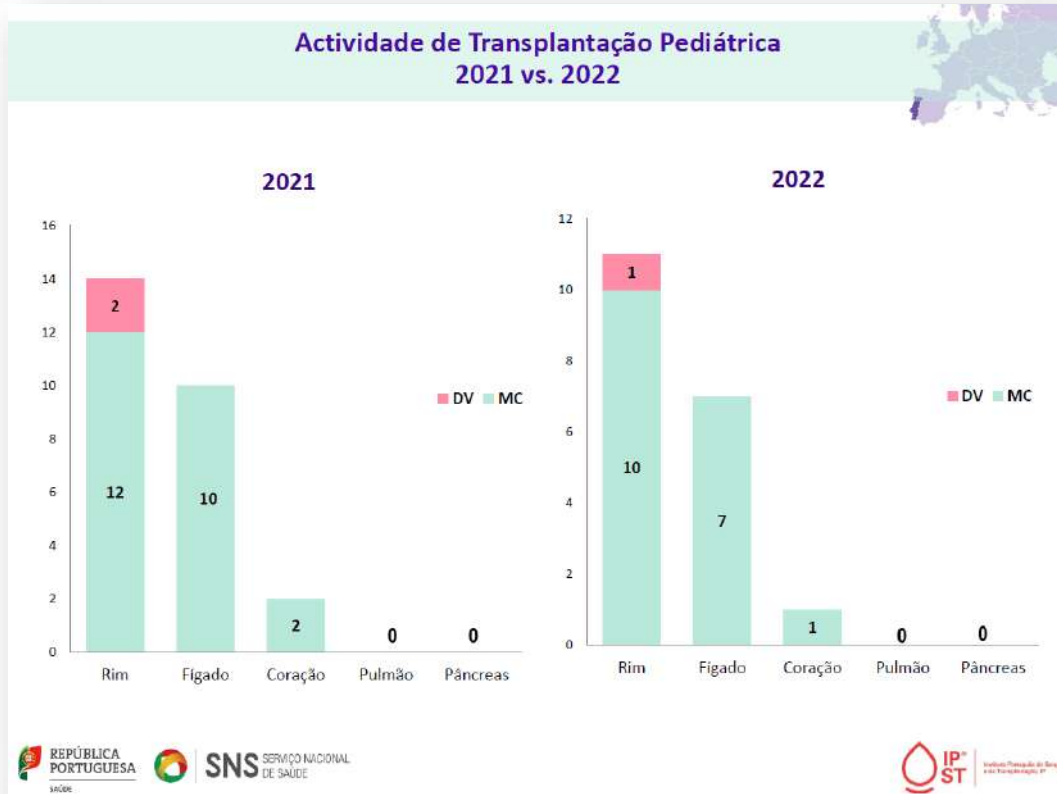
Transplantação Nacional 2012 - 2022



Programa Nacional de Doação Renal Cruzada

Evolução do número de pares cruzados transplantados 2015-2022





Doação e Transplantação de Órgãos, Tecidos e Células 2022

- Aumento da taxa global de doação
 - Recuperação da atividade da doação em PCC
 - Aumento da taxa de doação em vida
- Diminuição da taxa de aproveitamento de órgãos
- Aumento do Nº órgãos colhidos e transplantados
 - Diminuição do transplante cardíaco e do transplante hepático
- Diminuição ligeira do número total de doentes em lista ativa a aguardar transplante

Doação e Transplantação de Órgãos, Tecidos e Células 2022

- Aumento do Nº tecidos colhidos
 - Modalidade de dador falecido
- Diminuição ligeira do Nº tecidos aplicados
- Diminuição da taxa de aproveitamento de córneas

ANEXO 2

EVIDÊNCIAS CIENTÍFICAS

CLINICAL AND TRANSLATIONAL RESEARCH

The Impact of Exercise Training on Liver Transplanted Familial Amyloidotic Polyneuropathy (FAP) Patients

Maria Teresa Tomás,^{1,2,6} Helena Santa-Clara,¹ Paula Marta Bruno,³ Estela Monteiro,⁴ Margarida Carrolo,¹ Eduardo Barroso,⁴ Luis B. Sandinha,¹ and Bo Femholf⁵

Background. Liver transplantation is nowadays the only effective answer to adjoin the outcome of functional limitations associated with familial amyloidotic polyneuropathy (FAP), a neurodegenerative disease characterized by sensory and motor polyneuropathies. Nevertheless, there is a detrimental impact associated with the after-surgery period on the fragile physical condition of these patients. Exercise training has been proven to be effective on reconditioning patients after transplantation. However, the effects of exercise training in liver transplanted FAP patients have not been scrutinized yet.

Methods. The study aimed to evaluate the effects of a 24-week exercise training program (supervised or home-based) on body composition, muscle strength, and walking capacity of liver transplanted FAP patients. To fulfill this goal, a sample corresponding to 33% of all FAP patients who underwent a liver transplantation in the area of Lisbon between January 2006 and December 2008 were followed over time. Three evaluation periods were accomplished: M1 (pre-exercise training period), M2 (immediate post-exercise training period), and M3 (24 weeks after M2). The former allowed an assessment of the impact of detraining in these patients.

Results. The exercise training program improved body composition (lean mass and total body skeletal muscle mass), weight, and walking capacity. The improvements were more pronounced within the patients with supervised exercise training compared with the patients on the home-based program. In general, the benefits of the exercise training perdure even after a 24-week detraining period.

Conclusions. Exercise training results in significant improvements on the physical condition of liver transplanted FAP patients.

Keywords: Liver transplant, Familial amyloidotic polyneuropathy, Exercise training, Home-based exercise, Detraining

(*Transplantation* 2012;95: 00–00)

Familial amyloidotic polyneuropathy (FAP) is a neurodegenerative disease caused by the extracellular deposition of insoluble amyloid fibers, mostly synthesized within the liver (1, 2). In terms of life expectancy for patients, FAP is a devastating disease causing death within 10–20 years

after the first symptoms (3). The disease is characterized by a slowly progressive peripheral sensorimotor and autonomic neuropathy resulting in severe weight loss, renal failure with proteinuria, visual impairments, and motor incapacities coupled with muscle weakness and atrophy (4). Portugal constitutes the largest focus of FAP worldwide, with an estimated prevalence of 105×10^{-5} (5). The second largest

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The authors declare no conflicts of interest.

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M. T. T. was responsible for designing and performing the experimental work and participated in the data analysis and writing and editing of the article. H. S.-C. was involved in the research concept and design and the writing and editing of the article. P. M. B. was engaged in statistical analysis and writing of the article. M. C. participated in the data analysis and writing and reviewing of the article. E. M. was a clinical and methodology advisor and contributed to the writing and reviewing of the article. E. B. was a clinical advisor and collaborator on the writing of the article. L. B. S. contributed to the data discussion and interpretation and editing of the article. B. F. was involved in data analysis and writing of the article.

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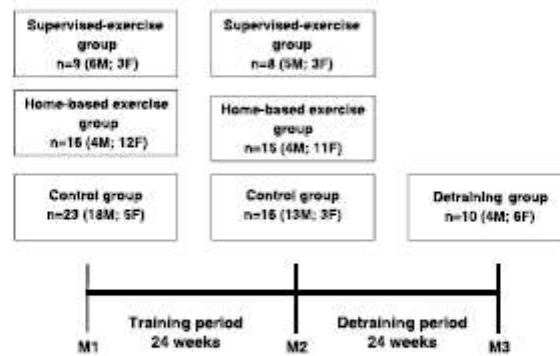


FIGURE 1. Sequence diagram of the evaluation moments of the study. The study included three distinct evaluation moments: a baseline assessment (M1), an assessment made after a 24-week training period (M2), and a third assessment performed 24 weeks after the final of the training period (M3). During the training period, nine patients left the study: one male (M) patient from the supervised exercise group, one female (F) patient from the home-based exercise group, and five males and two females from the control group. A group of 10 patients who participated in one of the training groups were also evaluated at M3.

core of the disease appears in Sweden, with a prevalence of 91×10^{-5} (6); the other relevant foci include Japan and Spain (7, 8).

Liver transplantation is the only therapy that halts the progression of the disease (9). Although the survival after transplantation has improved greatly in the last decade, the combination of the surgery with immunosuppressant medication is still associated with several comorbidities, including dyslipidemia, hypertension, diabetes, obesity, osteoporosis, sarcopenia, muscle pain, and metabolic syndrome (9). Physical function is also limited in patients who underwent a liver transplantation (10–12) and associations between poor prognosis and reduced physical function have been reported (10, 13). Exercise training can improve

exercise capacity, body composition, and muscle strength following the different types of transplantation (9, 14–16). It is likely that many of the common comorbidities associated with FAP liver transplantation can be improved through exercise training.

In this study, we propose to evaluate the effect of exercise training on body composition, muscle strength, and exercise capacity in liver transplanted FAP patients. Because many of these patients live in distant areas with some travel restrictions, we compared the effectiveness of supervised exercise training sessions with home-based exercise training sessions. We also checked for the impact of 24-week detraining period on the physical condition of the patients who had undergone training.

TABLE 1. Baseline assessment (M1) of patients distributed by groups, n=39

Variables	Supervised exercise group	Home-based exercise group	Control group
Number of patients	8	15	16
Age (years)	34.3	35.1	33.2
Weight (kg)	60.0±6.0	61.2±3.3	66.1±2.9
Height (m)	1.71±0.03	1.66±0.02	1.71±0.02
BMI (kg/m ²)	20.4±1.6	22.3±1.3	22.6±0.8
mBMI	802.7±67.2	865.8±46.5	910.8±43.2
Posttransplantation time (mo)	4.3±1.2	3.1±0.3	4.2±0.3
Inpatient time (d)	14.5±1.2	20.1±3.4	15.9±1.2
Prednisone (mg/d)	11.6±2.9	13.0±1.1	9.8±1.2
Tacrolimus (mg/d)	4.9±0.6	6.5±0.7	6.0±0.3
Number of patients in each PND score			
PND I	6	11	13
PND II	2	3	1
PND IIIA	0	1	2

Values are reported as frequency or mean±SEM.

BMI, body mass index; mBMI, modified body mass index; PND, polymyopathy disability scoring system.

RESULTS

Between January 2006 and December 2008, a total of 120 PAP patients underwent liver transplantation at Hospital Curry Cabral, one of the three hospitals where this procedure was performed in Portugal. From these patients, 48 were recruited to the study and assigned to one of the three groups: supervised exercise group (n=9), home-based exercise group (n=16), and control group (n=23). The three moments of evaluation were defined: a baseline assessment (M1), a second assessment immediately after a 24-week training period (M2), and a third assessment 24 weeks after the final of the training period (M3; Fig. 1). This last assessment was done to a group of 10 patients who participated in one of the training groups to check for the impact of a detraining period. During the training period, nine patients left the study and their results were excluded from statistical analysis.

The baseline characteristics of all patients are shown in Table 1. No significant differences were detected among groups for any of the evaluated characteristics. Globally, the average age of the patients enrolled in this study was 54.7 years, with a body mass index (BMI) of 22.0/3.9 kg/m², an

inpatient time of 17.2/8.9 days, and a posttransplantation time of 3.8/1.9 months. According to the polyneuropathy disability (PND) scoring system (17), 30 patients were classified as PND I, 6 patients as PND II, and 3 patients as PND IIIA. There were no patients in score IIIB or IV. Also, none of the patients exercised regularly before the transplantation.

After the training period, several significant differences (P<0.05) were found among the three groups (Table 2).

A post-hoc test done after an analysis of covariance showed significantly higher values in weight, BMI, total lean mass, right upper limb lean mass, dominant lower limb lean mass, total body skeletal muscle mass, skeletal muscle index, and walking capacity for the supervised exercise group followed by the home-based exercise group and the control group. The differences in the proximal femoral bone mineral density (BMD) were also significant, with the control group presenting the highest results. We must also notice that one patient (female) from the home-based group changed her PND score from IIIA to II between M1 and M2. No changes were observed between M2 and M3 in PND scores.

