

# BMJ Open Fatigue and its associated factors in liver transplant recipients in Beijing: a cross-sectional study

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## ABSTRACT

**Objectives:** Fatigue is a highly prevalent symptom experienced by patients who underwent the liver transplantation. However, the influencing factors of fatigue are poorly understood by healthcare professionals. The aim of this study was to examine the intensity, interference, duration and prevalence of fatigue in liver transplantation recipients and to explore the influencing factors of post-transplantation fatigue.

**Design:** A cross-sectional design was used in this study.

**Methods:** A convenience sample of liver transplant recipients was recruited at an outpatient transplant clinic of a general hospital in Beijing, China. Self-report survey data were provided by liver transplant recipients using the Fatigue Symptom Inventory (FSI), the Hospital Anxiety and Depression Scale (HADS), the Perceived Social Support Scale (PSSS) and the Athens Insomnia Scale (AIS). Demographic, clinical and psychosocial parameters were evaluated as fatigue influencing factors.

**Results:** Participants (n=285) included 69 women and 216 men. Fatigue was found in 87.0% of liver transplant recipients. Mean scores of fatigue intensity items were 4.47±2.85, 1.93±1.97, 3.15±2.13 and 2.73±2.42 (most fatigue, least fatigue, average fatigue in the week prior to assessment and fatigue at the point of assessment). The mean score of fatigue interference was 2.27±2.09. The number of days fatigued in the week prior to assessment was 2.26±2.02 and the amount of time fatigued each day was 2.75±2.44. Spearman's correlation analysis showed that fatigue intensity was positively associated with anxiety, depression and insomnia ( $p<0.001$  for all), while fatigue interference was positively associated with gender, anxiety, depression and insomnia ( $p<0.05$  for all). In the multiple linear regression analysis, anxiety and insomnia were positively associated with fatigue intensity ( $p<0.001$ ), and insomnia, depression and anxiety were positively associated with fatigue interference ( $p<0.001$ ).

**Conclusions:** Fatigue is common in liver transplant recipients, and it is strongly associated with insomnia, anxiety and depression.

## INTRODUCTION

Fatigue is generally described and measured as a multidimensional phenomenon,

## Strengths and limitations of this study

- This study examined the intensity, interference, duration and prevalence of fatigue in patients after liver transplantation in China.
- This is the first study to explore the influencing factors of post-transplantation fatigue in liver transplantation recipients in China.
- A single-centre cross-sectional survey may lead to problems about the representativeness of the liver transplantation recipients in China.

including experienced fatigue and physiological fatigue: experienced fatigue is usually defined as an overwhelming sense of tiredness, lack of energy and feeling of exhaustion, while physiological fatigue has been defined as an exercise-induced reduction in maximal voluntary muscle force.<sup>1</sup> Fatigue is a common symptom among patients with chronic disease, such as cancer survivors, multiple sclerosis, neurological illnesses, post-stroke patients and so on.<sup>2-5</sup> It reported that many patients with end-stage liver diseases experienced severe fatigue and the fatigue reduce their level of physical activity and quality of life.<sup>6 7</sup> The pathogenesis of fatigue in cirrhosis is complex, with numerous associated peripheral and central nervous system (CNS) features.<sup>8</sup> Cholestasis causes degenerative CNS change affecting areas of the brain regulating autonomic dysfunction and sleep, and these changes lead directly to some manifestations of fatigue and the associated cognitive impairment. In addition to this, autonomic dysfunction contributes to the impact of this metabolic change by limiting the capacity of the muscle to respond through increased proton/lactate efflux from cells and outflow from tissues.<sup>8</sup> Sarcopenia, a frequent complication in cirrhosis, while the loss of skeletal muscle mass may lead to patients' fatigue, was reported to have adverse effect on patients' recovery and

postliver transplantation survival.<sup>9</sup> Another complication in cirrhosis, hepatic encephalopathy, may be another reason for patients' fatigue, for it is related to anaemia and fat-free mass depletion.<sup>10</sup> Many studies found that fatigue among patients with end-stage liver diseases was associated with their depression, autonomic dysfunction and sleep disturbance.<sup>11 12</sup>

