Impact of an early physiotherapy program after kidney transplant during hospital stay: a randomized controlled trial

Impacto de um programa precoce de fisioterapia após transplante renal durante a internação: um estudo clínico randomizado controlado

Abstract

Introduction: Cardiorespiratory and musculoskeletal dysfunctions are common in the postoperative period of kidney transplant patients and are often accompanied by low exercise tolerance. Objective: The purpose of this study was to evaluate the impact of an early physiotherapy program during hospital stay on functional capacity and peripheral and respiratory muscle strength after kidney transplant. Methods: An open, randomized clinical trial was conducted in patients undergoing living donor kidney transplant. Sixty-three patients were included (intervention group - IG: n = 30; control group - CG: n = 33). IG received an early physiotherapy program from first postoperative day until hospital discharge and CG received standard care. The variables of interest were measured preoperatively and at discharge except for respiratory muscle strength and vital capacity (VC), which were also measured on the first postoperative day. Functional capacity was evaluated through six-minute walk test (6MWT); peripheral and respiratory muscle strength using a dynamometer and manovacuometer, respectively; and VC through spirometer. Results: After surgery, there was a reduction in functional walking capacity and peripheral muscle strength without different between groups (p > 0.05); however, respiratory muscle strength was significantly higher in IG (p < 0.001) at hospital discharge, when comparing with CG. Conclusions: An early physiotherapy program during hospitalization for patients undergoing living donor kidney transplant caused a lower reduction in respiratory muscle strength and without additional benefits in the functional capacity, when compared to a control group, although the clinical relevance of this finding is uncertain.

Keywords: kidney transplantation; physical therapy modalities; muscle strength; vital capacity.

Resumo

Introdução: Distúrbios cardiorrespiratórios e musculosqueléticos são comuns no período pós-operatório de pacientes de transplante renal, e são frequentemente acompanhados por baixa tolerância a exercícios. Objetivo: O presente estudo pretendeu avaliar o impacto de um programa precoce de fisioterapia durante a internação sobre a capacidade funcional e força muscular periférica e respiratória após transplante renal. Métodos: Foi realizado um estudo clínico randomizado aberto com pacientes submetidos a transplantes renais com doadores vivos. Sessenta e três pacientes foram incluídos (grupo de intervenção - GI: n = 30; grupo de controle - GC: n = 33). O GI recebeu o programa precoce de fisioterapia a partir do primeiro dia de pós-operatório até a alta hospitalar e o GC recebeu tratamento padrão. As variáveis de interesse foram medidas no pré-operatório e na alta, exceto por força muscular respiratória e capacidade vital (CV), que foram medidas no primeiro dia de pós-operatório. A capacidade funcional foi avaliada através do teste da caminhada dos seis minutos (TC6); força muscular periférica e respiratória com o uso de um dinamômetro e um manovacuômetro, respectivamente; e a CV por meio de um espiômetro. Resultados: Após a cirurgia houve reduções na capacidade funcional de caminhar e na força muscular respiratória sem diferenças entre os grupos (p > 0,05); contudo, a força muscular respiratória foi significativamente mais elevada no GI (p < 0,001) no momento da alta hospitalar em comparação ao GC. Conclusões: O programa precoce de fisioterapia oferecido durante a internação dos pacientes submetidos a transplantes renais com doadores vivos produziu uma menor redução da força muscular respiratória e não resultou em benefícios adicionais na capacidade funcional, apesar da relevância clínica desse achado ser incerta.

Palavras-chave: transplante renal; modalidades de fisioterapia; força muscular; capacidade vital.
INTRODUCTION

Several studies have shown that patients with chronic renal failure have reduced physical exercise capacity.1,2 Despite the benefits of kidney transplant for end-stage renal failure, cardiopulmonary and musculoskeletal dysfunctions are common after surgery.3-6 As with any intra-abdominal procedure, patients undergoing kidney transplant have impaired postoperative pulmonary function due to general anesthesia and diaphragmatic inhibition.7,8 Postoperative muscle weakness and reduced exercise tolerance9 are also frequently seen after surgery and may have an important impact on a patient’s quality of life.10,11 It is unclear whether this is a result of disease-related changes in skeletal muscle physiology or due to a reduction in physical activity after the transplantation.12

In recent years, there has been increasing interest in exercise interventions for patients with chronic renal diseases.13 However, there is no specific exercise program recommended for kidney transplant recipients. A systematic review suggested, based on trials with low methodological quality, that the benefits of such interventions are nuclear.14 Far too little attention has been paid to the effects of an exercise program after kidney transplantation,6 especially regarding the best time to start a program, how long to continue a program, and the level of intensity the activities should require.

