

Zur streng vertraulichen Einsichtnahme

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Safety of Whole-Body Vibration Exercise for Heart Transplant Recipients

Sicherheit von Ganzkörpervibrationstraining bei herztransplantierten Patienten

Zusammenfassung

Fragestellung: Die positiven Wirkungen des Ganzkörpervibrationstrainings (WBV) werden bis dato in der Rehabilitation nach Herztransplantation nicht eingesetzt, obwohl gerade diese Patienten oft eine ausgeprägte Muskelschwäche und Osteoporose zeigen. Ziel dieser Studie war es, die Sicherheit eines WBV sowie die kardiovaskulären und metabolischen Reaktionen bei herztransplantierten Patienten zu untersuchen. **Material und Methode:** 14 männliche, klinisch stabile, herztransplantierte Patienten wurden in diese Studie eingeschlossen. Als Intervention führten die Patienten eine Einheit Ganzkörpervibrationstraining am Galileo 2000 durch. Die Herzfrequenz, systolischer und diastolischer Blutdruck, die Plasmalaktatkonzentration, sowie die BORG-Skala wurden zur Bestimmung der objektiven und subjektiven Belastung während WBV herangezogen. **Ergebnisse:** Abbruchgrund bei WBV war bei jedem Patienten die lokalisierte Muskelschwäche der Beinmuskulatur. Die durchschnittliche Versuchsdauer betrug 248 Sekunden (Range 51 – 607). Herzfrequenz, systolischer und diastolischer Blutdruck sowie die Plasmalaktatkonzentrationen erreichten während des WBV Werte wie bei aerobem Ausdauertraining. Es kam bei keinem Patienten zu unerwarteten Zwischenfällen. **Schlussfolgerung:** Die Ergebnisse dieser Pilotstudie weisen darauf hin, dass WBV bei herztransplantierten Patienten sicher durchführbar ist. Bei einer Ein-

Abstract

Purpose: The benefits of whole-body vibration exercise (WBV) have not yet been recognized in heart transplant recipients although these patients often show a severe loss in skeletal muscle strength and bone mineral density over time. At present, WBV is not generally recommended for rehabilitation of transplant patients. The purpose of this study was to document the safety, cardiovascular responses and metabolic changes to WBV in heart transplant patients. **Material and methods:** 14 male clinically stable heart transplant recipients were included in this study. The subjects were exposed to one set of whole-body vibration using the Galileo 2000 device. Heart rate, systolic and diastolic blood pressure, blood lactate concentration and the Borg scale were used to determine objective and subjective exertion during WBV. **Results:** In every patient WBV was terminated due to muscular fatigue. The mean duration of exercise was 248 seconds (range, 51 – 607 seconds). Heart rate, systolic and diastolic blood pressure, lactate concentrations and the Borg score increased during WBV to levels achieved during aerobic exercise. No patient experienced adverse events. **Conclusion:** The results of this pilot study indicate that WBV is feasible and safe in heart transplant recipients. The cardiovascular and metabolic response of an acute bout of WBV is similar to that of standard aerobic exercise.

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heit WBV entspricht die kardiovaskuläre und metabolische Antwort von Herztransplantierten jener bei aerobem Ausdauertraining.

Schlüsselwörter

Sicherheit · Ganzkörpervibrationstraining · Herztransplantation · Muskelschwäche · Osteoporose

Key words

Safety · whole-body vibration exercise · heart transplantation · muscle weakness · osteoporosis

Introduction

Orthotopic heart transplantation is an effective treatment option for individuals with end-stage heart failure. Nearly 3500 people throughout the world benefit from this procedure every year. Owing to ongoing surgical, pharmacological and diagnostic advancements, more than 70% may expect to live an additional 5 years after the time of their surgery [1,2].

Although survival outcomes have been well studied in the past several years, less attention has been given to the issue of post-transplant functional capacity. Often overlooked as a major source of morbidity in transplant recipients are severe losses in skeletal muscle mass, strength and trabecular bone mineral density, which accompany long periods of inactivity and the long-term use of prednisone [1,3]. It has been suggested that muscular weakness and fatigue are the primary limiting symptoms in the activities of daily living for many heart transplant patients [1]. It is estimated that the skeletal muscle strength of transplant recipients is 60–70% of that in age-matched controls [4]. Although glucocorticoids are not the sole factor implicated in the pathogenesis of post-transplant osteoporosis, they play a major role in its development [3].

