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EDITORIAL

Preoperative Aerobic Capacity – Is There a Role for Routine Evaluation in Liver Transplantation?

Capacidade Aeróbia Pré-operatória – Existe um Papel para a Avaliação da Rotina no Transplante de Fígado?

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End-stage liver disease is a systemic condition leading to multiple visceral and metabolic disorders. Regardless of liver cirrhosis etiology, its 5-year mortality reaches 85% without liver transplantation (LT).[1] The occurrence of a major complication is an important turning point in the natural history of the disease; it is predictive of decreased survival and should prompt discussion about the optimal timing for LT. Given the discrepancy between the increasing number of candidates and the limited availability of liver grafts, there is a need to identify patients most likely to benefit from LT.

In comparison with other surgical procedures, liver transplantation has a significant mortality rate in the early post-transplant period. Early post-transplant mortality is both related to patient's pre-transplant condition and to the quality of the donor organ. Clinical scoring systems, such as Child–Pugh–Turcotte (CPT) classification and Model for End-Stage Liver Disease (MELD) score, have been developed to better evaluate the severity of preoperative liver disease, but they do not consistently predict post-transplant survival.[2]

It has been increasingly recognized that patients with chronic liver disease (CLD) develop progressive impairment of their fitness and exercise capacity.[3–5] There are a number of potential mechanisms that explain the reduced exercise capacity: (i) Disturbed metabolic response to exercise characterized by a shift in oxidative fuels from glucose to lipid to sustain exercise in cirrhotic patients; (ii) malnutrition, muscle wasting, and muscle weakness that are present in more than a half of these patients; (iii) cirrhotic cardiomyopathy, a chronic cardiac dysfunction related to liver cirrhosis, and unrelated to the etiology characterized by a chronotropic incompetence and incapacity to reach the predicted maximal cardiac frequency; (iv) anemia, found in up to 75% of patients in transplant waiting list; (v) beta-blocker therapy that may inhibit the adaptive cardiac response to anemia, resulting in a synergic deleterious effect on maximal exercise capacity and (vi) a multifactorial pulmonary gas exchange impairment.[3–6]

Cardiopulmonary exercise testing (CPET) is a safe, noninvasive, and dynamic measure that represents the gold standard for the determination of exercise capacity and cardiorespiratory reserve. It generates measures of several aspects of aerobic capacity (AC), which is the ability of the body to consume and use oxygen during exercise.[7] During CPET, numerous cardiac, respiratory and metabolic functional parameters are measured while the workload is progressively increased on an electronically braked cycle ergometer until the patient is exhausted. The evaluated parameters include the peak oxygen consumption (VO_2 peak) achieved during testing and the point at which an apparent shift occurs from aerobic to anaerobic metabolism [i.e., the anaerobic threshold (AT)] that is often reported as a percentage of VO_2 max or VO_2 peak. Together, these broadly

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indicate the ability of the cardiopulmonary system to deliver oxygen to the peripheral tissues and the ability of the tissues to use that oxygen.[3,5,7] Maximal exercise capacity is a strong and independent predictor of death from any cause. Thus, VO_2 peak has been used to predict the risks of perioperative morbidity and mortality and to select good candidates for lung surgery, heart transplantation, or rehabilitation programs.[3] Similarly, recent studies have also shown that VO_2 peak is significantly lower in patients with CLD and suggested that CPET can help the clinician during the screening process to accurately identify patients at high risk of post-LT mortality.[6–9] Studies suggest that CPET is the only test that can detect early all presumed contraindications for LT including unstable coronary artery disease, severe cirrhotic cardiomyopathy, and porto-pulmonary hypertension.[3,5]

Focusing on these data, in this issue of GE, Mancuzo et al[11] presented a study assessing the association between AC, liver disease severity and postoperative LT outcome (length of ICU stay, length of hospitalization and postoperative mortality). This study included 47 candidates on LT waiting list who performed CPET tests less than 90 days before LT. MELD and CPT scores were calculated to assess liver disease severity. In contrast to previous studies, Mancuzo et al found that AC measured by VO_2 peak was comparable to that of healthy sedentary individuals. These differences may be explained by differences in disease severity of the cirrhotic patients enrolled in previous studies. Indeed, Mancuzo et al observed that patients with a MELD score <18 had a significantly higher VO_2 peak compared to those in the MELD > 18 subgroup. Similar findings were observed in other studies that showed a negative correlation between the disease severity determined either by MELD score or CPT classification and VO_2 peak values.[2,10–12] Mancuzo also found an independent association between AC and the length of hospitalization, a similar finding to that of Bernal et al[12]. However, a significant association between AC and ICU stay or post-LT mortality was not established in the present study. It is important to highlight that post-LT mortality was too small in this series, which can explain the lack of association. All three previous studies, despite some limitations, comparing pre-LT exercise capacity with post-LT outcomes found significant independent associations between the preoperative VO_2 peak value and post-LT survival. Indeed, in a study of Prentis et al among 135 liver transplant candidates, those with greater VO_2 peak (>60% predicted VO_2 peak) experienced better 12-month survival ($87.5 \pm 11\%$ vs $53.3 \pm 12\%$, $p = 0.05$) and in another recently published study, VO_2 at ventilatory threshold (<9 mL/min/kg ideal body weight) was the only predictive factor of mortality after LT.[11,12] Exercise capacity may, therefore, be a prognostic factor for post-LT survival.

A precise measure of VO_2 during exercise would be especially interesting if it could be used to assess post-LT risk of death, to gauge ability to perform physical work, and to support the benefit of well-conducted rehabilitation programs in the pre- and post-LT course.

Although more robust data will be needed before making specific recommendations about a routine use of CPET in pre-LT evaluation, it seems that CPET provides a useful preoperative tool to assess the global health status of LT candidates, to detect their comorbidities, to rule out major contraindications for surgery, and eventually, to predict their post-operative course.

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