

# Quality of life in liver transplant recipients during the Corona virus disease 19 pandemic: A multicentre study

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**Abbreviations:** COVID-19, Coronavirus Disease 19; ISTAT, Italian National Institute of Statistics; LT, liver transplantation; QoL, quality of life; SF-12, The Short Form health survey; PCS-12, Physical Component Summary; MCS-12, Mental Component Summary; IPAQ, International Physical Activity Questionnaire; MET, Metabolic Equivalent Task; SD, standard deviation; SA, sedentary activity.

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#### Abstract

**Background:** Liver transplant recipients require specific clinical and psychosocial attention given their frailty. Main aim of the study was to assess the quality of life after liver transplant during the current pandemic.

**Methods:** This multicentre study was conducted in clinically stable, liver transplanted patients. Enrollment opened in June and finished in September 2021. Patients completed a survey including lifestyle data, quality of life (Short Form health survey), sport, employment, diet. To examine the correlations, we calculated Pearson coefficients while to compare subgroups, independent samples *t*-tests and ANOVAs. To detect the predictors of impaired quality of life, we used multivariable logistic regression analysis.

**Results:** We analysed data from 511 patients observing significant associations between quality of life's physical score and both age and adherence to Mediterranean diet ( $p < .01$ ). A significant negative correlation was observed between mental score and the sedentary activity ( $p < .05$ ). Female patients scored significantly lower than males in physical and mental score. At multivariate analysis, females were 1.65 times more likely to report impaired physical score than males. Occupation and physical activity presented significant positive relation with quality of life. Adherence to Mediterranean diet was another relevant predictor. Regarding mental score, female patients were 1.78 times more likely to show impaired mental score in comparison with males. Sedentary activity and adherence to Mediterranean diet were further noteworthy predictors.

**Conclusions:** Females and subjects with sedentary lifestyle or work inactive seem to show the worst quality of life and both physical activity and Mediterranean diet might be helpful to improve it.

#### KEYWORDS

COVID-19, liver transplant, quality of life

## 1 | INTRODUCTION

Coronavirus Disease 19 (COVID-19) is an acute respiratory disorder caused by the SARS-CoV-2 zoonotic virus actually responsible of a global pandemic.<sup>1-3</sup> People are experiencing dramatic clinical and psychological consequences, severe economic and social crisis and wide restrictions of personal and social freedom, culminating in lockdown and quarantine.<sup>1</sup> The Italian National Institute of Statistics (ISTAT) reported, in the last annual report of "Fair and sustainable well-being (BES 2020)," that the uncertainty related to the current

#### Key points

- Liver transplant recipients show specific clinical and psychosocial frailty.
- Female gender, sedentary lifestyle and work inactivity are associated to a low levels of quality of life.
- Physical activity and Mediterranean diet enhance the quality of life.

health, economic and employment crisis has led a vast part of the population to express worry for the next 5 years.<sup>4</sup>

Today, many subpopulations could require specific clinical and psychosocial attention, given their risk factors in terms of mental and physical health. Among them, patients who underwent liver transplantation (LT) are especially vulnerable, and previous research indicated higher depression and need for social support than general population.<sup>5</sup> Transplant recipients often experience negative psychological outcomes, such as re-experiencing, avoidance, a sense of anticipation and responsibility towards the donor, clinicians and family members.<sup>6–8</sup>

LT represents the standard of care for patients with severe acute or chronic liver diseases or hepatocellular carcinoma, with 1- and 5-year patient survival rates of more than 90% and 70% respectively.<sup>9,10</sup> With these remarkable survival rates, quality of life (QoL) should represent today a chief independent measure of transplant outcome.<sup>11,12</sup> Notably, the goal of LT should be not only to achieve an acceptable QoL, but to return to the levels present before the onset of liver disease.<sup>13,14</sup>

Considering the relevance of QoL in the overall assessment of the success of LT, this study was undertaken to examine the QoL of a large population of LT recipients during the COVID-19 pandemic. Specifically, we aimed (a) to analyse the correlation between personal data, lifestyle patterns, physical activity, employment and adherence to Mediterranean diet and QoL of LT recipients during the COVID-19 pandemic; and (b) to detect the predictors of impaired QoL.

## 2 | MATERIAL AND METHODS

### 2.1 | Patients

This cross-sectional, multicentre study was conducted in clinically stable, adult patients who underwent LT and were followed-up in seven Italian Hepatology Units. Inclusion criteria were the following: age  $\geq 18$  years, LT performed at least 12 months earlier, and absence of clinical events during the last 6 months. Multiorgan transplant or re-transplantation, vascular or biliary complications, systemic disorders (e.g. cardiovascular disease, cancer, infection, recurrence of pre-LT liver disease), unstable conditions, hospital admission in the last 6 months represented the exclusion criteria. Human Immunodeficiency Virus infection, deafness, inability to carry out a telephone interview in full understanding or holiday in the last 4 weeks were additional exclusion criteria.