We conducted a randomized clinical trial with the intention of producing evidence about the role of early exercise intervention for patients undergoing living donor kidney transplant. Thus, the aim of this study was to evaluate the impact of an early physiotherapy program during hospital stay on functional capacity and peripheral and respiratory muscle strength after kidney transplant. We hypothesized that patients who received an early physiotherapy program were more likely to walk longer distances and present greater respiratory muscle strength at hospital discharge than those who received only standard care.

METHODS

STUDY DESIGN

This study was a randomized, parallel-group, pragmatic, open trial. The study protocol was registered at The Brazilian Clinical Trials Registry (RBR-65G6XZ) and approved by the local Ethics Committee (protocol 0271/11). All participating patients provided informed consent. After signing the informed consent document, patients underwent a baseline assessment. After surgery patients were randomly assigned into one of two groups: control (CG) and intervention (IG).

The randomization scheme was computer generated and carried out by an investigator who was not involved with the recruitment and treatment of patients. The allocation was concealed by using sequentially numbered, sealed, and opaque envelopes. On the first day of treatment, the envelope was opened by the physiotherapist who provided the treatments. Patients were informed that they would receive one of two different physiotherapy approaches. In the postoperative period, all patients were assessed for the same variables from the preoperative period.

PARTICIPANTS

Adult patients (≥ 18 years old) admitted for living donor kidney transplantation in a tertiary hospital (Hospital do Rim e Hipertensão, São Paulo, Brazil) were included in this study. Patients were excluded using the following criteria: longer than 24 hours spent in mechanical ventilation and the intensive care unit, reoperation, intraoperative death, or any contraindications to performing the proposed measurements and/or treatment.

INTERVENTIONS

All groups received preoperative information about the importance of coughing and early mobilization by a physiotherapist. Patients in the CG received the standard care at our institution, with daily visits from a physiotherapist to encourage unsupervised mobilization, which included deambulation in the corridor and three sets of 10 repetitions of deep breaths.

Patients in the IG received daily supervised physiotherapy sessions with duration of approximately 30 minutes from postoperative Day 1 (1st PO) until hospital discharge. The specific physiotherapy protocol was as follows: 1st PO Day: patients (1) performed three sets of 10 repetitions of breathing exercises associated with elevation of the upper limbs in a seated position, (2) walked in a 30-meter corridor (four laps) assisted by a physiotherapist who encouraged an increase in intensity and speed according to the patient’s tolerance and (3) performed five repetitions of step exercises using a 25 cm step.

2nd PO Day: the same as 1st PO Day with the inclusion of (1) resistance exercises for upper limbs (three
sets of 10 repetitions of shoulder diagonals and elbow flexions) with the training load determined by tolerance (on average, women and men used 2 Kg and 4 Kg weights, respectively), and (2) two repetitions of stair climbing exercises (going up and down a 12-step flight of stairs, 25 cm each step). From 3rd PO Day until discharge: the same as 2nd PO Day with an increase of the stair climbing (one repetition per day) and walking exercises (one lap per day). During the sessions, all patients performed the exercises with rest intervals of at least two minutes between the sets.

OUTCOMES
The outcome measure of primary interest was functional walking capacity (6MWT) measured preoperatively and at discharge. The secondary variables were: respiratory muscle strength (maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) and vital capacity, which were measured preoperatively, on the first postoperative day, and at discharge; and peripheral muscle strength of upper and lower limbs, which were measured preoperatively and at discharge. The functional walking capacity was assessed by the 6MWT and performed according to the procedures described by the American Thoracic Society (ATS, 2002).15

Peripheral muscle strength was assessed by measuring the maximum force of voluntary isometric contraction using a dynamometer sensor “strain gauge” (TRF_200, EMG System of Brazil) with a sensitivity of 2 mV/V and a maximum capacity to measure up to 200 kgf.16

To record the signals from the dynamometer, we used the signal acquisition system model EMG200 (EMG System of Brazil), composed of an A/D converter with a16-bit resolution and a sampling frequency programmed at 200 Hz per channel, a low pass filter of 100 Hz and gain amplification of 600 times, thus, rejecting the common module > 100 dB. The data were stored in files using the same software, V1.2 EMGlab, by the same manufacturer.17

For the lower limbs (LL) in a straight position, we assessed the chain of the knee extensor muscles in the limb contralateral to the patient’s surgical incision (Figure 1a). The muscle group analyzed for upper limb (UL) strength was the chain of the elbow flexor contralateral to the arteriovenous fistula, which is the dominant member in the absence of the fistula (Figure 1b). Normal predicted values of UL and LL strength were calculated using the values proposed by Bohannon.16

Respiratory muscle strength was assessed using a manovacuometer (GlobalMed) connected to a nozzle with an orifice diameter of 2 mm to prevent the facial muscles contributing by generating pressure. The patients remained seated during the assessment. Three measurements were made, each starting from functional residual capacity for MIP and total lung capacity for MEP. The highest of the three measurements were recorded.

