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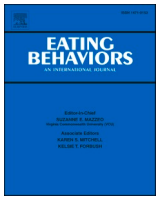

A cross-sectional study on the prevalence of eating disorders in liver transplanted patients with type 2 diabetes and/or overweight/obesity

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ABSTRACT

Liver transplantation (LT) associates with weight gain and metabolic complications. However, risk of eating disorders post-transplantation and factors influencing their onset remain poorly understood. This study aimed to fill this knowledge gap by characterizing the risk of having eating disorders or Orthorexia Nervosa (ON) according to the EAT-26, BES and Bratman screening questionnaires in 104 liver transplant recipients (mean age 62.5 years; median time from LT 6 years) with type 2 diabetes and/or overweight/obesity. Eighty-two patients (78.9 %) had diabetes; mean BMI was 30.1 ± 5.9 kg/m^2. Risk of eating disorders was observed in 6.9 %–10.8 % and the risk of orthorexia (Bratman test score > 4) was observed in 60.5 % of patients. A significant association was found between BMI and the likelihood of having eating disorders considering EAT-26 (OR = 0.17, $p = .009$). The absence of a direct link between diabetes and the risk of having eating disorders suggest multifactorial influences on post-transplant eating behaviors. The study highlights the importance of proactive screening to evaluate eating behaviors in liver transplant recipients to define tailored interventions and optimize post-transplant outcomes. Limitations refer to the observational nature of the study and the absence of pre-transplant data. Further research is warranted to validate these findings, elucidate temporal relationship between transplantation and the onset of eating disorders, and explore potential mechanisms underlying these associations. Such insights are crucial for developing effective strategies to mitigate the impact of eating disorders on post-transplant health and well-being.

1. Introduction

Liver transplantation (LT) is a life-saving intervention for individuals with end-stage liver disease. Preserving nutritional status and psychological well-being of these patients is challenging, with emerging evidence suggesting that nutritional inadequacy and the development of eating disorders constitute critical yet under-recognized aspects of post-LT care (Palmese et al., 2019). These disorders not only pose immediate health risks but also significantly impact long-term outcomes, including morbidity and mortality (Amianto et al., 2015; da Luz et al., 2018).

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) recognizes eating disorders as a spectrum of conditions with shared features but distinct diagnostic criteria. Anorexia Nervosa (AN), Bulimia Nervosa (BN), and Binge Eating Disorder (BED) are well classified, even if they may overlap in symptom presentation. It's worth mentioning that some atypical behaviors, such as Orthorexia Nervosa (ON), are not yet classified as an independent diagnostic category and are not included in the DSM-5. Indeed, ON shares similarities with AN in terms of rigid food rules and obsessive thoughts about food, being usually referred to as a disturbed eating behavior more closely allied with obsessive-compulsive disorders (Brytek-Matera, 2012). However, whether ON should be considered as a unique eating disorder or just a behavior is still matter of debate (Costa et al., 2017).

LT is a condition associated with a risk of weight gain and simultaneously with a risk of developing alteration in feeding behaviors in response to multiple factors (Anastácio & Ferreira, 2018; Anastácio, 2016; Correia et al., 2003; Ferreira et al., 2019, 2020; Linardon & Mitchell, 2017; Schaumberg et al., 2016), potentially resulting in

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disorders classified in the DSM-5, such as AN and BED, or in atypical tendencies, such as ON. Cirrhosis is the main cause of LT in Italy with a growing prevalence of cirrhosis secondary to metabolic disease. This medical condition requires very stringent nutritional indications (Plauth et al., 2019); yet strict dieting is a recognized risk factor for eating disorders (Stice et al., 2017). Indeed, in a previous article, we observed that patients affected by steatotic liver disease presented with higher risk of BED (Brodosi et al., 2023). Other risk factors for LT recipients to develop altered feeding behaviors include: corticosteroids, which can lead to increased appetite (Berthon et al., 2014; Jiménez-Pérez et al., 2016; McCoy et al., 2017) and stimulate consumption of highly palatable foods (Rodrigues et al., 2017); immunosuppressive drugs, a recognized risk factor for weight gain (Charlton et al., 2017); cyclosporine and tacrolimus, which can lead to metabolic derangement (Correia et al., 2003).