Liver transplantation (LT) has emerged as the best liver replacement therapy of choice and an excellent life-saving treatment option for patients with end-stage liver disease. However, the role of LT for the relief of fatigue in patients with end-stage liver disease is unclear. The literature comparing fatigue severity in patients with cirrhosis before and after LT determined that LT recipients had a significant improvement on fatigue scores after LT.<sup>13 14</sup> However, some scholars doubted the conclusion and pointed out that there may be some bias in these studies: the group of patients was small and had a considerable drop-out rate (mainly due to death or to the withdrew from the study after LT), for whom died or withdrew after LT might have more fatigue than those stayed in the study.<sup>14-16</sup> In addition, compared with the general population and community controls, LT recipients' fatigue scores were significantly worse.<sup>13 14</sup> High rates of fatigue prevalence (66%) have been reported after successful LT,<sup>17</sup> and fatigue is still a major problem in patients after LT.

The theory of unpleasant symptoms (TOUS) asserts that there are three categories of factors influencing a patient's symptom experience: physiological factors, psychological factors and situational factors.<sup>18</sup> Physiological factors include anatomical/structural, physiological, genetic, illness-related and treatment-related variables; psychological factors include both affective and cognitive variables; situational factors include the individual's social environment and physical environment.<sup>19</sup> Fatigue, as a common symptom in patients after liver transplant, might be influenced by these diverse factors. Severe fatigue may reduce LT recipients' daily activities and hinder their recovery and return to work. For those recipients who had been back to work, chronic fatigue may reduce their work efficiency and increase security risks. In addition, long-term fatigue may increase negative emotions. This cross-sectional study examines the fatigue of liver transplant recipients in China and explores whether demographic variables, insomnia, social support and mood disorders were associated with fatigue, thereby providing a basis for health professionals to facilitate the development and implementation of specific interventions to relieve the fatigue of liver transplant recipients.

## PARTICIPANTS AND METHODS

### Participants

This investigation employed a cross-sectional design to assess the fatigue status in liver transplant recipients and its influencing factors. Two hundred and eighty-five adult

liver transplant recipients were recruited, using a convenience sampling strategy, when they visited transplant follow-up clinics in one general hospital in Beijing, China from April to November 2015. Recipients who met the following criteria were eligible to participate: (1) at least 18 years old, (2) 3 months or more post-LT, (3) functional liver graft, (4) ability to speak and read Chinese, and (5) willingness to participate in this study. Patients who had multiple organ transplants or who had more than one liver transplant were excluded from this study.

### Measurement

A structured questionnaire was used to assess fatigue, physical status, psychological variables and situational factors of liver transplant recipients. The questionnaire was composed of five sections examining: demographic information, fatigue, anxiety and depression, insomnia and social support. It was completed in the transplant follow-up clinics. Demographic information included current age, gender, body mass index (BMI), employment status, education, marital status, whether the transplant was self-paid or paid by national insurance, and family financial income. Transplant-specific information, such as the date of transplant and whether the liver was from a living or deceased donor, was also collected. According to the TOUS, these aforementioned variables, which may influence LT recipients' fatigue symptoms, can be divided into three categories. Physiological factors included recipients' age, gender, BMI and duration after LT (calculated by the date of transplant and the date of assessment). Psychological factors included anxiety, depression and insomnia, while situational factors included recipients' employment status and social support.