TABLE 2. Results of body composition, muscle strength, specific strength, and exercise capacity for patients distributed by groups obtained at the baseline assessment (M1) and after 24 weeks of exercise training (M2), n=39

Variables	Supervised exercise group		Home-based exercise group		Control group		P
	M1	M2 ^a	M1	M2 ^a	M1	M2 ^a	
Weight (kg)	60.0/6.0	69.2/1.4	61.2/3.3	64.6/1.0	66.1/2.9	62.9/1.0	0.003 ^{b,c}
BMI (kg/m ²)	20.4/1.6	24.4/0.5	22.3/1.1	22.6/0.4	22.2/0.8	22.4/0.4	0.005 ^{b,c}
mBMI	302.7/67.2	984.1/34.6	865.8/46.5	929.6/24.9	910.8/43.2	913.4/24.3	NS
Total lean mass (kg)	43.4/3.3	48.9/0.9	41.7/2.1	47.0/0.7	49.9/1.9	45.1/0.7	0.009 ^c
Right upper limb lean mass (kg)	2.3/0.3	2.8/0.1	2.2/0.2	2.6/0.05	2.9/0.2	2.5/0.05	0.002 ^{b,c}
Left upper limb lean mass (kg)	2.2/0.2	2.5/0.1	1.9/0.1	2.4/0.05	2.7/0.2	2.3/0.05	NS
Dominant lower limb lean mass (kg)	6.6/0.6	8.0/0.7	6.5/0.4	7.3/0.1	7.9/0.4	7.6/0.1	0.001 ^{b,c}
Total body skeletal muscle mass (kg)	20.3/1.9	24.4/0.4	19.6/1.2	22.5/0.3	24.9/1.3	21.9/0.3	0.001 ^{b,c}
Skeletal muscle index (kg/m ²)	6.9/0.4	8.5/0.2	7.1/0.3	7.9/0.1	8.5/0.3	7.6/0.1	0.001 ^{b,c}
Fat mass (kg)	13.9/3.2	17.5/1.0	16.4/2.0	15.6/0.7	13.2/0.7	15.1/0.7	NS
Fat mass (%)	22.2/3.1	24.9/1.0	26.2/2.3	23.4/0.7	19.5/2.0	23.3/0.7	NS
Total BMD (g/cm ²)	1.1/0.04	1.1/0.01	1.2/0.03	1.1/0.01	1.2/0.03	1.1/0.01	NS
Proximal femoral BMD (g/cm ²)	0.8/0.04	0.8/0.01	0.9/0.03	0.8/0.01	0.9/0.04	0.9/0.01	0.017 ^d
Proximal femoral T-score	-1.7/0.31	-1.1/0.07	-0.8/0.21	-1.2/0.05	-0.7/0.25	-1.0/0.05	NS
Proximal femoral Z-score	-1.6/0.32	-1.0/0.07	-0.7/0.21	-1.1/0.05	-0.6/0.26	-0.9/0.05	NS
Right handgrip strength (kgf)	29.5/3.9	39.8/1.5	31.0/2.7	35.3/1.1	36.9/2.9	38.0/1.1	NS
Left handgrip strength (kgf)	29.0/2.5	36.6/1.2	29.0/3.8	35.1/0.9	35.6/3.4	34.8/0.8	NS
Quadriceps strength (Nm)	32.3/4.2	49.4/5.1	36.1/2.9	51.3/3.7	51.1/5.5	50.6/3.7	NS
Right upper limb specific strength (kgf/kg)	11.1/1.1	14.1/0.5	14.3/0.8	13.7/0.4	12.9/0.9	14.6/0.4	NS
Left upper limb specific strength (kgf/kg)	13.5/1.3	14.8/0.5	14.9/0.9	14.9/0.4	13.2/1.0	14.7/0.4	NS
Dominant lower limb specific strength (Nm/kg)	5.0/0.5	6.3/0.6	5.6/0.5	7.1/0.4	6.4/0.5	7.0/0.5	NS
6MWT (m)	506.2/42.1	573.3/14.0	491.2/36.1	550.5/10.2	530.9/36.8	553.6/10.6	NS
Walking capacity (kg km)	29.7/2.6	39.1/1.2	30.7/2.9	34.9/0.9	35.3/3.2	34.4/0.9	0.011 ^{b,c}

Values are reported as mean/SEM. P values reported are related to analysis of covariance.
^a After adjustment for baseline values.
^b Home-based group different from supervised group on post-hoc test.
^c Control group different from supervised group on post-hoc test.
^d Control group different from home-based group on post-hoc test.
 BMI, body mass index; mBMI, modified body mass index; 6MWT, 6-min walk test; BMD, bone mineral density; NS, not significant.

The results obtained 24 weeks after the cessation of the exercise program (M3; n=10) showed no significant differences compared with the results measured immediately after the end of the exercise program (Table 3).

DISCUSSION

The link between exercise and improved physical condition has been well established in patients after the different types of transplantation (18-20). One question that still remained to be answered was about the impact of exercise training on FAP patients with liver transplantation. Can exercise be an added value to recondition patients in the delicate period after the transplantation?

This study is unique in that a training intervention was tested in FAP patients who had undergone a liver transplantation, and the subjects were still early in their recovery (<1 year).

The findings from this study demonstrate the positive effects of exercise training on the patient's body composition, muscle strength, and walking capacity. It further demonstrates that supervised exercise training and home-based training are both acceptable and feasible within this

population. This feature is quite important as home-based programs give more flexibility to patients, which could enhance the degree of participation to the exercise program.

With respect to weight, both groups that did the exercise training reported significant weight gains. Modified BMI (mBMI) shows the highest increase in the supervised exercise group. Although those changes were not statistically significant, they might have a clinical importance because mBMI is a more accurate index for nutritional status and correlated with survival for FAP patients (21). In FAP patients, weight gain is of major importance as the disease is characterized by gastrointestinal problems causing malabsorption and malnutrition (22). Moreover, the observed weight gain mainly resulted from gains in lean mass, which are associated with improvements in daily living activities and quality of life (23, 24).

The observation of a higher increment in muscle mass than in strength could be explained by the typical peripheral nerve lesions of this patient population. We can speculate that extending the exercise training could positively contribute to decrease this impairment. Nevertheless, the obtained increase in muscle mass is by itself a substantial gain of

TABLE 3. Results of body composition, muscle strength, specific strength, and exercise capacity for a group of patients evaluated at the baseline assessment (M1), immediately after exercise period cessation (M2), and after a 24-week detraining period (M3), n=10

Variables	M1	M2	M3	P
Weight (kg)	62.0±5.3	67.5±6.3	67.7±6.0	0.025 ^a
BMI (kg/m ²)	22.0±1.6	24.0±2.1	24.1±2.0	0.025 ^a
mBMI	872.7±76.7	977.6±104.8	994.4±105.2	NS
Total lean mass (kg)	42.4±2.8	46.1±3.0	44.8±3.3	NS
Right upper limb lean mass (kg)	2.2±0.2	2.4±0.3	2.4±0.3	0.048 ^a
Left upper limb lean mass (kg)	2.0±0.2	2.2±0.2	2.2±0.2	NS
Dominant lower limb lean mass (kg)	6.5±0.5	7.1±0.6	7.2±0.6	NS
Total body skeletal muscle mass (kg)	39.8±1.6	41.5±1.9	41.7±2.0	0.048 ^a
Skeletal muscle index (kg/m ²)	7.0±0.4	7.6±0.5	7.7±0.6	NS
Fat mass (kg)	17.0±3.0	20.1±3.8	20.9±3.7	0.048 ^a
Fat mass (%)	26.2±2.8	28.1±3.2	29.4±2.9	NS
Total BMD (g/cm ²)	1.1±0.0	1.08±0.02	1.08±0.02	0.026 ^b
Proximal femoral BMD (g/cm ²)	0.78±0.03	0.78±0.03	0.78±0.02	NS
Proximal femoral T-score	-1.4±0.2	-1.5±0.2	-1.5±0.1	NS
Proximal femoral Z-score	-1.3±0.2	-1.4±0.2	-1.4±0.1	NS
Right handgrip strength (kgf)	28.4±3.0	32.9±3.2	32.9±3.8	0.026 ^a
Left handgrip strength (kgf)	27.1±3.1	30.5±3.4	30.7±3.5	0.026 ^a
Quadriceps strength (Nm)	36.6±3.5	42.9±2.2	46.8±3.8	0.046 ^b
Right upper limb specific strength (kgf/kg)	13.0±1.0	13.9±0.7	13.8±1.0	NS
Left upper limb specific strength (kgf/kg)	13.5±1.1	14.4±1.0	14.5±1.1	NS
Dominant lower limb specific strength (Nm/kg)	5.8±0.6	6.2±0.4	6.7±0.3	NS
6MWT (m)	512.3±38.7	569.8±45.9	563.1±38.3	<0.000 ^{ab}
Walking capacity (kg km)	31.1±2.6	37.8±3.6	37.8±3.5	<0.000 ^{ab}

Values expressed as mean±SEM. P values reported are related to Friedman test.

^a M1 different from M2 on post-hoc test.

^b M1 different from M3 on post-hoc test.

^c M2 different from M3 on post-hoc test.

^d Post-hoc tests were not able to show any difference among M1, M2, and M3.

BMI, body mass index; mBMI, modified body mass index; 6MWT, 6-minute walk; BMD, bone mineral density; NS, not significant.

the exercise training as it contributes to a better skeletal muscle index, which is directly related to a decrease in the patient's future risk of disability.

The differences observed in BMD were small, which could be due to the type and duration of the exercise training program. The exercise prescription did not have the main purpose of challenging bone mass, so the intensity, loads, and duration were not enough to provide powerful results between groups in BMD (25).

Compared with other studies with transplanted patients (26, 27), the 6-min walk test (6MWT) performance of the FAP patients in the baseline assessment was lower. This is likely to be related to the nutritional problems associated with FAP disease (22). Nevertheless, after the exercise intervention, patients already reached similar results compared with other studies with 12 months after liver transplantation (14, 28, 29). Another variable that is also below comparable values from other studies (30–32) in the baseline assessment was the walking capacity. This variable is a measure of the energy and work required for walking, which is a basic activity of daily life. Patients who participated in the exercise groups had a significant increment in their walking capacity. Moreover, the major increment on this variable was reached among patients who gained more weight. Thus, despite the body weight gain, these patients still walked larger distances.

With respect to the detraining period, no significant changes on body composition, muscle strength, and walking capacity were reported. This shows that the gains obtained during the exercise training period were still preserved throughout a 24-week detraining period.

In conclusion, this study demonstrates that a regular exercise program of moderate intensity produces benefits in the physical condition of liver transplanted FAP patients with less than 12 months after transplantation. It also shows that if attending to a supervised exercise program is not an option, a structured home-based exercise program can be recommended to these patients. Moreover, the results indicate that the significant increments in body composition and exercise capacity were maintained when patients stop exercising for 24 weeks. The findings from this study provide support for a continued investigation on the effects of longer periods of exercise training on the physical condition and global quality of life of liver transplanted FAP patients.

MATERIALS AND METHODS

Subjects

This study was done with 39 liver transplanted FAP patients whose surgery had been performed between 2 and 12 months. The study protocol was approved by the ethical review boards of the Hepatopancreatic and Transplantation Centre of Hospital Curry Cabral and the Faculty of Human Kinetics at Technical University of Lisbon.