The sum of all these risk factors explains the growing evidence that LT recipients are highly susceptible to altered eating behaviors (Anastácio & Ferreira, 2018; Ferreira et al., 2017, 2019, 2020) that may lead to the onset of eating disorders. Nonetheless, literature on the prevalence of these conditions, the associated risk factors, and the clinical implications is still scarce. To date, only one study has systematically examined the eating behavior, weight gain over time and development of obesity in patients who underwent LT, concluding that uncontrolled eating and cognitive and emotional distortions are more common in recipients with obesity (Ferreira et al., 2017). Another study investigating the influence of psychological state on food intake in patients undergoing LT showed no correlation between weight gain and depression and anxiety (McCoy et al., 2017). A study of food dependence and abuse in patients undergoing LT found that 5.1 % of patients met the criteria for food addiction – this is generally defined as a clinically significant dependence from food ingestion – and 39.8 % for food misuse – i.e., that behavior meeting criteria for experiencing food addiction without clinical significance. However, food misuse did not directly relate to development of metabolic complications (Saab et al., 2017).

An exhaustive analysis of eating patterns evaluating the prevalence of both altered and pathological eating behaviors after LT is the crucial starting point to elucidate the mechanisms underlying the potential development of an eating disorder or other nonspecific tendencies, thereby facilitating a more effective clinical management to prevent their onset. From this perspective, investigating the dietary patterns of high-risk individuals, such as those with comorbidities like diabetes or obesity (Jebeile et al., 2023; Niemelä et al., 2024) would be of primary importance, but there is currently no study addressing this. Moreover, little information is currently available on the prevalence of eating disorders and ON in LT recipients, thus limiting the identification of potential risk factors which may help to define proper post-transplant assessment plans.

The aim of this study is the evaluation of risk of having an eating disorder in transplanted patients affected by type 2 diabetes and/or overweight or obesity. In addition to this, the study aimed to shed more light on potentially pathological tendencies related to healthy eating in LT recipients.

2. Materials and methods

2.1. Study design

This is a non-profit, observational, cross-sectional, non-pharmacological, single-center study. For the purpose of the study, screening questionnaires already validated in Italy but never used in this specific clinical context were administered to evaluate the risk for patients to have eating disorders and altered feeding behavior (i.e., Orthorexia Nervosa – ON). Following regular clinical practice, patients who underwent LT with either excess weight or metabolic derangement were referred to the Department structure for Metabolic Diseases and Clinical Nutrition of the 'Azienda Ospedaliero Universitaria di Bologna' (AOUBO) by the transplant center of IRCCS AOUBO. Inpatients visits at the Nutrition Center typically take place every 6 months in long-term LT, in conjunction with the visit at the Internal Medicine Department hepatologic visit. A closer follow-up at the Clinical Nutrition might be organized, if necessary, in case of weight gain or worsening of glycemic control, for instance. Metabolic Clinical practice is based upon approved clinical guidelines for treatment of type 2 diabetes (Mannucci et al., 2023), dyslipidemia (Mach et al., 2020) and obesity (Amerio et al., 2017).

The study took place at the Metabolic Diseases Unit of the IRCSS AUBO; the participation to this study was offered to consecutive patients during regular inpatient visits if the inclusion criteria were met. One hundred four participants were enrolled from January 2021 to December 2023 and were asked to complete three screening questionnaires: Eating Attitude Test – EAT-26 (Garner et al., 1982); Binge Eating Scale – BES (Gormally et al., 1982); Bratman test (Bratman & Knight, 2004). No extra inpatient visits occurred. Patients underwent routinary inpatient visits, which included collection of anamnestic data, concomitant medication, blood test analysis and nutritional assessment inclusive of collection of anthropometric measurements (height, weight, BMI, waist circumference). Questionnaire scores were calculated and analyzed to assess the risk of having an eating disorder (Anorexia Nervosa, Bulimia Nervosa, Binge Eating Disorder) or Orthorexia Nervosa.