### Fatigue

The Fatigue Symptom Inventory (FSI) was adopted to assess the transplant recipient's fatigue during the past week. The scale was developed by Hann *et al*<sup>20</sup> in 1998. Yang Shoumei *et al*<sup>21</sup> translated FSI into Chinese and used it in 121 Chinese patients with cancer receiving chemotherapy. This 13-item self-report measurement was designed to measure the fatigue intensity (4 items) and duration of fatigue (2 items) as well as a subscale (7 items) which measures the extent to which fatigue interfered with quality of life. The intensity items require a respondent's rating of the most, least and average fatigue in the week prior to assessment, and fatigue at the point of assessment on an 11-point scale (0=not at all fatigued and 10=extreme fatigue). The average of four intensity item scores is the intensity scale score, with a higher score indicating more intense fatigue. Two duration items assess fatigue duration, including the number of days in the week prior to assessment (0-7 days) and the amount of time each day (0=none of the day and 10=the entire day) fatigue was present. The interference items assess the extent to which fatigue interfered with a respondent's general

activity level, ability to bathe and dress, work activity, ability to concentrate, relations with others, enjoyment of life and mood during the previous week prior to assessment using an 11-point rating scale (0=no interference and 10=extreme interference). The average of seven interference item scores is the interference scale score, with a higher score indicating more influence of fatigue to quality of life. The interference scale was found to have good internal consistency (Cronbach's  $\alpha=0.93$ ). In this study, the Cronbach's  $\alpha$  coefficient of FSI interference scale was 0.941.

### Anxiety and depression

Anxiety and depression of liver transplant recipients were measured by the Hospital Anxiety and Depression Scale (HADS), formulated by Zigmond and Snaith<sup>22</sup> to identify possible or probable anxiety and depression among patients in non-psychiatric clinical settings. Each of the HADS anxiety and depression subscales consists of seven related items. Each item is rated on a four-point scale from 0 to 3, yielding a maximum score of 21 for each subscale. A score of 8 or more with either subscale is considered to indicate a significant disorder. A score of 7 or less is considered normal. The optimal balance between sensitivity and specificity for both subscales was suggested by the original authors: a score of 8 or more for anxiety has a specificity of 0.78 and a sensitivity of 0.90, and for depression a specificity of 0.79 and a sensitivity of 0.83. The HADS has been translated into Chinese by Leung *et al*<sup>23</sup> in 1993. The Cronbach's  $\alpha$  coefficient of HADS anxiety and depression subscales in this study were 0.821 and 0.783, respectively.

### Insomnia

The Athens Insomnia Scale (AIS) was used to measure insomnia in liver transplant recipients. AIS was developed by Soldatos *et al*<sup>24</sup> and has been widely used in different populations around the world. It includes eight items: the first five pertain to sleep induction, awakenings during the night, final awakening, total sleep duration and sleep quality, while the last three refer to well-being, functioning capacity and sleepiness during the day. Each item scores from 0 (no problem at all) to 3 (a very serious problem). This gives a total score ranging from 0 to 24. A total score of 6 or more indicates insomnia. The Cronbach's  $\alpha$  of AIS was 0.89, and the test-retest reliability correlation coefficient was found to be 0.89 at a 1-week interval, with individual item values ranging from 0.70 to 0.86. The Cronbach's  $\alpha$  coefficient of AIS in this study was 0.874.

### Social support

The Perceived Social Support Scale (PSSS) was adopted to assess the liver transplant recipient's social support. PSSS was developed by Zimet *et al*<sup>25</sup> and demonstrated good internal reliability (Cronbach's  $\alpha=0.85-0.91$ ) and good stability (test-retest value=0.72-0.85). Huang *et al*<sup>26</sup> translated PSSS into Chinese and examined its

components with factor analysis. PSSS includes 12 items and the items were divided into three subscales relating to the source of the support (family, friends and significant other). Each of these subscales consists of four items, and each item ranges from very strongly disagree (score=1) to very strongly agree (score=7). The average score of 4 items in each subscale was the subscale score (range=1-7), and the average score of all 12 items was the total score (range=1-7), with higher scores indicating higher perceived social support from their social networks. In this study, the Cronbach's  $\alpha$  coefficient of PSSS subscales (family, friends and significant other) and scale as a whole were 0.815, 0.918, 0.813 and 0.917, respectively.