The values were expressed as absolute values and percentages, predicted according to Neder et al.18 The vital capacity was measured using a Wright’s spirometer (Ferraris Mark 8) connected to a mouthpiece. A nose clip was used to prevent air escaping through the nose. Patients were asked to perform a maximal deep inspiration and then exhale completely.19 At all-time points (preoperative, the first postoperative day, and discharge from hospital) measurements were performed in the following order: VC, MIP, and MEP.

STATISTICAL ANALYSIS
Sample size was calculated based on the functional parameters for the 6MWT, waiting a minimum difference of 75 ± 100 meters20 between pre- and post-intervention with a power of 80%. An alpha of 5% was determined and a sample of 28 patients per group were used. The interest variables were submitted to Kolmogorov-Sminov (K-S) normality test, and unless specified, the data were presented as mean and standard deviation. Was used the chi-square test to analyze the differences between groups of categorical variables.

To test the difference hypothesis of intra and intergroup variables (MIP, MEP, CV), we used an ANOVA repeated measures considering the factor group (CG e IG) and time (preoperative, 1st PO, discharge). The Tukey post-hoc test was used to identify such differences, if present. We used the paired t-test to analyze the difference of variables (LL, UL, 6MWD) between preoperative and discharge, and independent sample t-test to evaluate the difference of Δ6MWT between CG and IG. All analysis was performed using the SPSS for Windows, version 20 (SPSS Inc., Chicago, IL, USA). A p-value of 0.05 was considered significant.
Results

Seventy-two patients were recruited and 63 were included in the study, divided into a CG (n = 33) and IG (n = 30). Seven patients were excluded for the reasons presented in Figure 2. The preoperative and surgical characteristics of the patients are shown in Table 1. There was no difference in age, dialysis time, length of stay and clinical characteristics between the IG and the CG (p > 0.05).

Although there was a significant reduction (p < 0.001) in both groups compared to the 6MWT distance at discharge, no difference was found in relation to Δ6MWT between IG and CG (p = 0.29; Table 2). In the preoperative period, both groups presented similar predicted values (p > 0.05) for upper and lower limb strength (UL = CG: 97.8 ± 44.1% vs. IG: 116.1 ± 44.2%, and LL = CG: 102.1 ± 31.1% vs. IG: 122.5 ± 56.9%), without significant difference at hospital discharge (Table 2).

As expected, our results showed a significant reduction in the 1st PO respiratory muscle strength in both the CG (MIP = 9.0%, MEP = 34.9%) and the IG (MIP = 11.6%, MEP = 26.2%). While in hospital discharge, these values have not taken to the preoperative period, the IG showed a lower reduction of MIP (0.4% vs. 3.1%) and MEP (11.3% vs. 21.8%) relative to the CG (Table 3).

Both groups also showed reduction of VC on the first postoperative day (CG: 27.2% and IG: 20.5%; p < 0.001), with increase at hospital discharge, but no difference compared to preoperative values. However, IG showed values near the baseline (Table 3). The repeated measures ANOVA showed significant difference (p < 0.001) between the groups only for MIP and MEP. Both groups showed a significant reduction in serum creatinine at discharge, 2.1 (1.3) and 2.7 (1.1) mg/dL respectively for CG and IG but no statistical differences between groups.

Discussion

The results of this study showed that an early physiotherapy program for patients undergoing a living
Donor kidney transplant did not impact the patients functional walking capacity and peripheral muscle strength when compared to standard care. However, patients in the IG had better respiratory muscle strength when comparing with CG. To the best of our knowledge, only one study evaluated the effect of exercise training in the immediate postoperative period of kidney transplant patients, however, focused on biochemical markers of graft function.\textsuperscript{21}

We hypothesized that the intervention used in the IG would be at least 20% more effective than simple orientations in improving 6MWT distance. However, this hypothesis has not been confirmed. In a recent systematic review, Heiwe and Jacobson\textsuperscript{14} showed evidence that an exercise program after transplantation has potential benefits for physical activity and walking capacity. However, in our study, we observed that functional walking capacity was similar between the group performing a supervised exercise program and the group receiving standard care.