The enrollment started on 1 June 2021 and ended on 30 September 2021.

Patients provided informed consent before participating in the study. Then, trained professional staff agreed on the date and time of a subsequent interview, during which the patient could answer by telephone to the composite questionnaire. We requested that the patient be alone in a silent space.

The first part of the survey consisted of a demographic questionnaire. In particular, the following personal and lifestyle data were recorded: gender, age, transplant date, referral centre, region of residence, education degree, presence of caregiver, alcohol and tobacco habits. Subsequently, patients completed 4 questionnaires in an estimated total time of 10–15 min.

### 2.2 | Questionnaires

#### 2.2.1 | The Short Form health survey

The Short Form health survey (SF-12) is a health-related QoL questionnaire consisting of 12 questions that measure 8 health domains to evaluate physical and mental health. The SF-12<sup>15</sup> represents a commonly used tool to assess health-related QoL. It is a shorter version of SF-36 developed by Ware et al.<sup>16</sup> Physical health-related domains include General Health, Physical Functioning, Role Physical and Body Pain. Mental health-related scales comprise Vitality, Social Functioning, Role Emotional and Mental Health. The SF-12 has demonstrated strong reliability and validity across many chronic illnesses and conditions.<sup>17–21</sup> We administered the SF-12, and for each participant, we calculated two summary scores of physical (Physical Component Summary, PCS-12) and mental (Mental Component Summary, MCS-12) health, using the weighted means of the eight domains.

In each of the nine European countries, there were wide correlations between the measures from the SF-36 and SF-12.<sup>22</sup> Correlations were also significant between scores based on three different estimation methods (standard items and scoring weights; standard items and country-specific scoring weights; and country-specific items and scoring weights). Mean scores were also comparable across estimation methods. Furthermore, there was a high degree of replication in the selection of 12 items for the SF-12 across 9 European countries and in comparison with items selected for the North-American SF-12 version.<sup>22</sup>

The SF-12 covers the same eight health domains as the SF-36 with considerably fewer questions, making it a more practical instrument.

#### 2.2.2 | The International Physical Activity Questionnaire-short version

The International Physical Activity Questionnaire (IPAQ) measures multiple domains of physical activity.<sup>23</sup>

The IPAQ-short version includes 11 items regarding time spent on walking, vigorous- and moderate-intensity activity, sedentary activity and demographic information (including education) and some last items concerning comprehension of the questionnaire. Information regarding physical activity was expressed in min per day and/or days per week.<sup>24</sup> Then, there are three levels (low, moderate, high) of physical activity proposed to classify populations. The

“high” category includes (a) vigorous-intensity activity on at least 3 days achieving a minimum total physical activity of at least 1500 Metabolic Equivalent Task (MET)-min/week or (b) 7 or more days of any combination of walking, moderate-intensity or vigorous-intensity activities achieving a minimum total physical activity of at least 3000 MET-minutes/week. The pattern of activity can be classified as “moderate” if (a) 3 or more days of vigorous-intensity activity of at least 20 min per day, or (b) 5 or more days of moderate-intensity activity and/or walking of at least 30 min per day or (c) 5 or more days of any combination of walking, moderate-intensity or vigorous-intensity activities achieving a minimum total physical activity of at least 600 MET-minutes/week. Individuals who do not meet criteria for high or medium categories are considered to have a “low” physical activity level.<sup>23</sup> The IPAQ has been developed as an instrument for cross-national evaluation of physical activity and has been validated in 12 countries including Italy.<sup>24,25</sup>

The IPAQ also provides an indicator of sedentary activity that is not included as part of any summary score of physical activity. Indeed, the IPAQ assesses time spent in sitting on a typical week expressed in “minutes” (Sitting Total Minutes/week = weekday sitting minutes  $\times$  5 weekdays + weekend day sitting minutes  $\times$  2 weekend days).<sup>23</sup>

The IPAQ is present in two versions: long and short. The long version of questionnaire appeared less pleasant and more confusing in comparison with the short one<sup>24</sup>; therefore, we used the short version.

### 2.2.3 | Employment

We also evaluated the post-transplant resumption of work with both closed and open ad hoc questions. Indeed, we designed a specialized employment questionnaire.

The enrolled subjects answered the following questions concerning the work activity: “Today, are you an active worker? Which kind of job (then classified in ‘blue’ or ‘white collar’ job) are you doing in the present period or have worked in the past respectively? If inactive, how long have you been in this state? Have you ever received an inability pension or has been in a protected categories (according to the Italian Law number 68/99)?”

If patients were inactive, the questionnaire was finished. If patients were active workers, the following question was proposed: “After LT, were you placed in the same job responsibilities of the pre-transplant period? If not, what task was you assigned after transplant? Who evaluated the return to work after transplant? If the return was valued by the Occupational Health Physician, were the tasks customized? Did you receive some limitations or prescriptions? If yes, which?”