Mechanical vibration has aroused great interest because it has been hypothesized that a low-amplitude, high-frequency stimulation of the whole-body (whole-body vibration exercise) could positively influence many risk factors of falling and related fractures by simultaneously improving muscle strength, body balance, and mechanical competence of bones [5–16]. Given the preliminary observations suggesting simultaneous improvements in muscle performance and bone characteristics, a low-amplitude, high-frequency mechanical vibration of the whole body such as whole-body vibration exercise is an intriguing bio-mechanical intervention from the health perspective, as it may improve not only the strength and balance of the subject, but simultaneously reduce bone fragility [5–16].

At the present time, whole-body vibration exercise is not commonly recommended for transplant patients, perhaps because of the complete absence of safety or efficacy data in these subjects. The purpose of the present study was to document the safety, the cardiovascular response and metabolic changes during a set of whole-body vibration exercise in patients following orthotopic heart transplantation.

Material and methods

Subjects

Fourteen male clinically stable heart transplant recipients (mean age 56 ± 11 years, range 28–68 years) were included in this study (Table 1). The heart transplantation had been performed on average 57 ± 58 months previously (range, 4–209 months). All subjects were participants of a regular post-HTX aerobic exercise group at the Department of Physical Medicine and Rehabilitation of the General Hospital of Vienna, where they performed extensive aerobic bicycle ergometer exercise three times a week (endurance capacity $64 \pm 18\%$, range 31–95%; training heart rate 118 ± 17 bpm). Informed consent was obtained from all participants and the protocol was in conformity with the Declaration of Helsinki.

Intervention (whole-body vibration exercise)

The subjects were exposed to whole-body vibration exercise with the Galileo 2000 device (Novotec Company, Pforzheim, Germany). They stood on a platform fixed on a sagittal axis which alternately pushes the right and left leg upwards and downwards at a frequency of 26 Hz (amplitude, 3 mm; peak acceleration, 78 ms^{-2}). The whole-body vibration exercise was performed with the entire feet placed on the platform and moderately ($60\text{--}70^\circ$) bent knees. The subjects stood barefoot in order to avoid footwear-dependent attenuation of the vibrations. To avoid biorhythmic changes, all subjects performed the experiment at the same time of the day between 10 a.m. and noon.

Outcome measurements

Heart rate, systolic and diastolic blood pressure, lactate levels and Borg scale (measured at baseline, exhaustion, 3 minutes of recovery, 5 minutes of recovery) were used to determine objective and subjective exertion during whole-body vibration exercise. Heart rate was monitored with suitable devices (Polar beat, Polar Electro Oy, Kempele, Finland) and arterial blood pressure was measured using the conventional manometer technique (Riva Rocci, Heintel Rudolf Company, Vienna, Austria). Subjectively perceived exertion was assessed by Borg's scale [17], and blood lactate concentrations were measured in arterialised blood from the the ear lobe (EBIO plus, Eppendorf, Hamburg, Germany).

Statistics

Descriptive statistics were calculated for all parameters. The Wilcoxon sign rank test was used to compare the values obtained at the various time points of examination. The level of significance was set at $p = 0.05$.

Table 1 Demographic data concerning the study population (n = 14, male)

