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ORIGINAL ARTICLE

Physical exercise in cirrhotic patients: Towards prehabilitation on waiting list for liver transplantation. A systematic review and meta-analysis

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KEYWORDS

Prehabilitation;
Adapted physical
activity;
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End stage liver
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Summary

Background: Early survival after Liver Transplantation (LT) is reduced among sarcopenic patients. Despite, Adapted Physical Activity (APA) before LT is rarely proposed for the risk to impair portal hypertension and its resulting complications.

Objectives: To assess the effects of APA program in adults affected by End Stage Liver Disease (ESLD) on hospital stay, 1-year mortality and morbidity after LT, adverse events (Primary outcomes). Secondary outcomes were changes in VO₂ peak, muscle morphology, 6 minutes walking distance test (6MWD), Body Mass Index (BMI), MELD, CHILD score and Hepatic Venous Pressure Gradient (HVPG).

Search methods: MEDLINE, EMBASE, Google Scholar and the Cochrane Library database were explored for randomized clinical trials (RCT).

Data collection and analysis: Data were collected by one review author on the type of study, participants, treatments used for primary and secondary outcomes. Review Manager 5.2 was used for the analysis.

Main results: Four RCT with 81 patients were included. Primary outcomes: no severe adverse event was observed, but no published data were available on hospital stay or mortality after LT. Secondary outcomes: CHILD, MELD and BMI were not worsened by physical activity. No significant muscle diameter, 6MWD and VO₂ peak changes were observed after exercise. Significant reduction in HVPG in the treatment group was observed in a single study (MD-2.5 mmHg; 95%CI [-0.76, -0.24]; P=0.03).

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Authors' conclusions: Knowledge in this field is still at an early stage. Evidence derived from small trials of medium quality on ESLD patients suggests that APA is safe, without increasing portal hypertension. Further research is very likely to have an important impact on our confidence in the intervention effect.

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Background

Liver transplantation (LT) is the only curative treatment of end-stage liver disease (ESLD), with 1 and 5-year survival rates of 87–95% and 68–87% [1–4], respectively.

ESLD patients often suffer from physical deconditioning [5–9], which is responsible of a reduction of aerobic capacity and participates to the multifactorial process of cirrhosis-induced sarcopenia. Its incidence is as high as 30–50% among ESLD patients [7,10–12], and severely decreases 1-year survival after LT down to 53–58% [7–9,12–14].

To date, strategies to optimize health status of ESLD patients before LT are lacking, especially in case of high MELD score and severe portal hypertension.

Description of the intervention

Prehabilitation through Adapted physical activity (APA) programs was developed before digestive, cardiovascular and lung surgery to increase VO₂ peak: a recent meta-analysis highlighted how the application of such a program could reduce all types of postoperative complications after intra-abdominal operations [15]. APA is not yet applied in the context of LT probably because of the lack of a standardized program available [16–19] and mainly because of fear of portal hypertension complications [10,20–22]. Within certain limits, ESLD patients could be trained to become more physically fit in order to improve the functional capacity of the cardiovascular system and to enhance preparedness to external stressors [23,24] as could be considered LT.

There are two main tools to evaluate aerobic capacity:

- measurement of oxygen consumption at peak exercise (VO₂ peak). The VO₂ peak is impaired in more than half of the ESLD patients, [25,26] and correlates with a higher 1-year mortality after LT [13,14], with the duration of the oxygen therapy and hospital stay after LT [27,28];
- the 6 minutes walking distance (6MWD) [27,29] before LT is inversely correlated with the native MELD score, and a pretransplant 6MWD < 250 m is a risk factor for death on the waiting list [29].

Portal Hypertension can be objectively assessed by one single objective test:

- hepatic venous pressure gradient (HVPG).

How the intervention might work

Regular exercise and physical conditioning have been shown to cause positive changes in cardiorespiratory function, physical performance [30,31] and portal hypertension in ESLD populations [23,32–36]. Moreover, evidence exist that sarcopenia is reversible in healthy and cirrhotic subjects after moderate-aggressive exercise rehabilitation [36–40]. Prehabilitation APA programs may increase 6MWD, VO₂ peak, muscle mass, BMI and HPVG, and thus reduce mortality after LT.

Why it is important to do this review

No consensus exists on the feasibility, effectiveness, intensity and duration of an APA program in patients affected by ESLD, and their potential benefit before and after LT. Moreover, reluctance is justified by the «frail» condition of cirrhotic patients, suffering from sarcopenia, increased fatigability and potentially life-threatening portal hypertension [10,20–22].

Methods

Study inclusion in the review was based on the patient, intervention, comparison, outcome and study design (PICOS) criteria [41] and on the Cochrane Handbook for Systematic Reviews of Intervention [42].

Criteria for considering studies for this review

Types of studies

Randomized clinical trials, no matter the language, year of publication or blinding. We considered for inclusion trials published as abstracts if they could fulfil the inclusion criteria of our review: the corresponding authors were contacted to inquire about missing information relevant to the review. Quasi-randomised studies were not considered for this review, as well as series, case control studies or comparative series.

Types of participants

Trials including cirrhotic patients, regardless of age, sex or aetiology were included, as well as patients undergoing prehabilitation APA before Liver Transplantation. Studies focusing on exercise program after LT, were not considered for inclusion. Experimental studies on animals were not considered.

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