Finally, we asked to provide an overall judgement about the return to work after transplant and about the physical demand required with the use of two Likert scales.

“On a scale of 1 (very easy) to 5 (very difficult), in general terms, as you would define your reintegration into work? On a scale of 1

(very easy) to 5 (very hard), how would you define your return to work from a physical point of view?”

### 2.2.4 | MEDI-LITE score

To evaluate adherence to Mediterranean diet, we used the MEDI-LITE score, proposed in 2014 and validated in 2017.<sup>26,27</sup> The MEDI-LITE score consists of nine items about daily consumption of fruit, vegetables, cereals, meat and meat products, dairy products, alcohol and olive oil and the weekly intake of legumes and fish.<sup>26</sup> For each food group, there are three categories of consumption. For foods typical of Mediterranean diet (fruit and vegetables, cereals, legumes and fish), 2 points are assigned to the highest consumption category, 1 to the middle category and 0 to the lowest category. As to olive oil, 2 points are assigned for regular use, 1 for frequent use and 0 for occasional use. Foods not representative of the Mediterranean diet (meat and meat products, dairy products) are scored as follows: 2 points to the lowest category, 1 to the middle category and 0 to the highest category of consumption. Finally, 2 points are assigned to the middle consumption category of alcohol (1–2 alcohol units/day), 1 to the lowest category (1 alcohol unit/day) and 0 to the highest category (>2 alcohol units/day). The final score ranges from 0 (low adherence) to 18 (high adherence to the Mediterranean diet).

The MEDI-LITE score revealed a noteworthy discrimination capacity of 85%. The MEDI-LITE score that best discriminated between adherents and non-adherents (optimal cut-off point) was 8.50. The sensitivity for this cut-off value was 96% and the specificity was 38%.<sup>27</sup> For this reason, the tool was used and proposed by many authors in dissimilar subgroups.<sup>28–31</sup>

## 2.3 | Statistical analysis

All analyses were conducted on SPSS (version 27.0). As first step, we examined the missing values. Pairwise deletion was used when a case had missing answers.

### 2.3.1 | Sample description

Descriptive statistics, such as frequencies, percentages, mean [ $\pm$ standard deviation (SD)] or median (and range and/or quartiles), were used to describe the sample’s characteristics.

### 2.3.2 | Preliminary analyses to select Quality of Life-related variables

To investigate the relationships between personal data, lifestyle patterns, physical activity, employment and adherence to Mediterranean diet and QoL, we computed the Pearson Product

Moment Correlation coefficients. To compare two or more subgroups, we used the independent samples *t*-tests (if two) and one-way ANOVAs (if more than two) with Bonferroni post hoc (i.e., multiple comparisons between every possible combination of pairs were carried out). In detail, Pearson's correlations were calculated for PCS-12 and MCS-12 scores, age and MEDI-LITE score. According to Cohen,<sup>32</sup> a correlation coefficient from .10 to .30 represents a weak or small association, a correlation coefficient from .30 to .50 is considered a moderate correlation and a correlation coefficient of .50 or larger is thought to represent a strong or large correlation. Differences in PCS-12 and MCS-12 scores were assessed using *t*-tests to compare gender, caregiver (yes, no), smoking (yes, no), independent groups and one-way ANOVAs to compare educational level (primary school, secondary school, high school and university), place of stay in Italy (north, centre, south) independent groups, occupation (blue collar, white collar, unemployed/retired), time from LT (1–5 yrs, 6–10 yrs, more than 10 yrs), alcohol consumption (no, occasionally, continuously), and level of physical activity (low, medium, high). As measures of effect size (Cohen, 1992), *d* was used for *t*-test (values from 0.2 to 0.5 are indicators of a small effect, values from 0.5 to 0.8 represent a medium effect and values from 0.8 a large effect), the partial eta squared ( $\eta^2$ ) for ANOVAs (values lower than 0.06 suggest a small effect, values from 0.06 to 0.14 a medium effect, values from 0.14 a large effect). Finally,  $\chi^2$  tests were used to compare dichotomized PCS-12 and MCS-12 scores and the above-mentioned categorical variables of the study. All together, these analyses were used to identify the potential predictors of impaired QoL.