Although it is clear that chronic kidney disease is associated with impairments in several systems,
TABLE 2  MUSCULAR STRENGTH AND FUNCTIONAL CAPACITY OF PATIENTS BEFORE AND AFTER TRANSPLANTATION OF CONTROL GROUP AND INTERVENTION GROUP

<table>
<thead>
<tr>
<th></th>
<th>CG (n = 33)</th>
<th>IG (n = 30)</th>
<th>p-value</th>
<th>Preoperative</th>
<th>Discharge</th>
<th>Preoperative</th>
<th>Discharge</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UL strength (N)</td>
<td>23.7 (8.7)</td>
<td>21.4 (9.9)</td>
<td>0.13*</td>
<td>25.2 (8.3)</td>
<td>22.2 (5.8)</td>
<td>0.06*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LL strength (N)</td>
<td>52.5 (18.0)</td>
<td>51.3 (16.7)</td>
<td>0.67*</td>
<td>53.2 (16.0)</td>
<td>50.8 (13.0)</td>
<td>0.44*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6MWD (m)</td>
<td>584.9 (99.2)</td>
<td>502.4 (100.9)</td>
<td>&lt; 0.001</td>
<td>598.7 (72.2)</td>
<td>537.6 (83.7)</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ6MWT (m)</td>
<td>-82.5 (78.9)</td>
<td>-61.1 (81.8)</td>
<td>0.29**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%predicted 6MWD</td>
<td>86.9 (12.6)</td>
<td>75.0 (15.6)</td>
<td>&lt; 0.001</td>
<td>88.7 (11.9)</td>
<td>79.5 (11.1)</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ%predicted 6MWT</td>
<td>-11.9 (11.3)</td>
<td>-9.2 (12.0)</td>
<td>0.36**</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Data are expressed as mean (standard deviation). CG, control group; IG, intervention group; UL, upper limbs; LL, lower limbs; N, newtons; 6MWD, six-minute walking distance; m, meters. *Paired t-test between preoperative and discharge. **Independent samples t-test between CG and IG.

TABLE 3  RESPIRATORY MUSCLE STRENGTH AND VITAL CAPACITY OF PATIENTS BEFORE AND AFTER TRANSPLANTATION OF CONTROL GROUP AND INTERVENTION GROUP

<table>
<thead>
<tr>
<th></th>
<th>CG (n = 33)</th>
<th>IG (n = 30)</th>
<th>p-values*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preoperative</td>
<td>1st PO</td>
<td>Discharge</td>
</tr>
<tr>
<td>MIP (cmH₂O)</td>
<td>78.6 (27.4)</td>
<td>69.6 (27.8)</td>
<td>75.2 (27.2)</td>
</tr>
<tr>
<td>%predicted MIP</td>
<td>67.1 (21.2)</td>
<td>58.1 (22.6)</td>
<td>64.0 (20.4)</td>
</tr>
<tr>
<td>MEP (cmH₂O)</td>
<td>102.3 (19.1)</td>
<td>61.7 (23.3)</td>
<td>75.2 (26.3)</td>
</tr>
<tr>
<td>%predicted MEP</td>
<td>84.4 (19.3)</td>
<td>49.5 (20.8)</td>
<td>62.6 (23.9)</td>
</tr>
<tr>
<td>VC (L/min)</td>
<td>3.3 (1.1)</td>
<td>2.4 (1.0)</td>
<td>3.0 (1.0)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (standard deviation). CG, control group; IG, intervention group; 1st PO, first postoperative day; MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; VC, vital capacity. *ANOVA repeated measures: 1st PO differed significantly from preoperative; a Discharge differed significantly from preoperative; b Discharge differed significantly from 1st PO.

including peripheral muscles14,22 our study population was younger and presented a lower duration of the disease and dialysis period compared to previous studies. Our patients had normal predicted values for UL and LL17 right before surgery, which corroborates this hypothesis. On the other hand, Petersen et al.23 demonstrated abnormal skeletal muscle function and an increase in muscle fatigability in hemodialysis patients with no other difference after kidney transplantation.

In our study, an exercise protocol commencing immediately after renal transplantation did not increase the distance walked in the 6MWT or peripheral muscle strength. It is well known that the capacity to perform physical activity, such as walking, may be limited by the muscular, cardiac or pulmonary systems.23 However, our patients have good clinical conditions and the majority of our study participants had arterial hypertension. Moreover, the duration of the intervention session and the number of sessions could be insufficient to promote measurable muscle strength differences with the outcome measures utilized. However, there is no consensus about these concerns and our exercise program was based on our institution’s physiotherapy routine.