Body Composition

Patients' height was measured to the nearest 0.5 cm with a stadiometer (SECA, Hamburg, Germany) and body weight was assessed to the nearest 0.1 kg using a standard scale (SECA, Hamburg, Germany). BMI (kg/m^2) was directly calculated from height and weight and used to calculate the nBMI (serum albumin level [g/L] \times BMI), a more accurate index for nutritional status in FAP patients (21).

Total body composition and proximal femur bone mass were estimated using dual-energy X-ray absorptiometry (DEXA; QDR-Explorer, Hologic,

Waltham, MA). The DEXA was calibrated daily, and scans and respective analyses were made by the same investigator.

The proximal femur BMD analysis included the values of total hip, Ward's triangle, and the neck of the proximal femur from the dominant lower limb (as opposed to the support lower limb). A reduced bone density (-1.0 T-score < -2.5) was considered osteopenia (33, 34). The upper and lower limbs were defined as reported previously (35).

Bone mineral content was subtracted from the total and regional lean mass to define the total and regional methionine lean mass. Total body skeletal muscle mass was calculated previously (36).

Skeletal muscle index was obtained by normalizing the skeletal muscle mass for height (kg/m^2) and used as a marker of physical disability risk (24).

Strength Assessment

The unilateral isometric strength of the quadriceps was measured on a dynamometer (system 3; Biodex, Shirley, NY) at a knee angle of 30° flexion from full extension in the dominant leg. All individuals were tested in a seated position, with the back supported against a backrest, with a hip flexion of 100° and fixed by stabilization straps across the chest, pelvis, and thigh of the tested lower limb. The shin pad was placed proximal to the ankle as reported previously (37). The peak force was defined as the best value obtained from three attempts (10 sec of contraction and 90 sec of rest).

The handgrip strength was assessed with a portable grip dynamometer F-Link (Biometrics, Gwent, UK). All measurements were taken according to the American Society of Hand Therapists.

The muscle quality was defined by the ratio of strength and lean mass. The ratio of isometric strength at the knee and leg lean mass obtained by DEXA was used to define dominant lower limb specific strength; the ratio of handgrip strength and upper limb lean mass was used to define right and left upper limb specific strength.

Functional Exercise Capacity

The FND scoring system was used to classify motor function I, sensory disturbances but preserved walking capability, II, impaired walking but without use of any walking stick, III, walking with help of one walking stick, IV, walking with help of two walking sticks, and V, patients are confined to a wheel chair or bedridden (17).

The 6MWT was performed according to the American Thoracic Society guidelines. The walking capacity of patients was assessed by multiplying the number of meters walked on 6MWT by each patient body weight.

Exercise Training

Supervised exercise group: The aerobic exercises were performed on treadmill, bicycle, and rowing ergometer with ratings of perceived exertion lower than 15 on Borg scale (RPE scale). The initial speed on the treadmill was determined from mean velocity performed on the 6MWT and initiated at 50% of this value with progressive increments of 10% every 3 weeks according to the perceived exertion and alternating with other ergometers (one ergometer per week). The muscle resistance training was mediated using Thera-Band equipment and other resistance training equipment (free weight, dumbbells, and exercises using body weight) in one to two sets, 8–12 repetitions, for each of the 8–10 exercises. Sensorimotor training was also performed with Thera-Band equipment, especially stability trainer and flexbar in one to two exercises lasting 40 sec each with three repetitions with 20 sec rest between sets. All exercises start and finished with a warm-up and a cool-down period of 10 min on average. The total time of each exercise session was approximately 60 min, three times a week, for a period of 24 weeks.

Home-based exercise group: This group trained at home for 24 weeks, with Thera-Band equipment (aerobic band, hand ball exerciser and Flex Bar of different resistances, ABS aerobic ball, and stability trainer), with similar prescription as the supervised exercise training group. Before the beginning of the program, patients attended a practice session and were instructed on the exercise program, equipment safety and proper method, and mechanics of each exercise. Every month, follow-up practice sessions were then provided coupled with a written exercise material. Every 2 weeks, exercise load

was increased by mixing the number of series repetitions and the intensity given by the resistance of different colors of the elastic bands.

Statistical Analysis

The analysis was done using SPSS for Windows version 17 (SPSS, Chicago, IL). Shapiro-Wilk and Levene tests were used to assess normality and homogeneity of variances, respectively. For the three-group baseline comparison, an analysis of variance was carried out. An analysis of covariance was performed to evaluate the effect of training between groups using the baseline assessment as a covariate. When required, follow-up tests were conducted to evaluate pairwise differences using Bonferroni adjustment. Due to the reduced sample size at M3, nonparametric test was chosen (Friedman analysis of variance with Dunn's post-hoc test) to evaluate the effect of detaining period (M1, M2, and M3 for $n=10$).

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Revisión de conjunto

¿Es perjudicial el ejercicio físico para el trasplantado de hígado? Revisión de la literatura

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RESUMEN

El trasplante hepático es un tratamiento que ha permitido mejorar de manera significativa la calidad de vida de los pacientes. Sin embargo, se debe ser más ambiciosos y buscar una mejora de su condición física a través de protocolos de entrenamiento que permitan una reincorporación total a las actividades de la vida diaria.

Se buscaron artículos en los idiomas español e inglés, en las bases de datos PubMed y Cochrane, hasta el año 2014. Todos los artículos fueron revisados por 2 autores para determinar si eran apropiados para su inclusión.

Se muestra una recopilación de estudios donde se consiguen mejoras en el estado físico de pacientes que han participado en programas de entrenamiento aeróbico, de fuerza, o en combinación de ambos, sin que esto suponga un riesgo para el injerto. No obstante, existe una falta de trabajos de alta evidencia científica, que establezcan una correcta programación del ejercicio, tutorizada por especialistas en la actividad física y el deporte.

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Is physical exercise harmful to liver transplantation recipients? Review of literature

ABSTRACT

Liver transplantation is a treatment that significantly improves the patients' quality of life. However, we should be more ambitious and seek an improvement in their fitness through training protocols allowing them to fully return to daily activities.

English and Spanish-language articles on PubMed and the Cochrane Library were searched until 2014. Articles were reviewed by 2 of the authors to determine if they were suitable for inclusion.

Keywords:
 Physical exercise
 Physical capacity
 Quality of life
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It is shown a compilation of studies that included patients who have participated in aerobic, strength, or both combined training programs, without implying a risk for the graft function. There is a lack of studies with high scientific evidence that establish a proper exercise program methodology, supervised by specialists in physical activity and sports.
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Introducción

Durante los últimos años, la sociedad ha experimentado un creciente interés por la salud a través de la actividad física y el deporte, concediendo cada vez mayor atención al bienestar físico y psicológico de las personas, tanto por los efectos saludables de su práctica habitual como por la relación que su ausencia mantiene con el desarrollo, mantenimiento y agravamiento de diversas enfermedades crónicas¹. Una vida activa tiene una importancia social verificable debido a los beneficios generados en las personas y en la propia sociedad². La promoción de la práctica de la actividad física debe ser una pieza importante no solo en la prevención y promoción de la salud de la población sana³, sino en grupos con alguna necesidad especial, como son las personas trasplantadas de hígado.

El trasplante hepático ortotópico (THO) se considera como el único tratamiento posible para aquellos pacientes que padecen hepatopatías terminales⁴. Pese a su gran complejidad quirúrgica, se ha convertido en una operación habitual en nuestro país. Como indican los informes, la tasa de supervivencia es muy alta, consiguiéndose unos índices de supervivencia al año del 80%. A pesar de que la curación de estos enfermos es el logro fundamental, se debe ser más ambicioso, ya que aunque aumenta la calidad de vida relacionada con la salud (CVRS)^{5,6} puede ser insuficiente para que el paciente se reincorpore totalmente a la vida diaria. Para ello, ya existen algunos equipos de investigación que incluyen programas de ejercicio físico como complemento al tratamiento habitual tras el trasplante⁷⁻⁹.

El objetivo de este trabajo es comprobar cuál es el estado de forma física de los pacientes antes del trasplante, los cambios que se producen por la propia intervención, y si al llevar a cabo programas de ejercicio adaptados a su estado de forma estos aceleran el proceso de recuperación física, sin afectar negativamente a su función hepática y al estado del injerto.

Metodología

Se realizó la búsqueda en los idiomas español e inglés, en las bases de datos PubMed y Cochrane, hasta el año 2014. Los términos de búsqueda (en diferentes combinaciones) fueron: cirrosis hepática, trasplante hepático, ejercicio físico, actividad física, programa de entrenamiento físico, entrenamiento aeróbico, entrenamiento de fuerza, y fisioterapia. Todos los artículos fueron revisados por, al menos, 2 autores para determinar si eran apropiados para su inclusión.

Resultados

Relación entre el estado de forma física y el paciente en el pretrasplante

Antes del trasplante, los pacientes experimentan un periodo largo de debilidad debido a un descenso de su estado de forma física en sus distintas variables. El nivel de enfermedad en esta fase parece estar relacionado con el nivel de condición física¹⁰. Los pacientes con cirrosis hepática padecen una afectación de la homeostasis proteica, derivando en problemas en la respuesta aeróbica y muscular¹¹ relacionados con la disminución en la cantidad de adenosín trifosfato, fosfocreatina y magnesio total en el músculo esquelético, produciendo un déficit de fuerza en las extremidades¹²⁻¹⁵ y en la capacidad muscular respiratoria¹⁶. Estos factores limitan la capacidad funcional en las actividades cotidianas, provocando un descenso de la CVRS y la sociabilidad¹⁷.

La capacidad que más se ha asociado a la CVRS es el estado de forma cardiorespiratorio o capacidad aeróbica, representado por el máximo consumo de oxígeno (VO_{2max})¹⁸. Para valorar la importancia que tiene esta variable, se puede indicar que la reducción del 10% de los valores de referencia en comparación con personas sanas de la misma edad está asociado con un incremento en el riesgo de mortalidad en un 12% en la población general¹⁹. En pacientes que van a ser trasplantados, el VO_{2max} se ve reducido entre un 80% y un 78%²⁰⁻²⁴ si se comparan con los valores de referencia. Esta técnica en combinación con otras permite saber en qué estado se encuentra el paciente antes del trasplante y extraer datos muy indicativos sobre su futuro tras la intervención²⁵⁻²⁹, actuando como un excelente predictor de enfermedad y muerte posttrasplante. De hecho, en un estudio sobre mortalidad durante los 100 primeros días, Epstein et al.¹⁸ hallaron que los pacientes que menor capacidad aeróbica poseían dentro de los 35 meses previos a la intervención tenían mayor peligro de muerte a posteriori. Otra prueba predictora de mortalidad en lista de espera y posttrasplante es la de 6-minute walking test, prueba de campo que sirve para calcular la capacidad aeróbica de los pacientes cuando no es posible hacerlo en condiciones de laboratorio. Cada aumento de 100 m en la prueba se asocia a un descenso de la mortalidad posttrasplante de un 52%³⁰. Este test se puede aplicar en un pasillo del propio hospital de 20 m de longitud³¹.

Para disminuir estos efectos negativos sobre la condición física del paciente, Etland et al.^{32,33} defendían la necesidad de ejercicio físico. Para comprobar los efectos que tenía el entrenamiento sobre pacientes con hepatitis, el mismo autor³⁴, llevó a cabo un estudio donde participaron 9 pacientes que realizaron 3 periodos de test para averiguar su VO_{2max} .

Uno al comienzo del entrenamiento, otro a las 4-5 semanas y el último a las 10-12 semanas. A las 4 semanas, el VO_{2max} había aumentado de forma significativa un 19% y a las 10-12 semanas un 29%. No se produjo ninguna complicación relacionada con el programa y la mayoría de los pacientes percibió una mejora en su capacidad funcional a la hora de afrontar tareas cotidianas.