### 2.3.3 | Multivariate analysis to identify predictors of impaired Quality of Life

A multivariable logistic regression analysis was performed to identify independent predictors of QoL. We used the 25th percentile/1st quartile as a cutoff to identify impaired QoL (1 = scores lower or equal to 25th percentile) versus not impaired QoL (0 = scores higher than the 25th percentile) as outcome variable, and to include both metric and categorical variables (dichotomous or polytomous) as independent predictors. As indicators of overall model evaluation, we referred to Hosmer–Lemeshow inferential goodness-of-fit test<sup>33</sup> (lower values and non-significance indicate a good fit to the data) and Nagelkerke  $R^{234}$  (values range from 0 to 1). The degree to which predicted probabilities agree with actual data is expressed as a classification table. Statistical significance of individual predictors was tested using the Wald chi-square statistic ( $p < .05$ ). The resultant predicted probabilities (odds ratios) can be used to determine if higher or lower probabilities are indeed associated with an event (i.e., impaired QoL) given the different levels of the predictor variables (e.g., being male or female). Odds ratios were associated with the 95% confidence interval.

### 2.3.4 | Sample size

For observational studies that involve logistic regression in the analysis, taking a minimum sample size of 500 is typically necessary to derive the statistics that represent the parameters.<sup>35</sup> The other recommended rules of thumb include the following:  $n = 100 + 50i$ , where *i* refers to number of independent variables in the final.<sup>35</sup> In line with the aims of the current study, we hypothesized that at least 8 predictors (gender, age, smoking and alcohol habits, employment, educational level, physical activity and adherence to Mediterranean diet will be included in the analysis) will account for the outcome variable. As such, we calculated to enrol at least 500 patients (i.e.,  $100 + [50 \times 8] = 500$ ).

## 2.4 | ETHICS STATEMENT

The present study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments,<sup>36</sup> and it was approved by the Local Independent Ethics Committee (“Comitato Etico Area Vasta Centro”) (approval number 20659).

The reporting of this study conforms to STROBE guidelines.<sup>37</sup>

## 3 | RESULTS

### 3.1 | Sample description

The questionnaire was administered to 511 patients (71% men) with a mean age of 63.1 yrs ( $SD \pm 10.8$ ). Data on socio-demographic and clinical information on tobacco and alcohol use are reported in [Table 1](#).

### 3.2 | Preliminary analyses to select Quality of Life-related variables

Means, standard deviations and bivariate correlations of the SF-12 physical (PCS-12) and mental (MCS-12) with age, sedentary activity score of the IPAQ (SA-IPAQ) and the MEDI-LITE score are shown in [Table 2](#). We observed statistically relevant correlations of the PCS-12 score with age and the MEDI-LITE score ( $p < .01$ ). Moreover, a significant negative correlation was observed between MCS-12 and the IPAQ sedentary activity score ( $p < .05$ ). All the other correlations were not significant.

Female patients scored significantly lower than male patients on the PCS-12 and MCS-12 ( $t[507] = 2.52, p < .05$ ; Cohen's  $d = .25$  and  $t[509] = 3.61, p < .001$ ; Cohen's  $d = .35$  respectively), indicating that, in general, women experienced lower physical and mental health. Additionally, those who had a caregiver scored significantly higher on the PCS-12 ( $t[507] = 2.22, p < .05$ ; Cohen's  $d = -.25$ ), but not on

TABLE 1 Main demographic, social and lifestyle patterns

Variable	N	%
Gender		
Male	362	70.8
Female	149	29.2
Education		
Primary school	60	11.7
Secondary school	197	38.6
High school	193	37.8
University	61	11.9
Place of residence		
North	231	45.2
Centre	197	38.6
South	83	16.2
Occupation		
Blue collar	111	21.7
White collar	141	27.6
Unemployed/Retired	259	50.7
Caregiver		
Yes	152	29.7
No	359	70.3
Hepatology Unit		
Bologna	167	32.7
Bolzano	38	7.4
Caserta	32	6.3
Faenza	27	5.3
Firenze	146	28.6
Modena	63	12.3
Pisa	38	7.4
Time from transplant (years)		
1-5	111	21.7
5-10	154	30.1
>10	246	48.1
Smoking		
Yes	116	22.7
No	395	77.3
Alcohol habit		
No	355	69.5
Occasional	124	24.3
Continuous	32	6.3

MCS-12 ( $t[509] = 1.33, p = .19$ ; Cohen's  $d = -.13$ ). Group mean PCS-12 and MCS-12 scores are displayed in [Figure 1](#).

One-way ANOVAs showed differences in the PCS-12 score by place of stay ( $F[2, 506] = 6.88, p < 0.01, \eta^2 = .026$ ), occupation ( $F[2, 506] = 9.98, p < 0.001, \eta^2 = .038$ ), level of physical activity ( $F[2, 506] = 22.89, p < 0.001, \eta^2 = .083$ ) and alcohol habit ( $F[2, 506] = 6.32, p < 0.01, \eta^2 = .024$ ). Post hoc tests revealed that patients from Central Italy showed higher physical health than patients

from other areas ( $p < 0.01$ ), inactive/retired patients experienced lower physical health than blue ( $p < 0.01$ ) and white ( $p < 0.01$ ) collars. Patients with low physical activity reported lower physical health than those with medium ( $p < 0.001$ ) or high ( $p < 0.001$ ) activity, and patients who occasionally consume alcohol showed better physical health than patients who never ( $p < 0.05$ ) or continuously ( $p < 0.01$ ) drink alcohol. Mean PCS-12 and MCS-12 scores in relation to these parameters are displayed in [Figure 2](#).