2.2. Study population

The inclusion criteria were as follows: 1) age $>$ 18 years; 2) a diagnosis of type 2 diabetes mellitus and/or overweight or obesity (Body Mass Index – BMI $\geq$ 25); 3) having undergone LT. We excluded every patient who was diagnosed with a psychiatric disorder (as identified in the Diagnostic and Statistical Manual of Mental Disorders-5) within 12 months before the enrollment visit and patients who assumed psychotropic drugs. These patients were excluded as an acute o subacute mental disorder not necessarily well compensated might have repercussion on eating attitude. On the contrary, we decided not to exclude patients who had previously received a diagnosis of either generalized anxiety or major depression as chronic liver diseases and transplantation are conditions intrinsically intertwined with the aforementioned conditions. We also did not rule out patients who were in chronic therapies for longer than 12 months with molecules part of the Selective Serotonin Reuptake Inhibitor (SSRI) or Serotonin Modulator and Stimulator (SMS) categories. Decision of not to exclude these patients was made because conditions such as depression and anxiety disorders are highly prevalent in patients with chronic liver disease or who underwent liver transplantation (Cotter & Beresford, 2022; Mullish et al., 2014), so excluding them would have constituted a relevant bias in our analysis.

Local Ethical Committee Area Vasta Emilia Centro approved the study (reference code 301/2021/Oss/AOUBo). Written consent from enrolled patients was obtained. This research was conducted in accordance with both the Declaration of Helsinki and Istanbul and was reported following the STROBE criteria (von Elm et al., 2008).

2.3. Diagnosis of type 2 diabetes and overweight/obesity

Type 2 diabetes was diagnosed based on the indications provided by the Italian Society of Diabetology, which have been defined in line with criteria of the World Health Organization (WHO). Diabetes was diagnosed when one of the following conditions was verified: a) glycated hemoglobin (HbA1c) $\geq$6.5 % (in two circumstances; measured with a method aligned with the Diabetes Control and Complications Trial – DCCT – standard); b) glycemia measured in the laboratory $\geq$126 mg/dL (in the morning, after 8 h of fasting, in two circumstances); c) glycemia $\geq$200 mg/dL in the second hour after an oral glucose load (in two circumstances); d) glycemia $\geq$200 mg/dL at any time of the day in the presence of typical disorders (symptoms) of the disease (one circumstance sufficient).

Overweight and obesity were diagnosed based on the BMI of the patients, in line with criteria established by the WHO, which defines a BMI over 25 as overweight, and a BMI over 30 as obesity. Participants with obesity were further categorized according to three severity classes (Timothy Garvey, 2019): class I (BMI ≥ 30 and lower than 35), class II (BMI ≥ 35 and lower than 40), class III (BMI ≥ 40).

2.4. Questionnaires

The following questionnaires were used to assess the risk of having eating disorder or ON:

Eating Attitude Test (EAT)-26: a 26-item questionnaire that assesses symptoms and concerns characteristic of eating disorders (AN, BN and BED). A total score of 20 or higher is usually considered as the cut-off point for suspected eating disorders. According to the final score, a category "Yes" (≥20) or "No" (<20) is assigned.

Binge Eating Scale (BES): 16-item questionnaire to assess the presence of a Binge Eating Disorder. The value is weighted and differs from item to item. A score below 17 is not considered pathological ("Improbable"), a score between 17 and 27 is categorized as "Possible" and a score > 27 as "Probable".

Bratman test: A 10-item questionnaire to assess the presence of Orthorexia Nervosa. The test is considered an indicator of the possible presence of orthorexia if a score ≥ 4 is achieved. If the score does not exceed 6, it is categorized as "Orthorexic trait", while a higher score is categorized as "Orthorexia" as associates to a higher probability of occurrence of orthorexia.

2.5. Statistical analyses

Patient characteristics for continuous variables were described by either mean and standard deviation (SD) or median and interquartile range (IQR) for normal and non-normal data, respectively. Categorical variables were described by count and percentage. Summary statistics were tabulated according to the levels of the EAT-26, BES and Bratman test. The normality assumption was tested using the Shapiro-Wilk test. Comparisons between groups were performed using the Kruskal-Wallis test (continuous data) and Fisher's exact test (categorical data). Univariate binary and multinomial logistic regression analyses were performed to estimate the risk of a positive response ("Yes", according to the EAT-26 score), a "possible" response according to BES, "Orthorexia" and "Orthorexic trait" (according to the Bratman test) for each baseline characteristic. Logistic regressions were performed by correcting data for sex and presence of type 2 diabetes. The results were presented as odds-ratios (OR) and tabulated with 95 % confidence intervals (95 % CI). All tests were two-tailed with an α-value of 5 %. All analyses were performed with SAS 9.4 (N.C. Cary USA).