Relación entre el estado de forma física y el paciente en el trasplante

Tras el trasplante, los pacientes experimentan fatiga incluso un año después de la intervención²¹. La fatiga se define como una excesiva sensación de cansancio, falta de energía y sentimiento de exhaustividad, que dificulta el disfrute de una vida normal.

Aadali et al.²⁶ y van den Berg-Emons et al.²⁷ midieron el nivel de fatiga que padecen los pacientes tras el trasplante. La naturaleza de la fatiga se midió con el Multidimensional Fatigue Inventory (MFI-20)²⁸ y el nivel de fatiga con la Fatigue Severity Scale (FSS)²⁹. Los primeros realizaron un estudio transversal con 130 pacientes. Estos sugirieron que el estado laboral y el tiempo de supervivencia después del trasplante están asociados con la función física y la fatiga, y que esta es sobre todo física y no psicológica, defendido por Talwalkar³⁰. Los segundos, por el contrario, argumentaban que la fatiga no era psicológica o por falta de motivación, sino por la baja condición física, ya que la padecían los que realizaban poca actividad física diaria. Ambos argumentan que la falta de ejercicio físico hace que la fatiga no mejore a lo largo del tiempo.

Respecto a la relación que existe entre la capacidad física aeróbica y la dependencia del paciente con el hospital, Dharancy et al.³¹ llevaron a cabo un estudio de 135 pacientes donde los que tenían un deterioro grave del VO_{2max} mostraban una tendencia hacia una duración media mayor de hospitalización y necesidad de oxígeno. Por tanto, se comprueba que la medición del VO_{2max} es una excelente herramienta para la evaluación de la capacidad funcional, tanto antes, como después del THO³².

Antecedentes de programas de ejercicio aplicados a pacientes trasplantados de hígado

Ante el problema de debilidad y fatiga que sufren estos pacientes tras la intervención, diversos autores han apostado por la implantación de programas de ejercicio tras el trasplante (tabla 1).

Varios autores³³⁻³⁴ aplicaron un programa de ejercicio con una duración de 6 meses, y en todos ellos se consiguió una mejora sustancial de parámetros como el VO_{2max} , la fuerza y la calidad de vida, esta última medida mediante cuestionarios de salud auto-percibida como el SF-36.

En el estudio de Beyer et al.³, con una muestra de 38 pacientes, se aplicó un programa de ejercicio que consistió en: las 3 primeras semanas tras el trasplante, todos los pacientes se incluyeron en un programa que consistía en un régimen de aislamiento de protección en una sala de cuidados semintensivos. Durante este período, los pacientes fueron atendidos con movilización postoperatoria precoz y realizaron ejercicios diarios con intensidad creciente, que incluían ejercicio aeróbico (andar y montar en bicicleta ergométrica) a un ritmo prescrito de forma individualizada. Una vez concluido el programa inicial, se les organizó en grupos pequeños y se aplicó un programa que consistía en ejercicios de calentamiento, ejercicios aeróbicos en bicicleta estática y de entrenamiento de fuerza, equilibrio y flexibilidad. La carga y la intensidad de los ejercicios fueron individualizados de acuerdo a la capacidad de trabajo del paciente. No se especifica a qué intensidad debían realizar los ejercicios, siendo este hecho un sesgo metodológico crucial que afecta habitualmente a un número relativamente importante de los trabajos de investigación realizados sobre el tema aquí analizado.

Después del alta, se les ofreció seguir realizando entrenamientos de una hora, 2 veces por semana, hasta 6 meses después de la intervención. Se les dio un programa de entrenamiento, cuyo contenido no especifican los autores, y se les instó a realizar dichos ejercicios en casa 2 o 3 veces por semana. Además, se les animó a participar en actividades físicas o deportes de no contacto después de salir del hospital. Al cabo de los 6 meses de entrenamiento, los pacientes habían

Tabla 1 - Niveles de evidencia y grados de recomendación de Oxford Centre³⁵ de los estudios incluidos

Autor	Tamaño muestral	Tipo estudio	Nivel de evidencia	Grado de recomendación
Osborne et al. ³⁶	15 artículos, 641 sujetos	Meta-análisis	1a	A
Beyer et al. ³	38 sujetos (25 hombres, 13 mujeres)	Descriptivo	2c	B
Tomás et al. ⁷	111 sujetos	Caso clínico	3b	B
Tomás et al. ¹⁰	48 sujetos: 3 grupos: entrenamiento presencial (8), entrenamiento en casa (5), grupo control (23)	Intersubjetivo y aleatorizado	2c	B
Pimenta et al. ¹¹	Grupo intervención: 6 sujetos (3 hombres, 3 mujeres). Grupo control: 15 sujetos sanos (12 hombres y 3 mujeres), con un perfil similar, organizados por edad e índice de masa corporal (IMC)	Descriptivo	2c	B
Van Ginneken et al. ¹²	38 pacientes. Sin grupo control	Descriptivo	2c	B
Emesoff et al. ¹³	119 sujetos (49 intervención y 70 control)	Intersubjetivo y aleatorizado	2a	B
Van den Berg-Emons et al. ¹⁴	18 sujetos, 18-65 años (sin grupo control). Un año tras THO	Descriptivo	2c	B

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mejorado su VO_{2max} en un 43%, la fuerza del cuádriceps entre un 60-100% y el rendimiento funcional en un 22-27%. Un año después del trasplante, la calidad de vida de los pacientes, interpretada como salud general autovalorada y medida con el cuestionario SF-36, había mejorado y era calificada como buena o excelente en todos ellos. Ya que todos eran independientes en las actividades cotidianas, y el nivel de actividad física se había incrementado.

En el estudio de Tomás et al.⁹ se aplicó un programa de entrenamiento a una paciente trasplantada por polineuropatía amiloidótica familiar, de los 6 a los 12 meses de la intervención. Dicho programa consistía en la realización de ejercicio aeróbico de intensidad moderada, cuyos ejercicios no se especifican en el texto, con una frecuencia de 3 sesiones semanales de 1 h. Al cabo de los 6 meses, la fatiga había descendido un 31%, el VO_{2max} aumentado un 21,6%, la fuerza del cuádriceps un 28,3%, y recorrió un 21,3% más de distancia en el 6-minute walking test.

En otro estudio, Tomás et al.¹⁰ estudiaron a 48 pacientes, divididos en 3 grupos: grupo entrenamiento presencial (9 sujetos), grupo entrenamiento en casa (16 sujetos) y grupo control (23 sujetos). El entrenamiento consistió en sesiones de 60 min, 3 días a la semana, durante 24 semanas. El grupo presencial comenzaba con 10 min de calentamiento y finalizaba con 10 min de vuelta a la calma. Como parte principal, se combinó entrenamiento aeróbico con entrenamiento de fuerza. El entrenamiento aeróbico se realizó en cinta, bicicleta o remo ergométrico con carácter de esfuerzo de 15 sobre 20 (moderado). La velocidad inicial en la cinta se marcó en un 50% de la velocidad conseguida en el 6-minute walking test. El entrenamiento de fuerza se realizó mediante la utilización de materiales elásticos, peso libre, mancuernas y el propio peso corporal, y se realizaban 1-2 series, de 8-12 repeticiones, para cada uno de los 8-10 ejercicios. Además, completaron un entrenamiento de equilibrio con plataformas inestables, para conseguir mejorar la propiocepción.

El grupo de entrenamiento en casa entrenó con bandas elásticas, y materiales para potenciar el agarre, como pelotas y barras de goma. La organización de las sesiones fue similar a la del grupo presencial. A estos pacientes se les enseñó a entrenar antes de comenzar el programa y se hizo un seguimiento una vez al mes.

El grupo de entrenamiento presencial consiguió mejores resultados en peso, índice de masa corporal (IMC), masa magra, y capacidad de marcha que el grupo que entrenó en casa, y este que el grupo control. No se obtuvieron diferencias significativas ($p > 0,05$) en la fuerza máxima del cuádriceps, extremidades superiores y extremidad inferior dominante. Sin embargo, calculando los porcentajes que muestran en su publicación, se puede observar que la fuerza del cuádriceps ha obtenido un incremento del 35% en el grupo de entrenamiento presencial, un 30% en el de casa y un descenso de un 1% en el grupo control. Sin embargo, en la fuerza de extremidades superiores, el grupo control fue el que más fuerza recuperó. En la fuerza del miembro inferior, los 2 grupos de entrenamiento consiguieron un incremento de un 21%, mientras que el grupo control únicamente mejoró un 8,5%. Además, se midió a 10 pacientes a las 24 semanas de la finalización del programa para comprobar si habían mantenido las adaptaciones. Los datos corroboraron la hipótesis.

En el estudio de Pirene et al.¹¹, un grupo de 6 pacientes (3 hombres y 3 mujeres) intervenidos 2 años atrás llevaron a cabo un entrenamiento de 6 meses de duración. Una vez finalizado, realizaron una subida al Kilimanjaro hasta alcanzar la altura de 5.895 m en un total de 7 días. La capacidad física y el nivel de susceptibilidad al mal agudo de montaña fue comparado con otro grupo de 15 sujetos (12 hombres y 3 mujeres) sanos, con un perfil similar, y organizados por edad e IMC. El nivel de esfuerzo percibido y los parámetros pulmonares en reposo se compararon prospectivamente con otro grupo de 6 pacientes de similar VO_{2max} y género. Como resultado hallaron que no hubo diferencias significativas en los distintos parámetros (saturación de oxígeno, tensión arterial, ritmo cardíaco, mal de altura y otros problemas médicos) durante las distintas etapas de ascenso. Esto sugiere que estos pacientes, si siguen un entrenamiento adecuado, pueden realizar actividades físicas intensas y tolerar la altitud, en similares condiciones a personas sanas.

Los estudios más completos en este campo los realizaron van Ginneken et al.¹², Krasnoff et al.¹³ y van den Berg-Emmons et al.¹⁴. En el estudio de van Ginneken et al.¹² estudiaron los efectos de un programa de entrenamiento sobre la reducción de la fatiga, la funcionalidad cotidiana, la participación en actividades, la CVRS, la ansiedad y la depresión. La muestra fue de 18 pacientes sin grupo control. Estos se incluyeron en un programa de 12 semanas, con ejercicio supervisado, 2 veces/semana, sesiones de 1 h (aeróbico y fuerza) y 4 sesiones de actividad en casa siguiendo indicaciones de entrenamiento, llevadas a cabo en las semanas 1, 4, 8 y 12. Estas se hacían con el propósito de estimular la actividad física. Las sesiones se organizaban en grupos de 2-4 pacientes, y las sesiones cotidianas eran llevadas a cabo individualmente. La metodología para las actividades de fuerza no se detalló en el texto. Evaluaron el nivel funcional pre y post, el nivel de participación, la calidad de vida, la ansiedad y la depresión mediante cuestionarios. Sacaron como conclusión que un programa de entrenamiento con ejercicio y consejo diario de actividad física influye significativamente en la funcionalidad cotidiana relacionada con la salud ($p = 0,007$), la variable que mejoró fue la autonomía en el exterior ($p = 0,001$), y dentro de la CVRS, las variables que mejoraron fueron: la funcionalidad física ($p = 0,007$), la vitalidad ($p = 0,019$), sobre pacientes que han sido trasplantados. A pesar de las mejoras, no hubo cambios en el nivel de actividad diaria, limitaciones físicas, relaciones sociales, ansiedad o depresión. Además, el programa no mostró beneficios en la fatiga a largo plazo. De todos modos, los autores argumentaron que un programa de 12 semanas es insuficiente para afectar a la sensación de los pacientes sobre su mejora del estado general de salud.

