

Overweight in liver transplant recipients

Excesso de peso em pacientes submetidos ao transplante hepático

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A B S T R A C T

This review aims to describe the incidence and prevalence of overweight and obesity after liver transplantation and the consequences associated with it. Literature review consultation was conducted in Medline / PubMed, SciELO, EMBASE and LILACS, with the combination of the following keywords: liver transplantation, overweight, obesity, weight gain. Overweight is incident on more than 60% of patients undergoing liver transplantation and obesity rates exceed 20% in the first year after surgery, during which occurs the largest relative weight gain. Studies have shown that between 60% and 70% of patients undergoing liver transplantation are overweight after the third year, 90% with abdominal obesity. Associated factors are, among others, advanced age, family history of overweight and excess weight prior to liver disease. The contribution of immunosuppressive medication remains controversial. Some of the consequences of overweight are liver steatosis, steatohepatitis, diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease and death.

Key words: Liver transplantation. Overweight. Obesity. Weight gain. Prevalence.

INTRODUCTION

Liver transplantation is the second most accomplished type of organ transplantation in Brazil, surpassed only by renal transplantation. In 2011, 1,492 liver transplants were performed by 55 teams registered across the nation¹. It is often the only solution to acute and chronic liver failure, improving the quality of life of patients² and increasing life expectancy^{3,4}. Over the past two decades, rates of post-liver transplantation survival increased to 85% in five years³ and to 56% after 20 years⁴, mainly due to advances in surgical techniques, in immune management and in pre, peri and postoperative care⁵.

However, the increased survival of patients undergoing liver transplantation was accompanied by the increasing prevalence of chronic diseases, usually higher than the prevalence found in the general population⁶. In this context, we highlight the excessive weight gain experienced by these patients, causing overweight and obesity. There are reports on obesity in 40% of the population already in the first post-transplant year⁷, and after three years of operation about 70% of patients have excess body weight⁸. Although no study has been able to demonstrate the relationship between overeating and post-transplant weight gain⁹⁻¹², it is known that patients undergoing liver transplantation rediscover the appetite

and pleasure of old eating habits after months of restrictions¹³. Also, they feel better and are able to feed in appreciable quantities. At the same time, they feel eager to regain the weight lost during the months of waiting for transplantation^{14,15}, since 75% of them are malnourished during this period¹⁶. Moreover, many patients do not return to work after surgery¹⁷ and those surviving for long periods have levels of daily physical activity significantly lower than the general population⁴. Besides these factors, all patients submitted to transplantation use immunosuppressive drugs, among which mainly cyclosporine or tacrolimus and, at least initially, corticosteroids. All these drugs are implicated in the genesis of posttransplant excessive weight gain and obesity^{18,19}. Although this gain can not affect the statistics of survival of patients in the short term, it is certainly involved in the incidence of diabetes mellitus, dyslipidemia, hypertension and metabolic syndrome in this population²⁰. This morbidity exposes patients to increased risk of heart and kidney diseases, as well as nonalcoholic graft steatohepatitis. All have important consequences on long-term mortality²¹.

Thus, this revision work was elaborated in order to describe the weight gain, incidence and prevalence of overweight and obesity after liver transplantation, as well as the risk factors described for this morbidity and its consequences.

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WEIGHT GAIN, INCIDENCE AND PREVALENCE OF OVERWEIGHT AND OBESITY

Weight gain after liver transplantation is crucial for the recovery of the patients' nutritional status. However, they usually gain more weight than they should. In a study of 597 patients⁸, the average weight gain increased from 1.8 kg 9.5 kg six months to three years after transplantation, leading to a prevalence of about 70% overweight (BMI > 25 kg/m²).

The incidence of obesity in the first postoperative year ranges from 15.5% to 40.7%^{7,8}, depending on the definition used, and continues to grow over the years after transplantation^{7,8}. Some authors have reported rates of overweight of 60% on the second year¹¹ and 70% on the third⁸. The works that have studied the incidence and prevalence of overweight and obesity after liver transplantation were summarized in Table 1.

The first postoperative year seems to be responsible for most of the weight gained after the operation^{8,10,22}. Patients seem to recover most of the weight lost during liver disease already in the first post-transplant year; 45% of them are overweight at the end of the first year versus 21% at the first post-transplant outpatient visit, and 43% prior to liver disease²³.

Patients with longer transplant time have an even higher prevalence of overweight²⁴. In a study with 143 patients undergoing liver transplantation with a median of four years since surgery, 58.1% were classified as having overweight by BMI and 69.9% by body composition. In the same study, 21% of individuals were classified as obese by BMI (e" 30 kg/m²) and 37.8% by body composition²⁵.