3. Results

3.1. Characteristics of the patients

The 104 patients included in the analysis – 69 males and 35 females – had a median age of 62.5 years (IQR: 56–67) and mean weight and BMI of 84.2 ± 18.7 kg and 30.1 ± 5.9 kg/m^2, respectively. The primary clinical indication for LT was cirrhosis secondary to viral hepatitis (43.3 % of cases). The median time from LT was 6 years (2–15 years). Overall, there were 82 (78.9 %) patients with diabetes, with a median diabetes duration of 10 years (Table 1). A total of 86 (83 %) participants was in the class of overweight (BMI ≥ 25) and, out of them, 48 (46 %) were classified as having obesity – 22 % within severity class I, 20 % within severity class II and 4 % within severity class III.

3.2. EAT-26 scale

Responses to the EAT-26 scale were recorded from 102 participants (2 patients did not answer), of whom 91 (89.2 %) reported a score indicating no risk of eating disorder. The 11 patients who were categorized as having symptoms and presenting characteristics suggesting the risk of having eating disorders had a mean BMI of 34.6 kg/m^2, which was significantly (F = 8.18; d.f. = 1, 100; $p = .005$) higher than the mean BMI of the remainder patients (29.5 kg/m^2) (Table 2). For every 1 kg/m^2 increase in BMI, the probability of having symptoms and characteristics related to eating disorders increased by 17 %, as shown by the OR of 1.17 (Wald $\chi^2 = 6.82$; d.f. = 1; $p = .009$) (Table 3). No other factor was significantly associated with EAT-26 scale scores.

Table 1
Patient's characteristics summary statistics, $N = 104$.

Characteristic		Statistics[a]
Age (years)		62.5 (56–67)
Weight (kg)		84.2 ± 18.7
BMI		30.1 ± 5.9
LT indication	*Autoimmunity*	4 (3.9 %)
	Excitotoxicity	9 (8.7 %)
	Virality	45 (43.3 %)
	Dysmetabolism	9 (8.7 %)
	Excitotoxicity and Virality	6 (5.8 %)
	Excitotoxicity and Dysmetabolism	5 (4.8 %)
	Virality and Dysmetabolism	2 (1.9 %)
	Cryptogenic cirrhosis	5 (4.8 %)
	Primary Biliary/Sclerosing Cholangitis	8 (7.7 %)
	All	2 (1.9 %)
	Other[b]	9 (8.7 %)
LT duration (years)		6 (2–15)
Diabetes years (N = 82)		10 (3–16)
Sex	*Female*	35 (33.7 %)
	Male	69 (66.3 %)
Diabetes		82 (78.9 %)

[a] Median (IQR) for age, LT duration, diabetes years, Mean ± SD for weight and BMI; N (%) on non-missing cases otherwise; LT: Liver Transplantation.
[b] This category included: hemochromatosis, neoplasms, *Amanita phalloides*, multiple hepatic adenomatosis, familial polycystic disease, HHV6 fulminant hepatitis, Caroli's disease.

Table 2
Patient's characteristics summary statistics[a] according to the Eating Attitude Test 26 results.