### Ethical considerations

Ethical approval had been obtained from the hospital and university ethics committee, which requires processes to ensure the confidentiality of all data. The purpose, risks and benefits of this study were explained to the patients before they were asked to participate. The patients were assured that participation was voluntary, and that choosing not to participate would not influence their clinical care. The organ transplant donors involved in our study were not from a vulnerable population and they were informed and voluntary to donate their organ.

### Data collection procedures

Investigators were trained before the survey to make sure that they were familiar with the requirements and methods of data collection. The principal investigator prepared survey questionnaires. Survey packets and a cover letter with a description of the project, response confidentiality, consent procedure and investigator contact information were packaged in unsealed envelopes. Packets were distributed to liver transplant recipients when they attended the liver transplant follow-up clinic. Written informed consent was obtained from all participants. The investigators were present at the clinic to answer patients' questions. Patients returned the survey packet at the clinic after they completed. Patients did not put their name or any other identifying information on the surveys.

### Statistical analysis

Original data were input into Excel software and checked by two research assistants. Data were statistically analysed using SPSS V.21.0 software. Data were summarised as the mean and SD or as frequency and percentages for all demographic, clinical and outcome measures. Spearman's correlation analysis was conducted to find the correlation relationship between fatigue intensity and demographic, anxiety, depression, insomnia and social support. To find the fatigue influencing factors among demographic, clinical and psychosocial parameters, multiple linear regression analysis was conducted. Statistical significance was set at  $p<0.05$ , two tails.

**RESULTS****Participant characteristics**

A total of 300 questionnaires were distributed and all were returned (the return rate is 100%), of which 15 were incomplete and therefore invalid. Data from the remaining 285 questionnaires were included in the

analysis. The characteristics of the 285 recipients are shown in [table 1](#).

**Intensity, interference, duration and prevalence of fatigue**

A total of 248 (87.0%) LT recipients reported fatigue on the average in the week prior to assessment (their

**Table 1** Liver transplant recipient characteristics

Variables	n (%)	Mean/SD	Range
Age (years)		53.31/10.18	26–75
Gender			
Male	216 (75.8)		
Female	69 (24.2)		
BMI			
<18.5	16 (5.6)		
18.5–23.9	137 (48.1)		
24.0–27.9	97 (34.0)		
≥28.0	35 (12.3)		
Employed			
Yes	107 (37.5)		
No	178 (62.5)		
Education			
Middle school or below	60 (21.1)		
High school or technical secondary school	71 (24.9)		
College degree or above	154 (54.0)		
Marital status			
Married	273 (95.8)		
Single/widowed/divorced	12 (4.2)		
Medical payment			
By self	58 (20.4)		
Public service or medical insurance	227 (79.6)		
Family income (¥/month)			
≤3000	64 (22.5)		
3000–6000	113 (39.6)		
>6000	108 (37.9)		
Economic burden			
No burden	28 (9.8)		
Mild	64 (22.5)		
Moderate	99 (34.7)		
Severe	94 (33.0)		
Donor			
Deceased	281 (98.6)		
Living	4 (1.4)		
Duration after LT (month)		59.80/46.93	3.02–314.17
Anxiety			
≥8	36 (12.6)	3.83/3.27	0–13
<8	249 (87.4)		
Depression			
≥8	39 (13.7)	3.41/3.23	0–13
<8	246 (86.3)		
Insomnia			
≥6	138 (48.4)	5.75/4.09	0–19
<6	147 (51.6)		
Social support			
Family		6.08/1.03	1–7
Friends		5.33/1.34	1–7
Significant other		5.45/1.17	1–7

BMI, body mass index; LT, liver transplantation.