Krasnoff et al.¹³ estudiaron, en 119 pacientes, los efectos combinados de un programa de ejercicio físico y consejo dietético después del THO. Las variables analizadas fueron: VO_{2max} , fuerza máxima del cuádriceps, composición corporal, ingesta nutricional y calidad de vida. Entre fueron examinados a los 2, 6 y 12 meses tras la intervención, y divididos en 2 grupos. Ambos grupos realizaron estos test: 1) prueba de esfuerzo en bicicleta ergométrica con analizador de gases para averiguar el VO_{2max} , fuerza muscular del cuádriceps en dinamómetro isocinético (Biodex 3), composición corporal con densitometría, cuestionario SF-36 (CVRS), cuestionario

Block 95 (ingesta nutricional). Cada paciente recibió indicaciones individualizadas sobre el entrenamiento y la dieta que debía seguir en casa. Respecto al ejercicio, únicamente debían realizar ejercicio cardiovascular (andar, bicicletas) al menos 3 días a la semana, unos 30 min por sesión, a una intensidad que comenzó con un 60-65% y progresó hasta un 75-80% o entre un 13-15 sobre 20 en la escala de esfuerzo percibido de Borg. Esta es una escala que va de 6 a 20, donde 6 es muy suave y 20 muy duro. No se incluyeron ejercicios de fuerza. En este estudio, el grupo que se ejerció mostró una mejora de un 24% del VO_{2max} ($p < 0,001$), mientras que la del grupo control no fue significativa. Ambos grupos obtuvieron mejoras en la composición corporal, fuerza muscular y calidad de vida, aunque no fueron significativas en la interacción entre grupos. Estos resultados demuestran los cambios beneficiosos que conlleva seguir un programa de ejercicio y una dieta controlada. Según los autores, en un nuevo estilo de vida debería iniciarse antes de los 6 meses tras el trasplante.

Van den Berg-Emmons et al.¹⁸ realizaron un estudio donde incluyeron a 18 sujetos trasplantados de hígado. Estos realizaron un programa de ejercicio de 2 sesiones a la semana de 1 h, durante 12 semanas. El entrenamiento albergó esfuerzo aeróbico y de fuerza. El primero consistía en bicicleta ergométrica durante 30 min, comenzando a una intensidad del 40-50% de la frecuencia cardíaca de reserva, utilizando el método Karvonen¹⁹. A las 12 semanas, debían pedalear al 60% de la frecuencia cardíaca de reserva. El entrenamiento de fuerza tenía una duración de 30 min por sesión y se entrenaban los grandes grupos musculares. La intensidad y número de repeticiones aumentaba a medida que pasaban las 12 semanas de una serie de 10-15 repeticiones al 30% de la repetición máxima (1 RM), a 3 series de 20 repeticiones al 60% de la 1 RM. Para comprobar los cambios producidos entre el comienzo y finalización del programa, se midió la capacidad aeróbica a través de un test de esfuerzo máximo en cicloergómetro y el 6-minute walking test. La fuerza máxima se midió en la musculatura de los cuádriceps y los isquiotibiales con un dinamómetro isométrico (Biodex). La prueba se realizaba 5 veces a 60° por segundo. Además, se evaluó la composición corporal y la fatiga. Los resultados de este estudio fueron satisfactorios. El VO_{2max} aumentó en un 10% ($p < 0,05$) y la fuerza únicamente se incrementó en la musculatura isquiotibial, en un 10% ($p = 0,04$). El IMC no sufrió cambios, sin embargo, el porcentaje de grasa corporal disminuyó significativamente ($p = 0,49$).

La clave de este estudio fue el ratio de adherencia al programa. Al ser presencial, obtuvieron un 93% de asistencia a las sesiones de entrenamiento. La limitación de este estudio fue la falta de grupo control.

Para mejorar el desarrollo de estos programas se debe saber más sobre el estado de las capacidades y los efectos que produce el ejercicio en este tipo de población, pero la documentación es escasa. Tan solo existen unos pocos estudios que utilizan la rehabilitación y la preparación física como parte del tratamiento pre- y posttrasplante. Los estudios anteriormente citados únicamente contemplan los efectos del programa sobre distintas variables físicas, pero están limitados en cuanto a número de pacientes, metodología y objetivación de la mejoría cardiovascular a largo plazo¹⁴.

Ningún estudio ha comprobado cómo afecta el ejercicio a otros parámetros clínicos, como la función renal, de estos pacientes.

Conclusiones

Mientras que muchos equipos quirúrgicos se han focalizado en el éxito de la propia cirugía, el ajuste de la terapia inmunosupresora y la normalización de la vida del paciente, pocos son los que han planteado incluir programas de readaptación física para mejorar la calidad de vida del paciente para el resto de su vida.

Parece ser que los pacientes que más se benefician del ejercicio son los que tienen peor condición física, es decir, los que pasan de un estilo de vida sedentario a activo. De modo que podría ser interesante comenzar con el programa lo más pronto posible (performance status de grado 0-1), ya que una mejora de la condición física incluso antes del trasplante, puede suponer un descenso en el riesgo de enfermedad y muerte posttrasplante. Hasta la fecha, se ha comprobado que el entrenamiento aeróbico andando a una intensidad suave o moderada es beneficioso. Sin embargo, son escasos los estudios de calidad metodológica que hayan desarrollado capacidades como la fuerza o la aptitud funcional. Por tanto, según los estudios publicados al respecto, se propone que la clave para la programación y ejecución correcta de un plan de entrenamiento físico consiste en aplicar la dosis necesaria para cada paciente, con un contenido de entrenamiento aeróbico (andar, bicicleta, natación, acu-aeróbico), de fuerza (bandas elásticas, máquinas, squagym) y de aptitud funcional (equilibrio, agilidad, flexibilidad). Una planificación correcta podría ser 2-3 entrenamientos por semana de 1 h, con ejercicios de tipo aeróbico, fuerza y aptitud funcional organizados de forma combinada, a una intensidad moderada. Como se ha demostrado, el entrenamiento a intensidad moderada no afecta negativamente a la función del nuevo injerto. Por tanto, teniendo en cuenta que intensidades más altas producen mayores incrementos en las distintas capacidades, un estudio interesante a realizar contendría un entrenamiento de estas características.

Conflicto de intereses

Este trabajo no ha recibido apoyos económicos ni existe conflicto de intereses por parte de ningún autor.

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Exercise Training in Solid Organ Transplant Recipients: A Systematic Review and Meta-Analysis

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Background. Exercise training is effective in improving the cardiovascular risk profiles of nontransplanted patients, but the health benefits and potential harms of routine exercise training after solid organ transplantation are unclear. This study aims to assess the health benefits and harms of supervised exercise training programs in solid organ recipients. **Methods.** We systematically reviewed all randomized controlled trials (RCTs) comparing the outcomes of exercise training programs in solid organ recipients against standard care. MEDLINE, EMBASE, the Transplant Library from the Centre for Evidence in Transplantation, and the Cochrane Central Register of Controlled Trials were searched to June 2012.

Results. In total, 15 eligible RCTs involving 643 patients (9 cardiac transplants [$n=250$ patients], 2 kidney transplants [$n=164$ patients], 3 lung transplants [$n=110$ patients], and 1 liver transplant [$n=119$ patients]) were included. Cardiac transplant recipients who engaged in an exercise program after transplantation showed significant improvement in maximal oxygen uptake (standardized mean difference, 0.77; 95% confidence interval, 0.10–1.45) but no improvement in the overall serum lipid profile, blood pressure, and glycemic control compared with standard care. Among other solid organ transplant recipients, no significant improvements in exercise capacity or cardiovascular risk factors such as incidence of new-onset diabetes after transplantation were observed, but all effect estimates were very imprecise.

Conclusions. Exercise training is a promising but unproven intervention for improving the cardiovascular outcomes of solid organ transplant recipients. Existing trials are small, of relatively short duration, and focused on surrogate outcomes. Large-scale RCTs are urgently required if resources are to be directed toward exercise programs.

Keywords: Exercise therapy, Review, Transplantation.

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Solid organ transplantation is the treatment of choice for the majority of patients with end-stage organ failure, but it is not without complications. Weight gain, muscle weakness, reduced exercise tolerance, and decreased aerobic capacity are prevalent among solid organ transplant recipients because of prolonged bed rest, inactivity, immunosuppression use, and resultant muscle deconditioning (1–3). Metabolic syndrome, a

complication of insulin resistance and a sedentary lifestyle, are also common after solid organ transplantation (4–6). A recent observational study reported a significant increase in the incidence of metabolic syndrome after liver transplantation, from 5.9% before transplantation to 50% after transplantation, with an associated increase in cardiovascular morbidity by at least threefold compared with those without metabolic syndrome (7). Cardiovascular disease is also a major cause of mortality and morbidity in other solid organ transplant recipients (8). The 5-year mortality from cardiovascular disease in cardiac and kidney transplant recipients are 30% and 19%, respectively

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research and data analysis and contributed to the writing of the article. J.C.C. designed and performed the research, analyzed the data, and revised the article. J.R.C. advised on the performance of the research and revised the article. S.C. advised on the performance of the research and revised the article. G.W. conceived, designed, and performed the research, analyzed the data, and wrote the article.

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(9, 10), with an overall mortality rate of at least 5- to 10-fold greater than the general population. With improvements in graft survival and infection deaths over the past two to three decades, death with a functioning graft, due to cardiovascular disease, is now a critical issue for solid organ transplant recipients.

Despite the magnitude and the severity of cardiovascular disease in the transplant population, there is a paucity of high-quality evidence regarding interventions for prevention and treatment. Solid organ transplant recipients have been systematically excluded from most trials of physical therapies (11). Exercise training consisting of a structured program of physical activity reduces cardiovascular risk factors in the nontransplantation setting (12). However, results of the few observational studies that have assessed the outcomes of exercise training in the transplant population are

contradictory, which may be due to confounding from the effects of immunosuppression and other comorbidities or residual selection bias (13-15). Despite this apparent lack of evidence, most clinical practice guidelines recommend exercise training as standard care for solid organ transplant recipients (16). The aim of our study was to determine the health benefits and harms of supervised exercise training programs in solid organ transplant recipients.

RESULTS

Search Results

Of the 506 records identified electronically, 102 were duplicates (see Fig. 1) and 350 were ineligible after abstract review. The remaining 54 articles were retrieved and reviewed

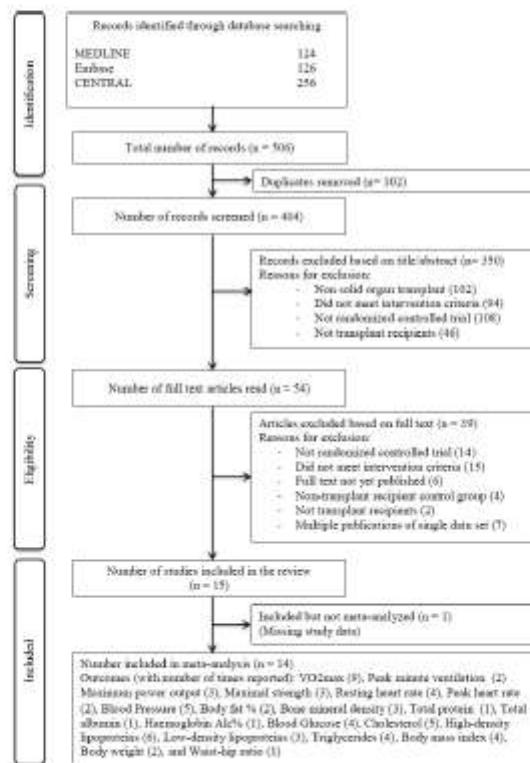


FIGURE 1. Process of studies selection.

in full-text form, with 15 randomized controlled trials (RCTs) found to be eligible and thus included. We contacted authors of three included RCTs for further detailed information and received information from two trials.