### 3.3 | Multivariate analysis to identify predictors of impaired Quality of life

Preliminarily, PCS-12 and MCS-12 outcome variables were dichotomized using the 25th percentile (corresponding to 41 and 42 respectively). Since inactive/retired patients reported lower PCS-12 scores when compared to blue and white collars, but no differences were detected between these two groups, the predictor variable "occupation" was transformed in a dichotomous variable (i.e., inactive/retired vs. blue/white collars). Similarly, because medium and high activity patients did not differ on PCS-12, the predictor "physical activity" was also dichotomised (i.e., low physical activity vs. medium/high activity). Finally, place of stay was not included as predictor because the variable is specifically related to the geographical characteristics of Italy and the geographical location of the Hepatology Units.

In [Table 3](#), we reported frequencies and percentages for each predictor and the relative statistics tests to compare the two groups defined upon the 25th percentile of the PMC-12 and MCS-12 scores (i.e., impaired vs. not impaired QoL groups). Except for the difference in the MEDI-LITE score that was observed also between groups based on the 25th percentile of the MCS-12, results are in line with the previous reported analyses, and they can be resumed as follows. Comparing the impaired versus not impaired physical health groups, higher percentages of female, unemployed/retired, low activity, low adherence to the diet, older patients belonged to the impaired group. Comparing the impaired versus not impaired mental health groups, higher percentages of female, sedentary activity and low adherence to the diet patients belonged to the impaired group.

The specific weight of each predictor is reported in [Table 4](#). Female patients were 1.65 times more likely to report impaired PCS-12 than males. Occupation and physical activity also displayed a significant positive in relation to QoL, indicating that workers or patients with medium/high activity were less likely to report impaired PCS-12 than unemployed/retired or low activity patients (Odds ratio 1.77 and 3.71 respectively). MEDI-LITE score was also a relevant predictor, and for each one-point increase in the score, the patient was .84 times less likely to report impaired QoL.

When mental health was analysed ([Table 4](#)), female patients were 1.78 times more likely to report impaired MCS-12 than male patients. Sedentary activity and the MEDI-LITE score were additional significant predictors, and for each one-point increase in the score, the patient was 1.51 more likely and .88 times less likely to report impaired MCS-12 respectively.

Variable	M	SD	(1)	(2)	(3)	(4)
(1) Age	63.08	10.78	—			
(2) MEDI-LITE	10.40	2.19	.02 <sup>a</sup>	—		
(3) SA-IPAQ	251.52	148.13	.01 <sup>a</sup>	.09 <sup>a</sup>	—	
(4) PCS-12	47.26	9.57	-.16 <sup>**</sup>	.20 <sup>**</sup>	-.08 <sup>a</sup>	—
(5) MCS-12	49.34	9.90	.05 <sup>a</sup>	.05 <sup>a</sup>	-.11 <sup>*</sup>	.09 <sup>a</sup>

Note: N = 506–511.

Abbreviations: MCS-12, Mental health score; MEDI-LITE, adherence to the Mediterranean diet score; PCS-12, Physical health score; SA-IPAQ, Sedentary activity score of the International Physical Activity Questionnaire.

<sup>a</sup>ns.

\* $p < .05$ ; \*\* $p < .01$ .

TABLE 2 Pearson's correlates between the metric variables in the study

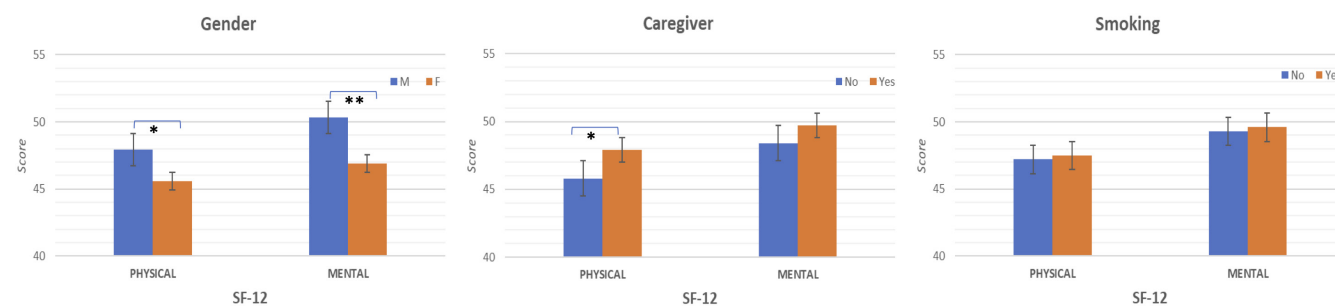


FIGURE 1 Mean scores of the physical and mental scores of the Short Form health survey (SF-12) across gender, caregiver presence and smoking habit (\* $p < .05$ , \*\* $p < .001$ )