	age	htx ¹	ethiology of CMP ²	concomitant diseases	medication
pat. 1	59a	17	idiopathic	hypertension, chronic renal failure	Lisinopril+Hydrochlorothiazid (Acecomb [®]), Lansoprazol (Agopton [®]), Prednisolon (Aprednislon [®]), Metoprolol (Beloc [®]), Pravastatin (Pravachol [®]), Ciclosporin (Sandimmun [®]), Benzbromaron (Uricovac [®]), Lisinopril (Acemin [®]), Amlodipin (Norvasc [®]), α -Tocopherolacetat (Biogelat Vit. E 400 [®]), Thiamin+Pyridoxin+Cynocobalamin (Neurobion forte [®]), Acetylsalicylic acid (Thrombo ASS [®]), Paroxetin (Seroxat [®]), Mycophenolatmofetil (CellCept [®])
pat. 2	68a	7	infectious	hypertension, chronic renal failure, prostatomegaly	Acetylsalicylic acid (Thrombo ASS [®]), Ciclosporin (Sandimmun [®]), Prednisolon (Aprednislon [®]), Mycophenolatmofetil (CellCept [®]), Atorvastatin (Sortis [®]), Lansoprazol (Agopton [®]), Benzbromaron (Uricovac [®]), Losartan (Cosaar [®]), Diosmin+Flavonoidfraktion (Daflon [®]), Alfuzosin (Xatral [®])
pat. 3	60a	12	ischemic	chronic renal failure	Azathioprin (Imurek [®]), Pantoprazol (Pantoloc [®]), Prednisolon (Aprednislon [®]), Ciclosporin (Sandimmun [®]), Acetylsalicylic acid (Thrombo ASS [®]), Pravastatin (Pravachol [®]), Xipamid (Aquaphoril [®])
pat. 4	50a	113	ischemic	hypertension, chronic renal failure, obesity, hypercholesterolemia	Ciclosporin (Sandimmun [®]), Sirolimus (Rapamune [®]), Prednisolon (Aprednislon [®]), Clopidogrel (Plavix [®]), Omeprazol (Losec [®]), Mycophenolatmofetil (CellCept [®]), Tocopherol (Ephynal [®]), Cilazapril (Inhibace [®]), Calcitriol (Rocaltrol [®]), Atorvastatin (Sortis [®]), Benzbromaron (Uricovac [®]), Trimethoprim (Motrim [®])
pat. 5	64a	118	ischemic	non-insulin-dependent diabetes mellitus, hypertension, chronic renal failure, hypothyroidism, obesity, hypercholesterolemia	Ciclosporin (Sandimmun [®]), Mycophenolatmofetil (CellCept [®]), Prednisolon (Aprednislon [®]), Acetylsalicylic acid (Thrombo ASS [®]), Tocopherol (Ephynal [®]), Atorvastatin (Sortis [®]), Clopidogrel (Plavix [®]), Calcitriol (Rocaltrol [®]), Gliclazid (Diamicron [®]), Benzbromaron (Uricovac [®]), Lisinopril (Acemin [®]), Levothyroxin-Natrium (Thyrex [®]), Thiamin+Pyridoxin+Cynocobalamin (Neurobion forte [®])
pat. 6	61a	51	ischemic	peripheral vascular disease, hypertension, hypercholesterolemia, hyperuricemia, obesity, hypothyroidism	Lisinopril+Hydrochlorothiazid (Acecomb [®]), Prednisolon (Aprednislon [®]), Azathioprin (Imurek [®]), Magnesiumcarbonat+Magnesiumoxid (Magnosolv [®]), Amlodipin (Norvasc [®]), Ciclosporin (Sandimmun [®]), Ciclosporin (Neoral [®]), Atorvastatin (Sortis [®]), Acetylsalicylic acid (Thrombo ASS [®])