Characteristics of Included Studies

The baseline characteristics of the studies are shown in Appendix 1 (see SDC, <http://links.lww.com/TP/A757>). A total of 643 patients from 15 RCTs (9 cardiac transplant [n=250 patients], 2 kidney transplant [n=164 patients], 3 lung transplant [n=110 patients], and 1 liver transplant [n=119 patients]) were included. Of the 15 included studies, only 14 trials provided extractable information for the meta-analyses. There were no found studies of pancreas, intestine, or combined solid organ transplant recipients such as heart/lung or kidney/pancreas.

Risk of Bias in Included Trials

Appendix 2 (see SDC, <http://links.lww.com/TP/A757>) shows the risk of bias assessment of all the included trials. Three of 15 (20%) trials were judged as high risk of bias. Allocation concealment was adequate in 6 of 15 (40%) trials and unclear in 9 (60%). None of the participants were blinded to the interventions in any of the studies. Investigators were blinded in only 3 (20%) trials. Methods of randomization were reported in only 4 (27%) studies. Publication bias was assessed using funnel plots, but there were insufficient studies to evaluate for such bias.

Study Outcomes

Clinical outcomes are summarized in Table 1. Major outcomes included exercise capacity such as maximal oxygen consumption ($\text{VO}_{2\text{max}}$); cardiopulmonary parameters such as resting heart rate and systolic and diastolic blood pressures; and serum cholesterol and bone mineral density (BMD). No studies were reported on cardiovascular-related events and cardiovascular or all-cause mortality. Given the limited number of studies that reported other specific outcomes such as quality of life (QoL) and body composition, the majority of findings for these outcomes were drawn from our systematic review instead of the meta-analysis. There was also statistically significant heterogeneity between the included studies. Studies were drawn predominantly from four different solid organ transplant populations. Not only were there differences between organ groups, there was also substantial variability in the types (aerobic, resistance, or both) of exercise training, the prescribed exercise intensity, duration of the exercise (4–84 weeks) intervention, and the time of intervention after surgery (immediately after discharge to >4 years after surgery).

Exercise Capacity

A statistically significant improvement in $\text{VO}_{2\text{max}}$ (6 trials, 175 patients, standardized mean difference [SMD], +0.77; 95% confidence interval [CI], 0.10–1.45; $P=0.03$; $I^2=77\%$) was observed among cardiac but not in kidney or liver transplant recipients who engaged in aerobic exercise training compared with standard care (Fig. 2). Overall, there was an increase in $\text{VO}_{2\text{max}}$ among all transplant recipients (10 trials, 485 patients; SMD, +0.47; 95% CI, 0.10–0.84; $P=0.01$; $I^2=72\%$; Fig. 2).

Compared with no supervised training, lung recipients who engaged in 3 months of supervised exercise training

postoperatively experienced an increase of 15% and 16% in the predicted $\text{VO}_{2\text{max}}$ and the maximum power output (W_{max}), respectively. There was also a significant increase in the predicted quadriceps strength of 16% compared with controls after a follow-up time of 9 to 12 months (17). However, no significant differences in the overall maximum oxygen capacity were observed when data from the two trials in lung transplant recipients were pooled (2 trials, 48 patients; SMD, +0.09; 95% CI, -0.80 to 0.98; $P=0.84$; $I^2=78\%$).

Findings from our meta-analyses also showed no significant increase in the overall peak minute ventilation (2 trials, 61 patients; mean difference [MD], +7.51 L/min; 95% CI, 7.63–22.53; $P=0.33$; $I^2=93\%$) or the W_{max} (3 trials, 104 patients; MD, +1.44 W; 95% CI, 0.47–3.36; $P=0.14$; $I^2=92\%$) among cardiac transplant recipients.

Body Composition

There was a consistent reduction in percentage body fat associated with exercise training compared with standard care in cardiac (1 trial, 32 patients; MD, -3.40%; 95% CI, -6.66 to -0.14; $P=0.04$) and liver (1 trial, 119 patients; MD, -3.40%; 95% CI, -8.03 to -2.77; $P=0.001$) transplant recipients. The overall effect size for the reduction across both organ groups was significant (MD, -4.67%; 95% CI, -6.66 to -2.57; $P=0.001$; $I^2=0\%$). In addition, we found a significant increase in the lumbar BMD (g/cm^2) among cardiac transplant recipients who underwent 6 months of resistance training (1 trial, 16 patients) compared with standard care. After the intervention period, patients who exercised had restored lumbar BMD to within 1% of their preoperative level, whereas the control group continued to lose lumbar BMD (-6.9%) (18). However, no significant improvements in BMD were observed in liver and lung transplant recipients who received exercise training compared with standard care (Table 1). BMD was not an included outcome in any of the trials performed in the kidney transplant populations.

A single study reported a significant increase in the serum total protein (MD, +0.99 g/dL; 95% CI, 0.78–1.20; $P=0.001$) and total albumin (MD, +0.90 g/dL; 95% CI, 0.64–1.16; $P=0.001$) between the exercise and the standard-care arms in kidney transplant recipients. Compared with standard care, there were no statistical differences in fasting serum glucose, serum cholesterol, high- or low-density lipoprotein, triglycerides levels, body mass index (BMI), lean body mass, or waist-to-hip ratio between the exercise and the standard-care groups in kidney, heart, and liver transplant recipients (19–21). A recent study conducted in the lung transplant population showed a trend of lower incidence of diabetes (6% vs. 25%; $P=0.11$) and fasting mean serum glucose (90 vs. 107 mg/dL; $P=0.13$) in the exercise group compared with the control arm. However, the effects were not statistically significant (17). In addition, no significant differences in BMI, serum cholesterol, and triglycerides were observed between the exercise and the control arms 1 year after lung transplantation (17). These studies were limited by the small number of participants and were likely underpowered to detect any significant differences between the two arms.

Cardiopulmonary Parameters

We found no consistent improvements in the resting heart rate (4 trials, 120 patients; MD, 1.12 beats per minute;

TABLE 1. Clinical outcomes

Outcome	Organ	n	Results [95%CI]	P	F (%)	Overall (all organs)	P	F (%)
Exercise capacity								
VO ₂ max, mL/min/kg	Heart	6	0.77 [0.10, 1.45]	0.03	77	0.47 [0.16, 0.84]	0.01	72
	Kidney	1	0.37 [-0.04, 0.78]	0.07	—			
	Lung	2	0.09 [-0.80, 0.98]	0.84	78			
	Liver	1	0.21 [-0.16, 0.57]	0.27	—			
Peak minute ventilation, L/min	Heart	2	7.45 [-7.63, 22.53]	0.33	93	7.45 [-7.63, 22.53]	0.33	93
	Heart	3	14.32 [-10.22, 38.86]	0.25	92			
W _{max} , W	Heart	3	14.32 [-10.22, 38.86]	0.25	92	14.32 [-10.22, 38.86]	0.25	92
	Heart	1	1.40 [-17.51, 20.31]	0.88	—			
Maximal strength, Nm	Heart	1	1.40 [-17.51, 20.31]	0.88	—	4.74 [-4.64, 14.12]	0.32	13
	Kidney	1	13.15 [-0.84, 27.14]	0.07	—			
	Kidney	1	-1.47 [-15.15, 12.20]	0.83	—			
	Liver	1	-1.47 [-15.15, 12.20]	0.83	—			
Cardiopulmonary parameters								
Resting heart rate, bpm	Heart	4	1.12 [-1.29, 3.53]	0.36	0	1.12 [-1.29, 3.53]	0.36	0
Peak heart rate, bpm	Heart	2	2.89 [-20.83, 26.60]	0.81	90	2.89 [-20.83, 26.60]	0.81	90
Systolic blood pressure, mm Hg	Heart	4	-4.06 [-18.83, 10.71]	0.59	77	-2.77 [-12.07, 6.54]	0.56	65
	Kidney	1	-1.20 [-9.36, 6.96]	0.77	—			
Diastolic blood pressure, mm Hg	Heart	4	-1.62 [-7.97, 4.72]	0.62	51	-1.35 [-5.22, 2.52]	0.49	26
	Kidney	1	-1.20 [-5.85, 3.45]	0.61	—			
Peak systolic blood pressure	Heart	1	-3.00 [-17.50, 11.50]	0.69	—	-3.00 [-17.50, 11.50]	0.69	—
Peak diastolic blood pressure	Heart	1	-1.00 [-6.38, 4.38]	0.72	—	-1.00 [-6.38, 4.38]	0.72	—
Mean arterial pressure, mm Hg	Heart	1	-10.10 [-22.62, 2.42]	0.11	—	-10.10 [-22.62, 2.42]	0.11	—
Body composition								
Body fat, %	Heart	1	-3.40 [-6.66, -0.14]	0.04	—	-4.61 [-6.66, -2.57]	<0.001	0
	Liver	1	-5.40 [-8.03, -2.77]	<0.001	—			
BMD, g/cm ³	Heart	1	0.10 [0.03, 0.16]	0.005	—	0.05 [-0.05, 0.14]	0.35	78
	Lung	1	0.10 [-0.08, 0.28]	0.29	—			
	Liver	1	-0.02 [-0.06, 0.02]	0.35	—			
	Kidney	1	0.99 [0.78, 1.20]	<0.001	—			
Total protein	Kidney	1	0.90 [0.64, 1.16]	<0.001	—	0.90 [0.64, 1.16]	<0.001	—
Total albumin	Kidney	1	0.90 [0.64, 1.16]	<0.001	—	0.90 [0.64, 1.16]	<0.001	—
Hemoglobin A1c, %	Heart	1	0.00 [-0.70, 0.70]	1.00	—	0.00 [-0.70, 0.70]	1.00	—
Glucose, mM	Heart	3	-0.63 [-1.51, 0.24]	0.16	0	-0.14 [-0.54, 0.25]	0.48	0
Total cholesterol	Kidney	1	-0.02 [-0.46, 0.43]	0.94	—	0.00 [-0.20, 0.21]	0.97	0
	Heart	3	-0.00 [-0.36, 0.36]	1.00	0			
High-density lipoprotein	Kidney	2	0.01 [-0.24, 0.26]	0.97	0	0.01 [-0.20, 0.21]	0.97	0
	Heart	2	0.03 [-0.24, 0.31]	0.82	0			
Low-density lipoprotein	Kidney	2	0.12 [-0.02, 0.25]	0.08	0	0.01 [-0.29, 0.30]	0.97	0
	Heart	2	0.06 [-0.26, 0.37]	0.73	0			
Triglycerides	Kidney	1	-0.31 [-1.10, 0.48]	0.44	—	-0.07 [-0.41, 0.27]	0.68	0
	Heart	3	-0.32 [-0.82, 0.18]	0.2	0			
BMI, kg/m ²	Kidney	1	0.14 [-0.31, 0.59]	0.55	—	0.25 [-1.20, 1.69]	0.74	0
	Heart	2	-0.74 [-2.75, 1.27]	0.47	0			
	Kidney	1	0.70 [-2.02, 3.42]	0.61	—			
	Liver	1	2.20 [-1.06, 5.46]	0.19	—			
Lean body mass, kg	Kidney	1	-2.10 [-6.82, 2.62]	0.38	—	-0.53 [-3.66, 2.60]	0.74	0
	Liver	1	0.70 [-3.48, 4.88]	0.74	—			
Body weight, kg	Heart	1	-15.10 [-26.73, -3.47]	0.01	—	-6.71 [-21.52, 8.11]	0.37	80
	Liver	1	0.10 [-6.44, 6.64]	0.98	—			
Fat mass, kg	Kidney	1	-1.80 [-6.06, 2.46]	0.41	—	-1.17 [-4.09, 1.76]	0.43	0
	Liver	1	-0.60 [-4.62, 3.42]	0.77	—			
Waist-to-hip ratio	Heart	1	0.03 [-0.08, 0.14]	0.60	—	0.03 [-0.08, 0.14]	0.60	—