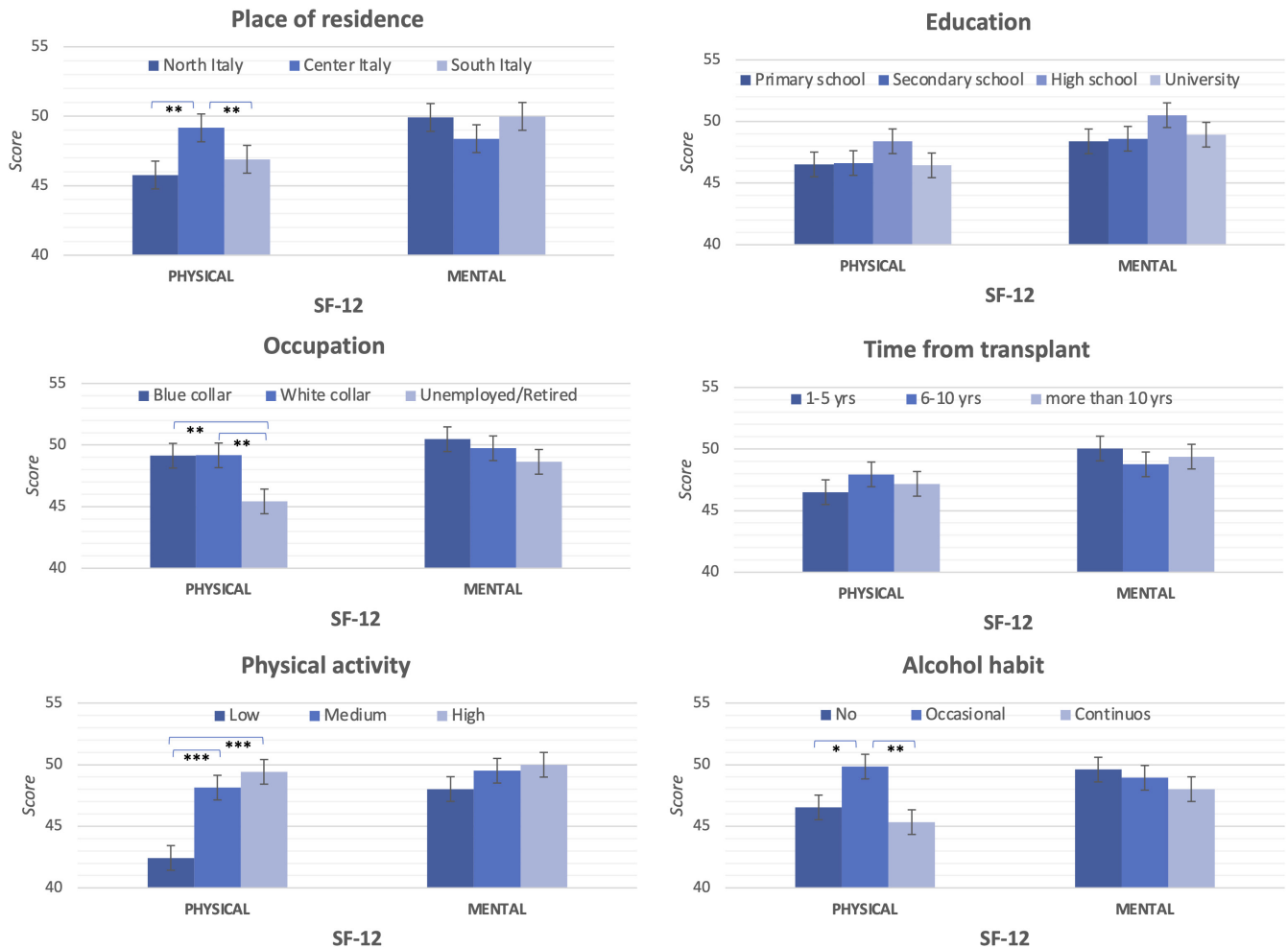
## 4 | DISCUSSION

To our knowledge, this is the first study reporting the QoL of LT recipients during the pandemic and exploring other important features of the patient's everyday life such as lifestyle patterns, physical activity, employment and eating habits. This multicentre study demonstrates that female gender, sedentary lifestyle and low adherence to a Mediterranean diet were independently associated with impaired QoL in both PCS-12 and MCS-12. Moreover, inactive status (vs. active work) and low (vs. medium-high) physical activity were significantly related to lower PCS-12. Interestingly, MCS-12 did not differ by place of residence, educational level, occupation, time from transplantation, level of physical activity or alcohol habit.