Although the prevalence of overweight and obesity are in clear ascendancy in recent years worldwide and in Brazil, yet the prevalence in the population undergoing transplantation is higher than in the general one. According to the latest data from the 2008 2009 Household Budget Survey, 50% of the adult Brazilian population has overweight, and 14.7%, obesity²⁶.

Still considering excess body weight, few studies have evaluated the prevalence of abdominal obesity in patients undergoing transplantation. In the study by Bianchi *et al.*²⁷, with 296 patients, the prevalence of waist circumference greater than 88cm for women and 102cm for men was 32 %²⁸. In the study by Anastácio *et al.*²⁵, 41.5% of the individuals were thus classified, and 88% had some degree of abdominal obesity (waist circumference greater than 80cm for women and 90cm for men)²⁵.

FACTORS ASSOCIATED TO WEIGHT GAIN, OVERWEIGHT AND OBESITY

The factors described are often older age^{8,29}, family history of overweight, high BMI prior to the disease

^{8,22,30}, post-transplant hypometabolism^{8,10}, post-transplant physical inactivity¹⁰, high donor BMI²², being married^{22,25}, few hours slept²⁵ and less dietary calcium intake²⁵.

Some authors demonstrated greater weight gain in patients undergoing liver transplantation for chronic liver diseases compared with those who were transplanted due to fulminant hepatic failure⁸. This is consistent with the theory of regain of the weight lost while waiting for transplantation. The highest incidence of obesity has also been observed in patients with a history of overweight or higher BMI prior to liver transplantation^{8,22,24,25,31}.

The use of immunosuppressive drugs as a risk factor for excess weight after liver transplantation is still controversial. Some studies have found an association with cyclosporine^{27,32} and steroids²² and weight gain or being overweight, but not all^{7,8,24}.

The contribution of the lower energy expenditure for the formation of overweight and obesity in patients undergoing transplantation also remains unclear. Richardson *et al.*¹² followed 23 patients after liver transplantation. They found a significant reduction in resting energy expenditure nine months after liver transplantation when compared with the pre-transplant period and controls. These authors also observed that the reduced resting energy expenditure after transplantation was an important predictor of increasing body fat mass after liver transplantation, though this association has not always been observed³³. Although it is not yet known whether it does or does not decrease after transplantation, certainly, the total energy expenditure of these individuals is reduced postoperatively. Patients undergoing liver transplantation generally reduce the level of physical activity. Besides, they retire when seriously ill while on the waiting list for transplantation. After the operation, most do not return to work¹⁷ and a minority have reasonable levels of physical activity, 24% according to Painter *et al.*³⁴. Other authors also found that levels of physical activity in patients undergoing liver transplantation are significantly lower than those of the general population⁴.

There are few data on food intake in liver transplant recipients. Nevertheless, none of the studies showed an association of dietary caloric intake with weight changes^{8,10,11,25}. This is possibly due to the methods used, since intake is usually assessed at the time of data collection and not continuously. Studies on the role of steroids in weight gain suggest that they stimulate appetite and increase intake of high-fat candies and food³⁵. Thus, patients tend to consume excess calories. In addition, patients undergoing liver transplantation feel freed from pre-transplant restrictions dietary and no longer have anorexia. They also have a higher sense of well-being and anxiety to regain the weight lost while waiting for transplantation¹⁵. Still, it is likely that patients return to old eating habits; the contribution of a history of overweight has been widely described as a risk factor for excessive weight gain and obesity^{8,22,24,25,31}.

Table 1 - Incidence and prevalence of excess weight, overweight and obesity after liver transplantation.