95% CI, -1.29 to 3.53; P=0.36), systolic blood pressure (4 trials, 109 patients; MD, -4.06 mm Hg; 95% CI, -18.82 to 10.71; P=0.59), and diastolic blood pressure (4 trials, 109 patients; MD, -1.62 mm Hg; 95% CI, -7.97 to 7.72; P=0.62) among cardiac transplant recipients who received exercise training compared with standard care. Similar to

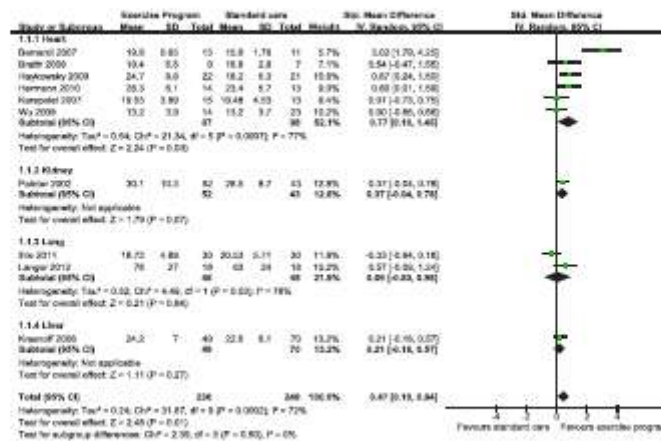


FIGURE 2. Maximum oxygen capacity (mL/min/kg) in cardiac transplant recipients.

the cardiac transplant patients, exercise training in kidney transplant patients showed no significant reduction in the systolic blood pressure (1 trial, 96 patients; MD, -1.20 mm Hg 95% CI, -9.36 to 6.96; *P*=0.77) and diastolic blood pressure (1 trial, 96 patients; MD, -1.20 mm Hg 95% CI, -5.85 to 3.45; *P*=0.61) compared with standard care. A single-center trial conducted in lung transplant recipients reported significantly lower values for the average 24-hr ambulatory diastolic (-9.00 mm Hg [-15.14 to -2.86]) and systolic (-16.00 mm Hg [-24.67 to -7.33]; *P*=0.01) blood pressure in the exercise compared with the control group (17). There were insufficient studies to evaluate exercise-induced changes in the cardiopulmonary parameters among liver transplant recipients (Table 1).

Quality of Life

Six (40%) of 15 studies (3 cardiac, 2 lung, and 1 liver) assessed the QoL outcomes in solid organ transplant recipients. One trial showed significant improvement by 0.61 points on the physical domain of the World Health Organization Questionnaire on Quality of Life among cardiac transplant recipients who received exercise training compared with standard care (22). Using the Hospital Anxiety and Depression Scales, there was significant reduction in patient-reported anxiety and depression. Using the Short Form-36 (SF-36) questionnaire, improvements in general health, bodily pain, and mental health were evident among those who underwent exercise training compared with those who did not engage in the exercise intervention (23).

Among those with lung transplants, no significant improvement in any of the QoL domains of the three QoL tools: SF-36, the German Quality of Life Profile for Chronic Diseases, and St George's Respiratory Questionnaire were observed between exercise training and standard care (24).

More recently, the study by Langer et al. (17) comparing supervised exercise training and no training in lung transplant recipients also showed no significant improvements in the levels of anxiety and depression as reported on the Hospital Anxiety and Depression Scales at 3 months and 1 year after the treatment period. On the contrary, significant changes in the self-perceived health status were observed in two of the physical component subscales (physical functioning and role functioning physical) of the SF-36 at 1 year among those who received the exercise training compared to those who received no training (17).

Adverse events, costs, compliance, graft function, cardiovascular, and all-cause mortality were not reported. Other outcomes including blood lipid profile and percent hemoglobin A1c are summarized in Table 1.

Investigation for Sources of Heterogeneity

Figures 3 shows the VO_{2max} among cardiac transplant recipients who received exercise training compared with no exercise training stratified by the duration of exercise intervention, the time of commencing exercise training after transplantation, the risk of bias of the included studies, and whether the patients received supervised or unsupervised training after transplantation.

Duration of Exercise Intervention

We found that the duration of intervention was an effect modifier for functional capacity in cardiac transplant recipients (*P* for heterogeneity=0.01). Specifically, cardiac transplant recipients who engaged in a longer period of exercise training (12-24 weeks) experienced a significant improvement in VO_{2max} (MD, +4.06 mL/min/kg 95% CI, 3.02-5.09; *P*=0.001; *I*²=0%) and W_{max} (MD, 26.8 W; 95%

CI, 22.57–31.31; $P=0.001$; $I^2=0\%$), whereas those who exercised for a lesser duration (≤ 8 weeks) had no significant improvement in their $\text{VO}_{2\text{max}}$ (MD, 1.15 mL/min/kg; 95% CI, -1.47 to 3.78; $P=0.39$; $I^2=48\%$) and W_{max} (MD, -7.70 W; 95% CI, -20.9 to 5.53; $P=0.25$; $I^2=0\%$).

Supervised Versus Unsupervised Training

Supervised exercise training was undertaken in three studies (96 patients). There was significant improvement in the $\text{VO}_{2\text{max}}$ among those who received supervised aerobic exercise training in cardiac transplant patients compared with standard care (MD, +4.6 mL/min/kg; 95% CI, 2.12–7.09; $P=0.001$; $I^2=0\%$) but not in those who engaged in home-based unsupervised regular exercise (MD, +2.17 mL/min/kg; 95% CI, -1.73 to 6.08; $P=0.005$; $I^2=83\%$).

Time after Transplantation

There was substantial variation in the length of time between the surgery and the commencement of the exercise program. We found that exercise training that commenced within 1 year after cardiac transplantation was associated with significant improvements in the overall $\text{VO}_{2\text{max}}$ (MD, +3.91 mL/min/kg; 95% CI, 2.85–4.97; $P=0.001$; $I^2=0\%$) compared with standard care, whereas those who commenced the exercise program 12 months after surgery showed no significant improvement in functional capacity.

Risk of Bias

We found that studies of low and unclear risk of bias showed significant improvements in the overall $\text{VO}_{2\text{max}}$ associated with exercise training compared with standard care (low risk of bias (1 trial; $n=27$); MD, +4.90 mL/min/kg [0.45–9.35]; $P=0.03$) and unclear risk of bias (4 trials; $n=111$); MD, +3.22 mL/min/kg [0.93–5.52]; $P=59\%$; $P=0.006$). However, this was not observed in the single study with high risk of methodologic bias.

Frequency, exercise intensity, and the types of exercise training did not affect outcomes in any of the included studies.

DISCUSSION

Our study findings suggest that regular exercise training is effective in improving exercise capacity compared with standard care in cardiac transplant recipients. Specifically, regimens that are of at least 12 weeks in duration, include supervision, and commence within 1 year after the transplant surgery appear to be the most effective. One recently conducted, randomized, controlled, trial suggests similar improvements in exercise capacity (increases in predicted $\text{VO}_{2\text{max}}$ and W_{max}) may be achieved through exercise training among lung transplant recipients (17). Despite favorable changes in the total body composition such as reduction in the overall body fat content among cardiac and liver transplant recipients, we identified no studies that were adequately powered to evaluate the longer-term patient important outcomes such as cardiovascular risk factors, cardiovascular, and all-cause mortality associated with structured exercise training in all solid organ transplant recipients.

Comparison With Other Studies

Reduction in exercise capacity is common after solid organ transplantation, particularly after cardiac transplantation. This reduction in exercise tolerance is in part due to the effects of immunosuppression, deconditioning due to prolonged hospital stay, graft dysfunction, and cardiac denervation (25). In cardiac transplant patients, exercise capacity is affected by denervation, which in turn reduces the overall responses to exercise compared with those in the general population. Introduction of a supervised exercise training program after cardiac transplantation, especially early after transplantation, has been consistently shown to improve the $\text{VO}_{2\text{max}}$ up to 12 months after transplantation (26,27). Our pooled analyses of these studies in the cardiac transplant population demonstrated, on average, a 10.2% increase in $\text{VO}_{2\text{max}}$ among those who received structured exercise training and rehabilitation after the surgery compared with recipients who did not. However, similar benefits were not observed in other solid organ transplant recipients. The lack of observed benefits may be attributed to the differences in the types, duration, and the intensity of exercise prescriptions, because none of these trials performed in other solid organ transplant recipients included supervised aerobic training programs with durations greater than 8 weeks.

W_{max} is highly correlated with the $\text{VO}_{2\text{max}}$ and is also an important predictor for exercise endurance (28). All but one study performed in the cardiac transplant population reported a significant increase in W_{max} (W) or physical workload among those who underwent structured exercise training. Contrary to findings from other studies, Wu et al. did not show any significant differences in functional or exercise capacity among those who received structured exercise training compared with standard care. In this study, inadequate randomization and the lack of allocation concealment have led to the imbalance of risk factors between the intervention and the control arms. Recipients in the control group (mean age, 51.6±12.8 years) were significantly younger than those who engaged in the exercise program (60.6±6.2; $P=0.05$), thus potentially confounding the overall effects of the intervention (22).

Reduction in exercise capacity is a particular concern for heart and lung transplant recipients who exhibit exercise capacity in the range of 40% to 60% of normal postoperatively (17, 29,30), which may impact on overall well-being and health-related QoL. Therefore, strategies to improve exercise capacity are considered as research and clinical priorities in thoracic organ recipients. Emerging data suggest that exercise training after transplantation improves exercise capacity, as assessed by 6-min walk distance, quadriceps force, total walking time, and self-assessed level of physical function, measured out to 1 year after transplantation (17).

Apart from exercise capacity, improvement in body composition such as reduction in the proportion of total body fat was also observed in cardiac and liver transplant recipients who engaged in exercise training and cardiac rehabilitation compared with those who did not. Similar findings have been reported in studies in the nontransplantation setting, whereby a combined supervised and unsupervised program of physical and exercise training program is effective in facilitating weight reduction, reducing total body fat and the incidence of type 2 diabetes mellitus in the general population.

The observed benefits are predominately driven by the amelioration of peripheral insulin sensitivity, insulin-mediated transport of glucose to muscles, increased transport of lipids to the liver, slower heart rates, and improved autonomic system functioning associated with increased aerobic fitness (31).

Strengths and Limitations

Our review has a number of strengths and limitations. Strengths include a systematic search of medical databases, data extraction and analysis, and trial quality assessment by two independent reviewers based on a prespecified protocol. Our review is limited by the small number of studies that lack longer-term follow-up to assess the efficacy and effectiveness of patient relevant rather than surrogate outcomes such as cardiovascular and all-cause mortality associated with physical and exercise training in solid organ transplant recipients. In a practical sense, it is impossible to blind patients and clinicians/investigators to the intervention of exercise training given its complexity and physical nature. This lack of blinding of assessors, in particular, may incur risk of bias in the assessment of outcomes, particularly when the assessment required some form of subjectivity.

Systematic reviews are the preferred method for summarizing evidence because they use explicit and reproducible methods to limit bias. We acknowledge that the limited number of participants in the included studies may preclude accurate assessment of heterogeneity beyond chance in our stratified analyses. Ideally, meta-regression, an extension to the subgroup analyses that allows assessments of the study characteristics on the effect estimates to be examined simultaneously, should be done to assess the independent effects of each characteristic on the overall outcome. However, this was not feasible due to the inadequate number of studies. Our subgroup analyses, although limited by the small number of participants in each of the included trials, show that the heterogeneity was partly explained by the effects of duration of the exercise intervention, whether the program was supervised or unsupervised, the risk of bias of the included studies, and the length of time after the surgery and commencement of the exercise program. Similar to findings in other settings such as those without solid organ transplants, a prolonged and sustained program in cardiac transplant recipients is important to maintain physical and psychologic improvements achieved with increased aerobic fitness (32). However, no significant differences were observed between the different exercise intensities and the number of exercise sessions per week. Compared with home-based programs, supervised exercise training with emphasis on behavioral change such as education about goal setting, self-assessment, and self-reward skills may lead to lifestyle modification and consequent longer-term outcomes such as sustainable weight loss and improved blood pressure control (33, 34).