pat. 7	42a	12	infectious	hypertension, hepatitis C, myopathy	Ciclosporin (Sandimmun [®]), Prednisolon (Aprednislon [®]), Mycophenolatmofetil (CellCept [®]), Lisinopril (Acemin [®]), Magnesiumcarbonat+Magnesiumoxid (Magnosolv [®]), Acetylsalicylic acid (Thrombo ASS [®]), Pravastatin (Pravachol [®]), Furosemid (Lasix [®]), Pantoprazol (Pantoloc [®]), Kaliumchlorid (KCl-Retard Zyma-Dragees [®]), Diosmin+Flavonoidfraktion (Daflon [®]), Benzbromaron (Uricovac [®]), Bromazepam (Lexotanil [®]), Thiamin+Pyridoxin+Cynocobalamin (Arca-Be [®] , Neurobion forte [®])
pat. 8	61a	73	idiopathic	chronic renal failure, peripheral vascular disease, obesity	Prednisolon (Aprednislon [®]), Azathioprin (Imurek [®]), Ciclosporin (Sandimmun [®]), Atorvastatin (Sortis [®]), Benzbromaron (Uricovac [®]), Lisinopril (Acemin [®])
pat. 9	67a	53	ischemic	hypercholesterolemia	Prednisolon (Prednisolon „Agepha“ [®]), Benzbromaron (Uricovac [®]), Pravastatin (Pravachol [®]), Tamsulosin (Alna ret. [®]), Tacrolimus (Prograf [®]), Magnesiumglutamat+Magnesiumcitrat+Magnesium-L-hydrogenaspartat (Magnesium Verla [®]), Amlodipin (Norvasc [®]), Mepartricin (Iperplasin [®]), Mycophenolatmofetil (CellCept [®]), Acetylsalicylic acid (Thrombo ASS [®]), α -Tocopherolacetat (Biogelat Vit. E [®]), Alendronat (Fosamax [®]), Ciclosporin (Neoral [®])
pat. 10	46a	4	idiopathic	hypercholesterolemia	Ciclosporin (Sandimmun [®]), Azathioprin (Imurek [®]), Prednisolon (Aprednislon [®]), Lisinopril (Acemin [®]), Acetylsalicylic acid (Thrombo ASS [®]), Omeprazol (Losec [®]), Spironolacton+Furosemid (Furo-Spirobene [®]), Pravastatin (Pravachol [®])
pat. 11	28a	209	idiopathic	no	Ciclosporin (Sandimmun [®]), Azathioprin (Imurek [®]), Prednisolon (Prednisolon „Agepha“ [®]), Benzbromaron (Uricovac [®]), Pravastatin (Pravachol [®])
pat. 12	55a	10	infectious	hypothyroidism	Ciclosporin (Sandimmun [®]), Mycophenolatmofetil (CellCept [®]), Prednisolon (Aprednislon [®]), Acetylsalicylic acid (Thrombo ASS [®]), Pravastatin (Pravachol [®]), Triazolam (Halcion [®]), Furosemid (Lasix [®]), Kaliumchlorid (KCl-Retard Zyma-Dragees [®]), Levothyroxin-Natrium (Thyrex [®]), Pantoprazol (Pantoloc [®])
pat. 13	60a	61	ischemic	non-insulin-dependent diabetes mellitus, hypertension	Ciclosporin (Sandimmun [®]), Mycophenolatmofetil (CellCept [®]), Prednisolon (Aprednislon [®]), Diltiazem (Dilzem [®]), Carvedilol (Dilatrend [®]), Pantoprazol (Pantoloc [®]), Thiamin+Pyridoxin+Cynocobalamin (Neurobion forte [®]), Magnesiumcarbonat+Magnesiumoxid (Magnosolv [®]), Benzbromaron (Uricovac [®]), Furosemid (Lasix [®]), Kaliumchlorid (KCl-Retard Zyma-Dragees [®])
pat. 14	67a	40	ischemic	hypertension, chronic renal failure, hypercholesterolemia	Kaliumcitrat, Kaliumhydrogencarbonat (Kalioral „Fresenius“ [®]), Atorvastatin (Sortis [®]), Magnesiumglutamat+Magnesiumcitrat+Magnesium-L-hydrogenaspartat (Magnesium Verla [®]), Benzbromaron (Uricovac [®]), Ciclosporin (Sandimmun [®]), Azathioprin (Imurek [®]), Prednisolon (Aprednislon [®]), Acetylsalicylic acid (Thrombo ASS [®]), Amlodipin (Norvasc [®]), α -Tocopherolacetat (Biogelat Vit. E 400 [®])