AUTHORS	N	Local	TYPE OF STUDY	Incidence / prevalence of excess weight, overweight and / or obesity comments about weight gain / BMI
Palmer et al. ²⁴	38	USA	Prospective; follow-up of 2.3 ± 1.9 years post-transplantation.	Incidence of excess weight after transplantation in 64.3% of normal weight / underweight patients before surgery (n = 18). All patients with excess weight before transplantation also had this condition after the operation (n = 11)
Munóz et al. ¹¹	21	USA	Prospective; follow-up to 2.8 ± 0.4 years after transplantation	Incidence of excess weight after transplantation in 67% of normal weight / underweight patients before surgery (n = 14). Incidence of obesity in 43% of normal weight / low weight patients before surgery (n = 9)
Stegall et al. ⁷	123	USA	Retrospective, with survivors of liver transplantation for at least one year	Incidence of obesity in 40.7% of the evaluated individuals one year after liver transplantation (n = 50)
Everhart et al. ²²	774	USA	Prospective; follow-up till the second year Post-transplant)	Incidence of obesity two years after transplantation in 21.6% of patients who did not have this condition before surgery (n = 69). Average BMI of 24.8 kg/m ² before transplantation, 27.0 kg/m ² after one year, and 28.1 kg/m ² after two years
Richards et al. ⁸	597	England	Prospective; follow-up till the third year Post-transplant)	Incidence of obesity in 24% (n = 76) of non-obese patients before transplantation in the first year and 31% (n = 95) in the third year after the operation. Incidence of overweight three years after transplantation in 67% (n = 166) of patients who did not have this condition prior to operation
Anastácio et al. ²⁵	143	Brazil	Cross-sectional, in patients with a median of four years post-transplant	Prevalence of overweight by BMI in 58.1%, in 69.9% by body composition and in 88% of patients by waist circumference. Prevalence of obesity by BMI in 21% and in 37.8% by body composition

IMPLICATIONS OF OVERWEIGHT AND OBESITY IN LIVER TRANSPLANTATION

There are several implications of obesity in patients undergoing liver transplantation. Studies have shown that the obesity of donor and recipient may influence operative results³⁶⁻⁴². Pre-obese patients are more likely, to develop primary graft dysfunction, delayed graft function after the operation and have increased risk of death^{36,37}. These findings have not been universal, however,³⁸.

Obesity can also affect the graft in the late postoperative period. In patients with general indications for liver transplantation, the incidence of steatosis ranges from 18%⁴³ to 40%⁴⁴ and the incidence of non-alcoholic steatohepatitis, from 9%⁴³ to 13%⁴⁴. Excess weight has been considered a risk factor for such types of involvement. Seo *et al.*⁴³ observed that 83% of patients who developed nonalcoholic fatty liver disease had weight gain 10% higher compared with pre-transplant BMI. Lim *et al.*⁴⁴ also observed that liver transplant recipients who developed nonalcoholic steatohepatitis had significantly higher BMI (32.5 ± 4.3 kg/m²) than those who did not develop this condition (22.9 ± 0.7 kg/m²).

In addition, excessive weight gain and excess weight are certainly related to comorbidities, such as dia-

betes, dyslipidemia, hypertension, metabolic syndrome, osteoarthritis and sleep apnea. They expose patients to increased risk of cardiovascular and renal diseases, and graft steatohepatitis²⁰, as it happens in the general population. Moreover, higher rates of such conditions are found in patients moderately (BMI between 35-40kg/m²) and severely obese (BMI > 40kg/m²) after five years of operation⁴⁵.

FINAL CONSIDERATIONS

Patients undergoing liver transplantation experience excessive weight gain, especially in the first post-transplant year, increasing over the years. Factors described as associated with weight gain and excess post-transplant weight are multiple, but the contribution of immunosuppressive medication remains controversial. Overweight and obesity after liver transplantation are associated with different consequences, ranging from higher recipient mortality to the development of various conditions – fatty liver, steatohepatitis, diabetes, hypertension, dyslipidemia and cardiovascular disease. Programs to prevent excessive weight gain should be implemented by multidisciplinary teams in the centers where these patients are followed.

R E S U M O

Esta revisão tem por objetivo descrever a incidência e prevalência de excesso de peso, sobrepeso e obesidade pós-transplante hepático e as consequências associadas a ele. Foi realizada revisão bibliográfica com consulta nas bases Medline/Pubmed, SciELO, EMBASE, LILACS com o cruzamento dos seguintes descritores: transplante hepático; sobrepeso; obesidade; ganho de peso. O excesso de peso é incidente em mais de 60% dos pacientes submetidos ao transplante hepático e as taxas de obesidade ultrapassam 20% já no primeiro ano do pós-operatório, período em que ocorre o maior ganho de peso relativo. Estudos revelaram que entre 60% e 70% dos pacientes submetidos ao transplante de fígado apresentam excesso de peso após o terceiro ano e quase 90% deles com obesidade abdominal. Os fatores associados são os mais variados, dentre os quais se destacam maior idade, história familiar de excesso de peso, excesso de peso anterior à doença hepática, dentre outros. A contribuição da medicação imunossupressora ainda permanece controversa. Dentre as consequências do excesso de peso estão a esteatose hepática, esteatohepatite, diabetes melito, hipertensão, dislipidemias, doenças cardiovasculares e morte.

Descritores: Transplante de fígado. Sobrepeso. Obesidade. Ganho de peso. Prevalência.

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