Characteristic			EAT-26		
		All patients N = 102[b]	No N = 91	Yes N = 11	*p*-Value
Questionnaire score		10.3 ± 6.8	8.7 ± 4.9	24.0 ± 3.9	/
Age (years)		63 (56–67)	63 (56–67)	63 (55–69)	0.545
Weight (kg)		84.4 ± 18.6	83.4 ± 18.1	93.0 ± 21.2	0.104
BMI		30.1 ± 5.8	29.5 ± 5.6	34.6 ± 5.8	**0.005**
LT duration (years)		7 (2–15)	8 (2–15)	4 (1–12)	0.520
Sex	*Female*	33 (32.4 %)	29 (31.9 %)	4 (36.4 %)	
	Male	69 (67.6 %)	62 (68.1 %)	7 (68.6 %)	0.744
Diabetes	*No*	21 (20.6 %)	18 (19.8 %)	3 (27.3 %)	
	Yes	81(79.4 %)	73 (80.2 %)	8 (72.7 %)	0.692
Diabetes years (*N* = 81)		10 (3–16)	10 (4–16)	5.5 (1.5–17.0)	0.502

[a] Median (IQR) for age, LT duration, diabetes years, Mean ± SD for questionnaire score, weight and BMI; N (%) on non-missing cases otherwise; LT: Liver Transplantation.
[b] N = 2 missing EAT-26 values (no answer).

Table 3
EAT-26 positive answer univariate risk (odds-ratio) estimates.

Risk factor		Odds-ratio (95 % CI)	p-Value
Age		1.02[a] (0.95–1.10)	0.541
Weight		1.03[a] (0.99–1.06)	0.109
BMI		1.17[a] (1.04–1.31)	**0.009**
LT duration (years)		0.97[a] (0.89–1.06)	0.501
Sex	*Female*	Ref.	
	Male	0.82 (0.22–3.02)	0.763
Diabetes	*No*	Ref.	
	Yes	0.66 (0.16–2.73)	0.564
Diabetes years		0.96[a] (0.87–1.07)	0.473

[a] By 1-unit increase; LT: Liver Transplantation; CI = Confidence Interval.

3.3. BES

The BES scores of 102 patients were analyzed, as one case had a missing answer. Only one participant scored as "Probable". Ninety-five (93.1 %) patients were in the "Unlikely" range for BES, while 7 (6.9 %) were categorized as "Possible". Overall, no variables were significantly associated with BES (Tables 4 and 5).

3.4. Bratman test

Forty-one (39.4 %) patients scored <4, indicating no risk according to the Bratman test, 56 (53.8 %) scored between 4 and 7, suggesting the risk of an orthorexic trait, and 7 (6.7 %) scored >7, indicating the risk of having ON. None of the baseline variables differed significantly between levels or showed a significantly higher or lower odds ratio for ON or orthorexic traits compared to patients who had no risk. Sex was the only variable that showed a significantly (d.f. = 2; $p = .034$) higher proportion ($n = 43$, 76.8 %) of male patients with orthorexic traits (Table 6). However, sex did not predict a significantly higher probability of being at risk to have orthorexic traits (Wald $\chi^2 = 0.46$; d.f. = 1; $p = .491$) or orthorexia (Wald $\chi^2 = 0.42$; d.f. = 1; $p = .519$) (Table 7).

Table 4
Patient's characteristics summary statistics[a] according to the Binge Eating Scale (BES) results.

Characteristic			BES[c]		
		All patients N = 102[b]	Improbable *N* = 95	Possible *N* = 7	p-Value
Questionnaire score		5.4 ± 6.3	4.1 ± 4.2	20.0 ± 3.3	/
Age (years)		63.0 (56–67)	64.0 (56–68)	59.0 (57–63)	0.228
Weight (kg)		84.1 ± 18.8	83.8 ± 19.2	87.7 ± 11.8	0.381
BMI		30.0 ± 5.8	29.7 ± 5.8	33.7 ± 5.2	0.083
LT duration (years)		7 (2–15)	7.5 (2.0–15.0)	6 (2–8)	0.535
Sex	*Female*	34 (33.3 %)	30 (31.6 %)	4 (57.1 %)	
	Male	68 (66.7 %)	65 (68.4 %)	3 (42.9 %)	0.218
Diabetes	*No*	21 (20.6 %)	18 (19.0 %)	3 (42.9 %)	
	Yes	81(79.4 %)	77 (81.0 %)	4 (57.1 %)	0.151
Diabetes years (*N* = 80)		10 (3–15)	10 (3–16)	6.5 (4.0–7.5)	0.234

[a] Median (IQR) for age, LT duration, diabetes years, Mean (SD) for questionnaire score, weight and BMI; N (%) on non-missing cases otherwise; LT: Liver Transplantation.
[b] $N = 2$ missing BES – no answer was observed;
[c] Excluding N = 1 BES "Probable" patient (score = 31).