We found that female patients had significantly lower scores than males in both PCS-12 and MCS-12. Of note, females experience numerous challenges in the post-transplant period, which may include greater risk for osteoporosis upon post-menopause metabolic changes.<sup>38</sup> Desai et al.<sup>39</sup> demonstrated that after LT, female gender was associated with a worse QoL (in PCS-12) than males. Notably, women show lower levels of QoL than men also in other contexts such as older adults<sup>40</sup> or patients with cardiovascular disease.<sup>41</sup> Thus, our data and those of previous studies indicate that clinical practitioners should pay special attention to LT female recipients seeking treatment and offer specialized medical and psychosocial resources to address their unique needs.

Our data about the positive impact of physical activity on QoL are coherent with data reported in other studies. Post-transplant physical activity, self-care, mobility and total energy expenditure were all associated with improved QoL in LT recipients.<sup>42</sup> Interestingly, involvement in group sport activities was associated with improved physical function and QoL.<sup>43,44</sup> According to our data, a sedentary lifestyle independently correlated with both MCS-12 and PCS-12 and patients reporting low physical activity had lower PCS-12 than subjects with medium and high activity. Along these lines, we also provide evidence that inactive or retired patients experienced lower PCS-12 than active workers, independently of the type of occupation (blue- or white-collar). Both physical activity and occupation maintained a significant positive correlation to QoL in the multivariate model, indicating that patients on a medium/high activity or an active working status are less likely to report impaired PCS-12 than unemployed/retired or low activity patients.

An original finding of the present study is that adherence to a Mediterranean diet is a significant and independent predictor of better QoL in LT. These data are in line with those recently reported<sup>45</sup> in a large cohort study in the Italian general population, demonstrating that adherence to a Mediterranean diet was related to an enhanced perceived QoL. A positive association between Mediterranean diet and QoL was also reported by Gailella-Zabalza et al.<sup>46</sup> who analysed data from Spanish patients affected by metabolic syndrome. To explain the link between diet and QoL, we should also consider that there are indirect connections between diet and lifestyle and mental



**FIGURE 2** Mean scores of the physical and mental scores of the Short Form health survey (SF-12) across place of stay, educational level, occupation, time from transplantation, physical activity and alcohol habit (\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ )

disorders, including socioeconomic conditions, obesity and existence of patterns related to chronic diseases.<sup>47</sup> Additional support to our findings is provided by recent data<sup>48</sup> from two retrospective Italian cohorts, showing that psychological distress from the COVID-19 quarantine was directly related to unhealthy diet variations.

The present study can be particularly important also because data on LT recipients' QoL from studies conducted before the COVID-19 pandemic are controversial. Some authors described a significant increase in QoL during the first year after LT in a relevant percentage of cases and a steady state in the subsequent years.<sup>49</sup> However, other authors reported criticisms about the QoL evolution during the years. Masala et al.<sup>50</sup> suggested that LT recipients are more prone to develop psychological and emotional distress and lower physical functioning than the general population. Drent et al.<sup>51</sup> reported that QoL after LT can be satisfactory but below the levels of the general population, and Burra et al.<sup>52</sup> suggested that QoL tends to significantly decline after LT.

The study reported herein is the first analysing the QoL during the COVID-19 pandemic in a multisite investigation that sampled a large cohort of LT patients across many Italian regions. While this is a major strength of our work, some limitations should be acknowledged. First,

the present study is based on self-reports, and objective measures of physical or mental well-being (e.g., physical mobility testing or cognitive testing) were not utilized. Future studies should employ objective measures along with self-report to better assess the QoL outcomes. Second, we utilized a cross-sectional study design and thus, causality could not be fully determined based on the current findings. Future longitudinal designs may decipher the distinction and directionality of the described associations. Third, owing to the cross-sectional design, we did not report assessment outside the time-window of the pandemic. In the future, longitudinal studies analysing the modifications from pandemic to post-pandemic period would be useful and interesting. Finally, we decided to include only patients in stable clinical conditions. Recent pathological conditions per se influence not only the QoL but also the other main issues that we analysed (sport, diet, work activity). For example, in the general population, hospitalization induces a reduction of both muscle strength and QoL in adults and elderly.<sup>53</sup> Therefore, the enrollment of unstable subjects would not have allowed us neither to accurately detect the possible modifiable predictors of impaired QoL nor to analyse the other aspects of the everyday life of LT recipients. On the other hand, the present study cannot represent the whole post-LT population.