**Table 2** Liver transplant recipients' scores on the FSI

	Range	Mean	SD
Intensity ratings (subscale score)		3.07	2.05
Most fatigue	0–10	4.47	2.85
Least fatigue	0–9	1.93	1.97
Average fatigue	0–9	3.15	2.13
Fatigue at the point of assessment	0–10	2.73	2.42
Duration ratings			
Number of days fatigued	0–7	2.26	2.02
Amount of time fatigued	0–10	2.75	2.44
Interference scale (subscale score)		2.27	2.09
General activity level	0–10	2.78	2.62
Ability to bathe and dress	0–10	1.39	2.13
Work activity	0–10	2.12	2.42
Ability to concentrate	0–10	2.21	2.22
Relations with others	0–9	2.26	2.34
Enjoyment of life	0–10	2.61	2.70
Mood	0–10	2.48	2.59

FSI, Fatigue Symptom Inventory.

average fatigue score >0). The intensity, interference and duration of fatigue are shown in table 2. Mean scores of fatigue intensity items were 4.47±2.85, 1.93±1.97, 3.15±2.13, 2.73±2.42 (most fatigue, least fatigue, average fatigue in the week prior to assessment and fatigue at the point of assessment). The number of days fatigued in the previous week prior to assessment was 2.26±2.02 and the amount of time fatigued each day was 2.75±2.44 (0=none of the day and 10=the entire day). The mean score of fatigue interference was 2.27±2.09. Ranking fatigue interference scores in descending order, the seven dimensions were fatigue interfered with general activity level, enjoyment of life, mood, relations with others, ability to concentrate, work activity, and ability to bathe and dress.

Considering that LT recipients who had longer time after LT may have better functional recovery and less fatigue than those who had LT in the short time, we divided 285 LT recipients into the early post-transplant recipient group (time after LT≤5 years) and late post-transplant recipient group (time after LT>5 years). We compared the FSI 13-item scores between the two groups with non-parametric test (none of the scores obeyed the normal distribution) and found that there were no significant differences between the two group scores (table 3).

### Association between fatigue and other variables

Neither the scores of fatigue intensity nor fatigue interference obeyed the normal distribution; Spearman's correlation analysis was adopted to find the association between fatigue and other variables. The correlations between fatigue intensity/interference and other variables are shown in table 4. Fatigue intensity was significantly and positively correlated with anxiety ( $r_s=0.454$ ,  $p<0.001$ ), depression ( $r_s=0.429$ ,  $p<0.001$ ) and insomnia ( $r_s=0.561$ ,  $p<0.001$ ), while fatigue interference was significantly and positively correlated with gender ( $r_s=0.119$ ,  $p=0.044$ ), anxiety ( $r_s=0.534$ ,  $p<0.001$ ), depression ( $r_s=0.489$ ,  $p<0.001$ ) and insomnia ( $r_s=0.541$ ,  $p<0.001$ ). There were no significant correlation between fatigue with age, BMI, employment status, duration after LT, and social support from others ( $p>0.05$ ).

### Influencing factors of fatigue

A multiple linear regression analysis was conducted to determine the influencing factors of fatigue as assessed by FSI intensity score and interference score. Variables which were significantly correlated with fatigue intensity and fatigue interference in the Spearman's correlation analysis (table 4, anxiety, depression and insomnia were

**Table 3** FSI scores in early and late post-transplant recipient groups.

	Mean rank (early postgroup, n=157)	Mean rank (late postgroup, n=128)	Z	p
Intensity ratings				
Most fatigue	140.51	146.05	-0.569	0.569
Least fatigue	139.66	147.09	-0.775	0.438
Average fatigue	139.25	147.61	-0.860	0.390
Fatigue at the point of assessment	137.83	149.34	-1.187	0.235
Duration ratings				
Number of days fatigued	143.32	142.61	-0.073	0.942
Amount of time fatigued	143.92	141.88	-0.226	0.822
Interference scale				
General activity level	149.65	134.84	-1.551	0.121
Ability to bathe and dress	143.78	142.05	-0.180	0.857
Work activity	141.29	145.10	-0.397	0.692
Ability to concentrate	143.21	142.74	-0.049	0.961
Relations with others	143.93	141.86	-0.215	0.830
Enjoyment of life	144.66	140.97	-0.383	0.702
Mood	146.38	138.86	-0.776	0.437

FSI, Fatigue Symptom Inventory.