Corroborating our findings, Heiwe and Jacobson14 showed that there is no evidence that an exercise protocol after transplantation promotes improvement in peripheral muscle strength. In relation to the influence of cardiac limitations on walking distance, it was not our aim to evaluate cardiac parameters. However, cardiovascular disease remains the major cause of mortality in kidney recipients24-26 and the majority of our study participants had arterial hypertension.

We did observe a reduction in the distance walked at discharge compared to the preoperative period in both groups and this could be related to the effects induced by the surgery. Based on previous studies, the
majority of kidney transplant recipients do not practice any type of exercise up to 12 months before and after transplant.\textsuperscript{24,27} The fact that our results show that patients from both groups had a lower functional capacity at discharge could be a predictor variable to maintain physical inactivity after transplantation.

However, we believe that the training group will become more physically active after discharge compared to the control group, since they were submitted to systematic and supervised physiotherapy immediately after surgery. Recently, Greenwood \textit{et al.},\textsuperscript{26} in a 12-week pilot randomized controlled trial, concluded that both aerobic training and resistance training interventions appear to be feasible and clinically beneficial in kidney transplant recipients. Based on this, we can imagine that an average of about seven days of training, as in our study, is not sufficient to achieve statistically significant differences. However, the aim of our study was to evaluate the effect of exercise program just during hospitalization.

Several studies have shown that compared to upper abdominal surgery lower abdominal surgery is less likely to promote a reduction in pulmonary volumes and respiratory muscle strength during the postoperative period.\textsuperscript{28} Our data are supported by results obtained from the Literature,\textsuperscript{29,30} however, we also observed that the exercise protocol induced a lower reduction in respiratory muscle strength and VC compared to the control group.

Grams \textit{et al.},\textsuperscript{31} in a recent meta-analysis assessing the effects of breathing exercises on the recovery of pulmonary function, showed that a significant improvement of maximal respiratory pressure can occur in patients who perform breathing exercises after upper abdominal surgery. Although the findings of Grams \textit{et al.} relate to upper abdominal surgery, it is well known that patients who undergo abdominal surgery, whether upper or lower, usually develop a restrictive lung pattern. Therefore, we believe that breathing exercises probably increase diaphragm mobility and improve respiratory muscle synergism.\textsuperscript{32}

In addition, the concept of the breathing exercise has changed over the years and only recently includes active upper and lower limb exercises, supervised walking, and the use of steps. These latter changes in body position, as well as breathing exercises, optimize basal area ventilation.\textsuperscript{33} In the present study, the IG performed upper and lower limb exercises combined with breathing exercises and used training loads of 2 kg and 4 kg for female and male participants, respectively. However, there is no consensus regarding the weight of the training load, the number of series, and the frequency of the exercise protocol, each of which could have been insufficient and could have influenced our results.

Our study has a few limitations. First, we did not evaluate clinical outcomes such presence of postoperative complications (pneumonia, etc.) or evaluation of the level of pain in the surgical incision. However, this topic was not one of the aims of our study. Second, these results cannot be generalized and extrapolated for other populations of kidney recipients (older patients, deceased donors recipients) because our study was carried out in non-elderly patients with a more recent diagnosis with few co-morbidities and only in living donor recipients with few time on dialysis.

In addition, we could not be evaluated the impact of graft function in a sample only with live donor recipients (very low probability of delayed graft function for instance). Finally, short intervention time may not have time enough for providing a positive outcome and we could not evaluate how much the unsupervised group exactly exercised, but as a matter of ethics, we could never stop them to do exercise. Probably our results show that an early postoperative physiotherapy protocol after kidney transplantation does not promote an additional benefit when it comes to functional capacity and peripheral muscle strength after renal transplantation because a short intervention time maybe not have time enough for providing a positive changes.

\textbf{Conclusions}

Our results show that an early postoperative physiotherapy protocol after living donor kidney transplantation promoted a lower reduction in respiratory muscle strength (especially in MEP), when compared to a control group, but the clinical relevance of this finding is uncertain. The protocol implemented does not promoted an additional benefit when it comes to functional capacity and peripheral muscle strength, without causing implications in days of hospitalization. Future investigations should be conducted in elderly patients who have been diagnosed with kidney disease for a longer time and have experienced a longer dialysis period, especially those who received deceased donor kidneys.
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