TABLE 3 Demographic, social and lifestyle patterns by physical and mental health (impaired/not impaired) groups

	PCS-12		p	MCS-12		p
	≤ 25th percentile (N = 127)	> 25th percentile (N = 382)		≤ 25th percentile (N = 126)	> 25th percentile (N = 385)	
	f (%)			f (%)		
Gender						
Male	80 (63%)	281 (74%)	.023	77 (61%)	285 (74%)	.006
Female	47 (37%)	101 (26%)		49 (39%)	100 (26%)	
Occupation						
Blue/White collar	46 (36%)	205 (54%)	<.001	53 (42%)	189 (52%)	.061
Unemployed/Retired	81 (64%)	177 (46%)		73 (58%)	186 (48%)	
Caregiver						
No	66 (36%)	106 (28%)	.071	45 (36%)	107 (28%)	.091
Yes	81 (64%)	276 (72%)		81 (64%)	278 (72%)	
Alcohol habit						
No	97 (74%)	256 (67%)	.030	86 (68%)	269 (70%)	.671
Occasional	20 (16%)	104 (27%)		30 (24%)	94 (24%)	
Continuous	10 (8%)	22 (6%)		10 (8%)	22 (6%)	
Physical activity						
Low	55 (43%)	66 (17%)	<.001	36 (29%)	85 (22%)	.137
Medium/High	72 (57%)	316 (83%)		90 (71%)	300 (78%)	
	M (SD)			M (SD)		
Age	65.00 (9.51)	62.39 (11.11)	.018	63.74 (10.00)	62.95 (11.03)	.639
MEDI-LITE	9.68 (2.23)	10.64 (2.14)	<.001	9.96 (2.32)	10.55 (2.14)	.009
SA-IPAQ	272.13 (175.42)	245.05 (137.72)	.12	275.16 (165.65)	243.79 (141.31)	.039

Note: Comparisons were made using  $\chi^2$  test (categorical variables) and *t*-test (metric variables).

Abbreviations: MEDI-LITE, adherence to the Mediterranean diet score; SA-IPAQ, Sedentary activity score of the International Physical Activity Questionnaire.

TABLE 4 Multivariable logistic regression analysis with physical and mental health (impaired/not impaired) as outcome variable

Variable	$\beta$	SE $\beta$	Wald's $\chi^2$	df	p	Odds ratio ( $e^\beta$ )	95% CI ( $e^\beta$ )
PSC-12							
Age	0.02	0.01	2.37	1	.12	1.02	0.99–1.04
Gender	0.50	0.24	4.33	1	.04	1.65	1.03–2.60
Occupation	0.57	0.24	5.65	1	.02	1.77	1.11–2.83
Caregiver	0.27	0.24	1.32	1	.25	1.32	0.82–2.11
Physical activity	1.31	0.24	29.96	1	<.001	3.71	2.32–5.93
MEDI-LITE score	−0.17	0.05	11.00	1	.001	0.84	0.76–0.93
Alcohol habit							
0 vs. 1 & 2	−0.15	0.44	0.08	1	.78	0.88	0.37–2.11
1 vs. 0 & 2	−0.60	0.50	1.47	1	.26	0.55	0.21–1.45
Overall model evaluation: Goodness-of-fit test: Hosmer & Lemeshow: $\chi^2 = 16.66$ , df = 8, p = .03. Nagelkerke $R^2 = .19$ . Correct classification: 76.6%.							
MSC-12							
Gender	0.57	0.22	6.86	1	.009	1.78	1.56–2.74
SA-IPAQ	0.001	0.001	4.27	1	.022	1.51	1.06–2.14
MEDI-LITE score	−0.13	0.05	7.84	1	.005	0.88	0.80–0.96
Overall model evaluation: Goodness-of-fit test: Hosmer & Lemeshow: $\chi^2 = 11.48$ , df = 8, p = .18. Nagelkerke $R^2 = .06$ . Correct classification: 76.1%.							

Note: Variable coding: Gender: 1 = male, 2 = female; Occupation: 1 = unemployed/retired, 2 = blue/white collar; Caregiver: 1 = yes; 0 = no; Physical activity: 1 = low, 2 = medium/high; Alcohol habit: continuous = 2; occasional = 1; no = 0; Physical/Mental health: 1 = impaired, 0 = not impaired. The model evaluation indicators suggested an acceptable goodness of fit for the PCS-12 and MCS-12 models.

Abbreviations: MEDI-LITE, adherence to the Mediterranean diet score; SA-IPAQ, Sedentary activity score of the International Physical Activity Questionnaire

In conclusion, considering LT recipients, females and patients with sedentary lifestyle or work inactive seem to show lower QoL scores than their counterpart. Sport activities and a Mediterranean diet might help LT recipients to improve their QoL. The transplant community might implement a network of information and support encouraging physical activity and adherence to a healthy Mediterranean-style diet. Further targeted studies should better investigate the gender differences by attempting to eliminate the clinical and social disadvantages of women.

#### CONFLICT OF INTEREST

Nothing to declare.

#### ETHICS APPROVAL STATEMENT

The present study was approved by the Local Independent Ethics Committee ("Comitato Etico Area Vasta Centro") (approval number 20659).

#### PATIENT CONSENT STATEMENT

Patients provided informed consent before participating in the study.

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#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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