¹htx: time since heart transplantation in months; ²CMP: cardiomyopathy as underlying disease before heart transplantation

Results

Every patient performed the whole-body vibration exercise up to the point of subjective exhaustion (Borg [18]). The exercise was terminated in all cases due to muscular fatigue. The mean duration of exercise was 248 seconds (range, 51–607 seconds). No patient experienced any adverse events.

Heart rate, systolic and diastolic blood pressure, lactate levels and Borg scale increased significantly during WBV, but did not reach levels higher than those achieved during aerobic exercise (Table 2). The maximum values for heart rate, systolic and diastolic blood pressure were registered at peak exercise; the highest lactate concentrations were measured after 3 minutes of rest (Table 2). Haemodynamic parameters returned to baseline during the recovery period.

Table 2 Mean and standard deviations of the investigated parameters (n = 14)

	baseline	exhaustion	recovery 3 minutes	recovery 5 minutes
Plasma lactate (mM/L)	1.2 ± 0.3	2.0 ± 1.6*	2.3 ± 0.8*	2.1 ± 0.7*
Heart rate (beats per minute)	98 ± 10	121 ± 20*	107 ± 15	104 ± 14
Systolic blood pressure (mmHg)	136 ± 17	158 ± 23*	139 ± 15	139 ± 15
Diastolic blood pressure (mmHg)	90 ± 13	93 ± 16	93 ± 13	91 ± 13

* p < 0.05, Wilcoxon sign rank test

The patients' heart rate at the termination of the trial was significantly higher than at baseline (0.001). The difference between heart rate at the termination of the trial and the training heart rate was not significant (Table 2). Systolic blood pressure at the termination of the trial was significantly higher than at baseline (0.001). The difference between the diastolic blood pressure of the patients at the termination of the trial and the value registered before the start of the study was not significant (Table 2).

Lactate concentrations at the termination of the trial (0.001), after 3 minutes of recovery (0.001) and after 5 minutes of recovery (0.001) were significantly higher than at baseline (Table 2).

Discussion

Exercise training is commonly recommended to patients after orthotopic heart transplantation. In recent years, extensive reviews have outlined guidelines for the prescription of exercise training for transplant patients [1, 18–21].

Whole-body vibration exercise is a new type of exercise currently being used as a training modality in sports, a therapeutic method in rehabilitation, and as a measure to counteract muscular atrophy and bone loss during immobilization and space flight [5–16]. It is assumed that this vibration evokes muscle contractions, probably via the monosynaptic stretch reflex [22]. The

benefits of whole-body vibration exercise seen in other patients have not yet been established in a large number of heart transplant recipients. This is a noteworthy observation, given the severe loss in skeletal muscle strength and bone mineral density experienced by heart transplant recipients. At the present time, whole-body vibration exercise is not commonly recommended for rehabilitation of transplant patients, perhaps because of the complete absence in the literature of any functional assessment of the transplanted heart during this type of stress. This may be one reason why many transplant centers do not prescribe this type of exercise to transplant recipients. The special anatomic circumstances of the transplanted heart, i.e. its specific reaction to cardiovascular stress, makes it necessary to separately investigate the post-transplant cardiovascular reaction, the internal metabolic strain, and the experienced load during whole-body vibration exercise [23–26].

All 14 heart transplant recipients tested in the present study completed their whole-body vibration exercise session without adverse events, although the patient group was very heterogeneous in respect of age and the period of time that had elapsed since heart transplantation. Heart rate, systolic and diastolic blood pressure, and lactate levels of heart transplant recipients increased during whole-body vibration exercise, which is consistent with healthy subjects [22]. In young healthy subjects, vibration exercise has been shown to have mild cardiovascular effects, e.g. heart rate rises to a maximum of approximately 130 beats per minute, which corresponds to 50% of the maximal oxygen uptake, and increase in systolic blood pressure, but slight drop in diastolic pressure. Blood lactate rose to about 3.5 mM [22]. In our patients all parameters as well as in healthy subjects returned to normal within 15 min of recovery. Despite these significant increases in the investigated parameters, values higher than those during aerobic exercise were not registered for any parameter (Table 2). Notably, the highest achieved heart rate of 121 (±20) beats per minute and the highest lactate concentration of 2.3 (±0.8) mM was markedly below the values reported in healthy young volunteers [22]. In contrast, systolic blood pressure achieved a markedly higher value in heart-transplanted subjects. On the one hand, this appears to have been due to concomitant diseases and medication of the heart transplant patients. On the other hand, the specific cardiovascular reaction of transplanted hearts may contribute to this result. All patients in the present study had to interrupt the bout due to early weakness of the leg muscles and not because of general exhaustion, although they performed no exercises but merely stood on the vibration plate with slightly bent knees. Thus, atrophy of the leg muscles seems to be the primary factor limiting optimal performance of heart transplant recipients during whole-body vibration exercise. Side effects of whole-body vibration exercise like itching erythema as shown by Rittweger et al. were not observed in the patients of this study [9].

Limitations of this pilot-study are the sample size, the difference in mean age of the study group, and in the time from transplantation. Nevertheless, the results of this safety pilot-study indicate that whole-body vibration exercise seems to be a feasible and safe method of rehabilitation and to improve functional health [27,28] in heart transplant recipients. Future controlled trials will have to evaluate the short- and long-term effects of

whole-body vibration exercise on balance, skeletal muscle strength and bone density in heart-transplanted patients.

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