Another limitation of this review is that 1 of 15 studies ($n=15$ of 643 subjects) met the inclusion criteria but did not provide sufficient data to contribute to the meta-analysis. This represents a potential source of bias.

Implications for Clinical Practice and Research

Based on the current available evidence, a program of prolonged supervised exercise training after transplantation is effective in improving the short-term exercise capacity and body composition such as total body fat in cardiac

transplant recipients. Despite the observed benefits of a structured exercise training program in preventing weight gain, reducing the incidence of type 2 diabetes, and improving cardiovascular risk among the high-risk nontransplanted population, the effectiveness of such interventions among transplant recipients has not been adequately addressed in the current literature. Longer-term, well-powered studies, with sufficient sample sizes and follow-up time analyzing the effects of exercise training in all solid transplant recipients, varied by intensities, modes, durations, and frequency on hard endpoints such as improvement in cardiovascular risk factors, including hypertension, diabetes, obesity and dyslipidemia, cardiovascular mortality, as well as graft survival, harms, and adverse effects of exercise training are warranted.

CONCLUSIONS

Trials to date have shown that exercise training is effective in improving the exercise capacity of cardiac transplant recipients. However, data assessing the cardiovascular benefits of exercise training in other solid transplant recipients are sparse. Quality trial-based evidence of longer-term health benefits such as QoL, sustainable weight control, and graft and patient survival is needed to determine if resources should be directed to exercise programs after solid organ transplantation.

MATERIALS AND METHODS

We conducted a systematic review based on standard methods (35) and reporting in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement (36).

Data Sources and Searches

To identify RCTs of exercise training in solid organ transplant recipients, we searched MEDLINE (1946–June 2012), EMBASE (2010–2012), Transplant Library from the Centre for Evidence in Transplantation, and the Cochrane Library database (Central Register of Controlled Trials) using relevant text words and medical subject headings that included all spellings of exercise intervention, organ transplantation, physical activity, and physiotherapy (see Appendix 3, SDC, <http://links.lww.com/TP/A257>). The search was limited to RCTs without age and language restriction. Reference lists from identified trials and review articles were manually screened to identify any relevant studies. The clinicaltrials.gov Web site was also searched for randomized trials that were registered as complete but not yet published.

Study Selection

Two authors (M.D. and G.W.) independently reviewed titles, abstracts, and full-text articles to determine study eligibility. We included RCTs if both reviewers agreed that an article described and compared the use of exercise training programs against standard care or compared two or more exercise training programs in all solid organ transplant recipients. We excluded trials comparing exercise to drug therapy or exercise and drug therapy to standard care. We included all solid organ transplant recipients (lung, liver, pancreas, heart, kidney, intestine, combined heart/lung, liver/kidney/heart/kidney, and kidney/pancreas) in the study. We excluded patients who received trans and cell transplants such as skin, bone marrow, cornea, and islet.

Data Extraction and Quality Assessment

Published reports were obtained for each trial and information was extracted using standardized data extraction forms and imported into a spreadsheet. Studies reported in non-English language journals were translated before assessment. When more than one publication of a trial existed, only the article with the most complete data was included. Further information was requested from the corresponding authors when necessary. The methodologic quality of included studies was assessed independently by the two authors (M.D. and G.W.) using the Cochrane risk of bias tool (36). Any discrepancies were resolved by discussion with consensus agreement.

Outcomes Measures

We included data on a broad range of outcomes including cardiovascular parameters (resting and peak heart rate, systolic and diastolic blood pressure, heart rate, and blood lipid profile), aerobic capacity (VO_{2max}, muscle strength, and W_{max} [W]), body composition (serum albumin and protein, serum cholesterol, high and low lipoprotein, triglyceride levels, serum glucose levels, incidence of diabetes, weight circumferences, BMI, and waist-to-hip ratio), flexibility scores (measured in centimeters), graft function (estimated glomerular filtration rate), QoL (SF-36 and Kidney Disease Quality of Life), adherence and dropout rates, adverse events, as well as cardiovascular and all-cause mortality.

Data Synthesis and Analysis

Results from individual trials were expressed as risk ratios with 95% CIs for dichotomous outcomes and continuous outcomes were expressed as MD or SMD if the same outcome was measured in different ways. Data were combined using a random effects model. Heterogeneity was quantified using the chi-square test and I² statistic (36) with preplanned subgroup analyses used to explore possible sources of heterogeneity, but because of insufficient data, this was not possible. Outcomes were stratified by transplanted organ (heart, kidney, lung and liver), duration and frequency of exercise training, exercise supervision, and time commencing training after transplantation (from months to years; heart, kidney, lung, and liver). P<0.05 was considered statistically significant. Where possible, publication bias was assessed using funnel plots (36). All analyses were conducted using Review Manager 5.

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ANEXO 3
PLANEAMENTO DE ATIVIDADES
E ORÇAMENTO

ÁREA EDUCAÇÃO

DESCRIÇÃO DE ATIVIDADES	META	RECURSOS		Observações
		Humanos / Logísticos / Financeiros	Valor (€)	
Produção de material informativo com foco na missão e os objetivos do GDTP para distribuição	Produção e divulgação de material informativo em diferentes formatos	Humanos: Direção, Designer, Voluntários Logísticos e Financeiros: Elaboração de material, impressão, aquisição, serviços, entrega e distribuição de material de publicidade.	1000€	<u>Atividade contínua</u> Mantém-se a habitual produção e envio de material informativo para divulgação.
Promoção do Website e canais de comunicação digital	Atualização e promoção do website e canais de comunicação digital	Humanos: Direção, Designer, Voluntários Logísticos e Financeiros: Domínio do website e apoio técnico de empresa/particular.	1000€	<u>Atividade contínua</u> Os custos previstos decorrerão apenas de apoio técnico com o website e respetivo alojamento.
Semana Europeia do Desporto	Participação em evento BeActive com o tema da Transplantação	Humanos: Direção, Voluntários Logísticos e Financeiros: Despesas de deslocação e participação no evento, material de promoção e divulgação.	250€	<u>Atividade pontual / Setembro</u>
Eventos associativos: - Dia do Transplante - Outros eventos	Participação em eventos	Humanos: Direção, Voluntários Logísticos e Financeiros: Despesas de deslocação e demais despesas de material informativo e outras associadas ao evento (GDTP ou parceiros).	250€	<u>Previsto Dia do Transplante – 20 de julho</u>

Subtotal: 2500€

ÁREA FORMAÇÃO / INVESTIGAÇÃO

DESCRIÇÃO DE ATIVIDADES	META	RECURSOS		Observações
		Humanos / Logísticos / Financeiros	Valor (€)	
Organização de Webinários	Realização de ações de formação online	Humanos: Direção, Voluntários, Profissionais Logísticos e Financeiros: Despesas de secretariado, material de divulgação, despesas associadas a oradores e organização.	250€	<u>Atividade periódica</u> Os custos dos webinários serão relativos a plataforma e eventuais despesas associadas a oradores.
Produção de vídeos educacionais	Produção e divulgação de conteúdos digitais educacionais	Humanos: Direção, Designer, Profissionais Saúde e Desporto, Voluntários Logísticos e Financeiros: Serviços na área tecnológica e audiovisual, material necessário e despesas associadas.	500€	Mantém-se a intenção de produção de conteúdos digitais. Estes trabalhos implicam contratação de serviços especializados.
Boas práticas de exercício físico na transplantação	Produção de manual de boas práticas	Humanos: Direção, Designer, Profissionais Saúde e Desporto, Voluntários, serviços de produção de conteúdos e audiovisual Logísticos e Financeiros: Serviços na área tecnológica e audiovisual, material necessário e despesas associadas.	1000€	Produção de conteúdos digitais.
Eventos no âmbito da formação	Eventuais eventos para os quais o GDTP é convidado	Humanos: Direção, Voluntários, Profissionais Logísticos e Financeiros: Despesas de deslocação e demais despesas de material informativo e outras associadas.	250€	

Subtotal: 2000€

ÁREA LAZER

DESCRIÇÃO DE ATIVIDADES	META	RECURSOS		Observações
		Humanos / Logísticos / Financeiros	Valor (€)	
Corridas e Caminhadas Solidárias de Agradecimento ao Dador	Realização de evento em Lisboa / Porto	<p>Humanos: Direção, Voluntários, Equipa organização eventos</p> <p>Logísticos e Financeiro: Despesas de gestão e organização do evento, empresa organização eventos, prémios, equipamentos, Kit, material de promoção e divulgação.</p>	20000€	<u>Atividade planeada para o 2º semestre 2023</u>
Evento Nacional pela Transplantação	Realização de evento em Lisboa	<p>Humanos: Direção, Voluntários, Equipa organização eventos</p> <p>Logísticos e Financeiro: Despesas de gestão e organização do evento, empresa organização eventos, prémios, equipamentos, Kit, material de promoção e divulgação.</p>	10000€	

Subtotal: 30000€

ÁREA COMPETIÇÃO

DESCRIÇÃO DE ATIVIDADES	META	RECURSOS		Observações
		Humanos / Logísticos / Financeiros	Observações	
Participação nos Jogos Internacionais: - Quotizações das Federações	Quotização de membro	Humanos: Direção, Voluntários Logísticos e Financeiros: Pagamento de quotizações como membro da organização	300€	
Participação nos Jogos Internacionais: - Jogos Europeus - Lisboa	Participação de equipa portuguesa	Humanos: Direção, Voluntários Logísticos e Financeiros: Pagamento de participação e transporte de atletas, equipamentos desportivos, outras despesas.	20000€	<u>Atividade anual / julho 2024</u>
Dispensa dos atletas ao abrigo do Decreto-Lei n.º 45/2013 de 5 de abril	Participação de equipa portuguesa	Humanos: Direção, Voluntários Logísticos e Financeiros: Pagamento de dispensa participação	5000	<u>Nota:</u> Medida de apoio à preparação e participação internacional das seleções ou outras representações desportivas nacionais, relativamente a dispensa temporária de funções (Artigos 11.º e 12.º do mencionado DL)
Organização dos Jogos Europeus para Transplantados e Dialisados 2024	Preparação / Organização do evento	Humanos: Direção, Voluntários, Equipa organização eventos Logísticos e Financeiro: Despesas de gestão e organização do evento, empresa organização eventos, deslocações necessárias.	400000€	

Subtotal: 425300€

DESPESAS DIVERSAS

DESCRIÇÃO DE ATIVIDADES	META	RECURSOS		Observações
		Humanos / Logísticos / Financeiros	Observações	
Despesas administrativas	-	Humanos: Direção, Voluntários Logísticos e Financeiros: Despesas associadas à manutenção das atividades correntes, despesas bancárias, material administrativo, etc.	2000€	Atividade contínua (base ano anterior)
Despesas associativas		Humanos: Direção, Voluntários Logísticos e Financeiros: Despesas de pagamento de rendas de sede e encargos associados, recursos humanos, formação para capacitação e recursos, equipamentos necessários, etc.	5000€	Atividade contínua (base ano anterior) (Renda, Energia, Água, Contabilidade)
Despesas de representação		Humanos: Direção, Voluntários Logísticos e Financeiros: Despesas de participação em eventos como representação, convidado e presença em reuniões institucionais.	2000€	Atividade contínua

Subtotal: 9000€

ORÇAMENTO FINAL

SUBTOTAIS	Valor (€)
EDUCAÇÃO	2500€
FORMAÇÃO / INVESTIGAÇÃO	2000€
LAZER	30000€
COMPETIÇÃO	425300€
DIVERSOS	9000€
TOTAL	468800€