Table 5
BES possible answer univariate risk (odds-ratio) estimates.

Risk factor		Odds-Ratio (95 % CI)	p-Value
Age		0.97[a] (0.89–1.05)	0.421
Weight		1.01[a] (0.97–1.05)	0.597
BMI		1.12[a] (0.98–1.28)	0.092
LT duration (years)		0.95[a] (0.86–1.06)	0.395
Sex	*Female*	Ref.	
	Male	0.35 (0.07–1.64)	0.182
Diabetes	*No*	Ref.	
	Yes	0.31 (0.06–1.52)	0.149
Diabetes years		0.90[a] (0.75–1.07)	0.234

[a] By 1-unit increase; LT: Liver Transplantation; CI = Confidence Interval.

4. Discussion

A review of the literature performed in the context of this study confirmed that data on eating disorders and altered eating behaviors in patients after LT is scarce, and the few that exists mainly focuses on BED. This is one of the first studies that evaluated the proportion of LT patients with either diabetes and/or with overweight/obesity at risk of having eating disorders and ON.

A crucial information that can be gathered from the analysis is that the risk of having an eating disorder in our clinical population ranged between 6.9 % for BED to 10.8 % for EAT-26 questionnaire. According to the Bratman test, 60.5 % of participants showed altered scores, being at risk of having either orthorexic trait or ON. There was a significant difference between the proportion of male and female patients exhibiting orthorexic behavior, with orthorexic traits being mainly observed in males. This result differs from previous reports showing a significant association with females (Rogowska et al., 2021) and a recent systematic review and meta-analysis reporting no significant differences in the proportion of orthorexia symptoms between female and male subjects (López-Gil et al., 2023).

To the best of authors' knowledge, no study assessed the prevalence of eating disorders and orthorexia in LT recipients with type 2 diabetes and/or overweight/obesity and data from this study could offer a first indication. Although we point out that our results were collected through screening tools from a small population, our data call for a higher attention to the potential occurrence of altered eating behaviors and the likelihood of developing an eating disorder in patients undergoing LT, which underscores the need of fostering collaboration among physicians from diverse specialties to precisely evaluate those patients who test positive to screening questionnaires. These tools are important to identify individuals at high risk, so as to send them to a timely psychiatric consultation for diagnostic evaluation of eating disorders and other pathologies associated with altered eating behaviors.

A correct diagnosis is crucial for therapeutic purposes, as there is evidence that strict dieting exacerbates eating disorders, which should instead be treated with a cognitive-behavioral approach (Habib et al., 2023). Early assessment of altered eating behaviors and diagnosis of eating disorders in liver-transplanted patients appear paramount also considering that cardiovascular diseases are among the main cause of death after LT, which is relevant considering the increasing indication for LT in patients with steatohepatitis due to metabolic dysfunction with secondary worsening of cardiovascular risk factors, such as hypertension, diabetes, and dyslipidemia (Gabrielli et al., 2024). Our results also suggest that careful screening for ON would be beneficial in LT recipients, possibly along with the assessment of other altered eating behaviors related to underlying pathologies that may increase morbidity and mortality in transplanted patients. Whether ON should be classified as a proper disorder is still matter of debate (Costa et al., 2017) and no validated screening or diagnostic tool is currently available; the Bratman test itself has been questioned as a valid tool, with some authors suggesting not to use it (Missbach et al., 2017). However, considering the scientific interest for this condition, the Bratman test is still largely

Table 6
Patient's characteristics summary statistics[a] according to the BRATMAN scale results.