**Table 4** Correlations between fatigue scores and scores on other variables

	Fatigue intensity		Fatigue interference	
	$r_s$	p Value	$r_s$	p Value
Age	-0.002	0.978	-0.013	0.821
Gender(1=male, 2=female)	0.101	0.088	0.119	0.044*
BMI	-0.032	0.594	-0.106	0.073
Employment	0.043	0.469	0.056	0.342
Duration after LT	0.073	0.219	-0.037	0.529
Anxiety	0.454	0.000*	0.534	0.000*
Depression	0.429	0.000*	0.489	0.000*
Insomnia	0.561	0.000*	0.541	0.000*
Family support	-0.062	0.301	-0.055	0.355
Friends' support	-0.038	0.520	-0.094	0.114
Significant others' support	-0.088	0.138	-0.089	0.132

\*p&lt;0.05.

BMI, body mass index; LT, liver transplantation.

associated with fatigue intensity; gender, anxiety, depression and insomnia were associated with fatigue interference) were entered into the regression analysis as independent variables. Through the backward and forward methods, it was found that anxiety and insomnia were included in the linear regression model of fatigue intensity, and insomnia, depression and anxiety were included in the linear regression model of fatigue interference (tables 5 and 6). The variables explained 31.3% (fatigue intensity:  $R=0.560$ ,  $R^2=0.313$ ) and 36.2% (fatigue interference:  $R=0.602$ ,  $R^2=0.362$ ) of the total variance, and each made a significant contribution to the prediction of fatigue ( $p<0.001$  for each variable). F value was 64.352 (fatigue intensity,  $p<0.05$ ) and 53.103 (fatigue interference,  $p<0.05$ ), indicating that the linear regression equations were statistically significant.

## DISCUSSION

### Fatigue is common among liver transplant recipients

Fatigue is often experienced after LT. In our study, 87.0% of liver transplant recipients on average reported fatigue in the week prior to assessment, indicating a high prevalence of fatigue in LT recipients. The result is in agreement with those from previously published studies (66–76%).<sup>17–27</sup> The average score of fatigue intensity during the previous week before assessment

**Table 5** Regression analysis of fatigue intensity in liver transplant recipients.

	$\beta$	SE	$\beta'$	t	p Value
Constant	1.350	0.182	–	7.409	0.000*
Insomnia	0.209	0.029	0.418	7.278	0.000*
Anxiety	0.135	0.036	0.216	3.754	0.000*

\*p&lt;0.05.

**Table 6** Regression analysis of fatigue interference in liver transplant recipients

	$\beta$	SE	$\beta'$	t	p Value
Constant	0.397	0.181	–	2.196	0.029*
Insomnia	0.167	0.029	0.326	5.836	0.000*
Depression	0.134	0.047	0.207	2.885	0.004*
Anxiety	0.118	0.048	0.184	2.463	0.014*

\*p&lt;0.05.

was 3.07 (10=extreme fatigue) and there were 2.26 days in the week prior to assessment that recipients experienced fatigue, indicating a frequent and mild fatigue the LT recipients experienced. Even 3 years after LT, fatigue was still the third most frequent and distressing symptom.<sup>28</sup> In our study, there were no significant differences between early and late post-transplant recipient groups in FSI 13-item scores, indicating that recipients' fatigue symptoms persisted for a long time after LT. LT recipients had slightly more fatigue, although compared with the pretransplant patients they still had a greater load of fatigue compared with normal individuals.<sup>13–14</sup> It is reported that apart from hepatic mechanism, extrahepatic mechanism may lead to fatigue in patients with liver diseases, including autonomic nervous system dysfunction, progesterone metabolites, psychological elements, mitochondrial dysfunction, cytokines and adipokines as well as structural cerebral abnormalities.<sup>16</sup> Extrahepatic mechanism and persistent organic brain injury caused by liver diseases before LT may explain why patients' fatigue persisted after LT.