Characteristic			BRATMAN			
		All patients N = 104	Normal *N* = 41	Othrorexic trait *N* = 56	Orthorexia N = 7	p-Value
Questionnaire score		4.1 ± 2.1	2.1 ± 1.0	5.1 ± 1.1	8.6 ± 0.8	/
Age (years)		62.5 (56–67.0)	64 (57–67)	62 (55–67)	64 (62–70)	0.456
Weight (kg)		84.2 ± 18.7	81.0 ± 18.9	86.6 ± 17.2	84.5 ± 27.9	0.348
BMI		30.1 ± 5.9	29.1 ± 5.6	30.7 ± 5.7	31.2 ± 8.2	0.306
LT duration (years)		7 (2–15)	8 (2–15)	6 (1–13)	12 (2–26)	0.409
Sex	*Female*	35 (33.7 %)	18 (43.9 %)	13 (23.2 %)	4 (57.1 %)	
	Male	69 (66.3 %)	23 (56.1 %)	43 (76.8 %)	3 (42.9 %)	**0.034**
Diabetes	*No*	22 (21.1 %)	12 (29.3 %)	8 (14.3 %)	2 (28.6 %)	
	Yes	82 (78.9 %)	29 (70.7 %)	48 (85.7 %)	5 (71.4 %)	0.138
Diabetes years (*N* = 82)		10 (3–16)	12 (4–15)	8.5 (2.5–15.5)	17 (14–20)	0.341

[a] Median (IQR) for age, LT duration, diabetes years, Mean (SD) for questionnaire score, weight and BMI; N (%) on non-missing cases otherwise; LT: Liver Transplantation.

Table 7
Bratman test univariate risk (odds-ratio) estimates for Orthorexia and Orthorexic trait.

Risk factor			Odds-ratio (95 % CI)	p-Value
Age	Othrorexic trait		0.99[a] (0.95–1.03)	0.512
	Othrorexia		1.04[a] (0.94–1.16)	0.454
Weight	Othrorexic trait		1.02[a] (1.00–1.04)	0.133
	Othrorexia		1.01[a] (0.97–1.05)	0.604
BMI	Othrorexic trait		1.05[a] (0.98–1.13)	0.180
	Othrorexia		1.06[a] (0.93–1.21)	0.380
LT duration (years)	Othrorexic trait		0.98[a] (0.94–1.03)	0.493
	Othrorexia		1.05[a] (0.95–1.15)	0.340
Sex	Othrorexic trait	*Female*	Ref.	
		Male	0.98 (0.94–1.03)	0.491
	Othrorexia	*Female*	Ref.	
		Male	0.59 (0.12–2.96)	0.519
Diabetes	Othrorexic trait	*No*	Ref.	
		Yes	2.48 (0.91–6.89)	0.077
	Othrorexia	*No*	Ref.	
		Yes	1.03 (0.18–6.09)	0.970
Diabetes years	Othrorexic trait		1.00[a] (0.95–1.07)	0.907
	Othrorexia		1.14[a] (0.95–1.37)	0.169

[a] By 1-unit increase; LT: Liver Transplantation; CI = Confidence Interval.

applied and there is evidence that it can be considered as a reliable self-report instrument providing information convergent with other tools (Meule et al., 2020). Developing a fully-validated instrument to detect orthorexic tendencies seems urgent considering the potentially high prevalence of ON in some patient groups. Moreover, a fully validated tool could help to better define also ON classification. Accordingly, we advise careful interpretation of the results from the current study concerning orthorexia.

The greatest strength of this study is that it is unique, as there is no data in the literature on the risk of developing eating disorders or ON after LT in patients with type 2 diabetes or overweight/obesity. One important result of our analyses is the significant association between BMI and the likelihood of having eating disorders, indicating that patients with a higher BMI are at higher risk. LT recipients with overweight and obesity, thus, may require close medical counselling after transplantation, in line with current knowledge. Obesity and eating disorders have been considered separate entities in the past, but there is increasing evidence of a higher prevalence of eating disorders in people with obesity (with bulimia nervosa and binge eating disorder being most strongly associated with obesity) (Treasure et al., 2020). We showed similar results in a previous study evaluating the risk of binge eating in patients with steatotic liver disease, which showed that the risk of having this disorder was associated with a higher caloric intake (Brodosi et al., 2023). Moreover, previous studies reported a significant association between excessive weight and altered eating behaviors in LT recipients, highlighting a direct link with the emotional state of the patients and with environmental triggers/stimuli (Ferreira et al., 2019, 2020). Results from the present cross-sectional study further support the hypothesis that increased body weight may favor the onset of an eating disorder, although not indicating a direct association with altered behaviors such as orthorexia. This could suggest that part of the post-transplant weight gain is related to dietary habits, maintenance of pre-transplant food choices and low physical activity as previously suggested (Camacho-Barcia et al., 2024), independently of other chronic conditions such as diabetes. Indeed, we found no association between diabetes and the risk of having an eating disorder or orthorexia, possibly suggesting that the role of this comorbidity is marginal.

Another interesting aspect of our study is the long follow-up period, as the analysis included patients who had received LT 2 to 15 years before enrollment, which could have hindered detecting a significant association between the time expired from LT and the risk of eating disorder. Indeed, immunosuppressive therapy is usually more intense in the first three months post-liver transplantation when alloreactivity is high, subsequently being minimized for a maintenance phase (Panackel et al., 2022). Clinical data collected from this study, thus, may suggest that the influence of immunosuppressive drugs on the onset of eating disorders could disappear after few years from transplantation, when emotional and external factors may play a pivotal role (Ferreira et al., 2019, 2020). If held true, this dynamic would highlight the importance of monitoring the eating behavior of LT recipients soon after transplantation; moreover, this would further corroborate the robustness of our data, as the influence of immunosuppressive medication on the questionnaire scores might be considered small or almost irrelevant.

This study has several limitations, firstly referring to its observational nature and to the consecutive enrollment of patients after that they were referred from the transplant center for nutritional/diabetic assessment according to the decision of the physician or surgeon who first saw the patient. This might have represented a confounding factor in the timing of detecting a risk for eating disorders or orthorexia. Moreover, eating habits were characterized only after transplantation with no possibility of comparison before and after surgery. A further concern refers to the low number of participants not having type 2 diabetes, which could have limited the power of our analyses when considering diabetes as explanatory variable. It is important to note also that the questionnaires used in this survey serve as screening tools and do not constitute formal diagnoses for eating disorders. The Bratman test, also, is a tool with intrinsic limitations, which raises concerns about the reliability of the results obtained from it (Missbach et al., 2017). Further studies would benefit from the analysis of a larger set of patients

and from the collection of data on their pre-transplant condition to determine whether diabetes, obesity and the risk of eating disorders or orthorexia occurred after transplantation. Also, further research should include more comprehensive, dedicated, validated diagnostic tools.

5. Conclusions

This is the first study providing evidence about the proportion of patients with type 2 diabetes and/or overweight or obesity showing the risk of having eating disorders or ON after liver transplantation. The risk of having eating disorders in these patients ranged between 6.9 and 10.8 % depending on the questionnaire. Altered Bratman score was observed in 60.5 % of patients, possibly suggesting the need of careful monitoring for ON after transplantation; however, data on orthorexia should be interpreted with caution as no validated tool currently exists to estimate this behavior and because the current study included a limited number of patients. The significant association found between body mass index and the likelihood of having eating disorders could highlight the intricate relationship between weight status and disordered eating behaviors. The absence of a direct link between diabetes and eating disorders may suggest multifactorial influences on post-transplant eating behaviors. Further research is needed to validate these findings and elucidate the temporal relationship between transplantation, risk of eating disorder and eating disorder onset. Nonetheless, the observed trends underline the importance of proactive screening and tailored interventions to address eating disorders in liver transplant recipients, thus optimizing post-transplant outcomes, reducing the risk of death after surgery and improving the quality of life.

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CRediT authorship contribution statement

Lucia Brodosi: Writing – review & editing, Writing – original draft, Conceptualization. **Michele Stecchi:** Writing – review & editing, Formal analysis. **Giovanni Vitale:** Writing – review & editing. **Beatrice Selvatici:** Writing – review & editing, Data curation. **Michela Genovese:** Writing – review & editing, Data curation. **Matteo Ravaioli:** Writing – review & editing, Supervision. **Matteo Cescon:** Writing – review & editing, Supervision. **Maria Cristina Morelli:** Writing – review & editing, Supervision. **Loris Pironi:** Writing – review & editing, Supervision.

Declaration of competing interest

All authors declare that they have no conflicts of interest.

Data availability

Data that support the findings of this study is available from the corresponding author, upon reasonable request

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