### Interference of fatigue with recipients' quality of life and daily activities

Fatigue has a major impact on quality of life and daily activities.<sup>29</sup> Berbke's research found that patients with more severe symptoms of fatigue had larger deficits in cardiorespiratory fitness than patients with less severe symptoms of fatigue, implying that cardiorespiratory fitness and body composition were impaired in liver transplant recipients and that fitness was related to severity of fatigue and quality of life.<sup>30</sup> It reported that liver transplant recipients experience physical fatigue and had reduced activity rather than mental fatigue and reduced motivation.<sup>17–31</sup> In our study, we found that fatigue among LT recipients had moderate interference on their quality of life, and general activity level was the most affected aspect. This was similar to results obtained in previous studies. Fatigue is a complex symptom and makes people feel malaise, exhaustion, lethargy, and loss of motivation and social interest,<sup>15</sup> which had an impact on recipients' enjoyment of life, mood, relations with others, ability to concentrate and work activity.

### Factors influencing fatigue intensity and interference in LT recipients

Several studies have found that sleep quality of LT recipients was associated with fatigue,<sup>32</sup> and that patients with

high fatigue severity were significantly more likely to have been taking sleep medication than patients with low fatigue severity.<sup>27</sup> In our study, insomnia was moderately positively correlated with fatigue intensity and fatigue interference, and the result of linear regression showed that insomnia was the influencing factors of fatigue among LT recipients, indicating that poor sleep quality is at increased risk of fatigue intensity and interference post-transplantation. Having poor sleep quality at night, recipients often felt tired and found it hard to concentrate in the daytime; their exercise decreased, finally affecting their physiological function and leading to their reporting more weakness and fatigue.

Another influencing factor of fatigue among LT recipients was mood disturbance. It was reported that high fatigue severity was associated with higher total mood disturbance.<sup>27 32</sup> We found that both anxiety and depression were positively correlated with fatigue intensity and fatigue interference, and the result of linear regression showed that anxiety was the influencing factor of fatigue intensity while anxiety and depression were the influencing factors of fatigue interference among LT recipients. Anxiety and depression in LT recipients may be due to recipients' experience of a major life event or because they have adopted the 'sick role' and have difficulty readjusting to a healthy role.<sup>33</sup> These negative emotions make recipients lose interest and enthusiasm for life, and may lead to their mental and emotional fatigue. In addition to this, mood disturbance and insomnia often interact with and aggravate each other, which may lead to patients' physical fatigue. Insomnia, anxiety and depression often coexist with fatigue and should be targeted by healthcare providers' interventions designed to reduce fatigue in LT recipients.

In our study, gender was correlated with fatigue interference, indicating that female recipients obtained more fatigue interference on their quality of life than male recipients. This result met with van den Berg-Emons *et al*<sup>17</sup>'s research, which found that women were more severely fatigued than men. No relations were found between fatigue with age, employment status and duration after LT in our study; however, there were different results in previous studies. It found that older recipients were more severely fatigued than younger recipients;<sup>17</sup> working and having undergone LT 4–5 years previously were associated with less physical fatigue than not working and having undergone LT 1–3 years previously.<sup>31</sup> The difference in results may be due to differences in sampling groups. In our study, recipients who had a LT <3 months previously were excluded, considering that their condition was not stable. These excluded recipients might have different fatigue sense compared with those included in the study. van den Berg-Emons *et al*<sup>17</sup> included recipients who were discharged 3 weeks or more, and Aadahl *et al*<sup>31</sup> excluded recipients who received their liver transplant <1 year because they are not long-time survivors.

## CONCLUSION

The current study showed that fatigue is common among liver transplant recipients in China and negatively influences the recipient's quality of life and daily activities. Anxiety, depression and insomnia were the influencing factors of fatigue intensity and fatigue interference. The recipients who had severe insomnia and mood disorders felt severe fatigue and greater influence caused by fatigue. It suggests that healthcare providers should pay more attention to recipients' fatigue and to other coexisting symptoms. Some intervention, such as rehabilitation programme, antidepressant drugs treatment and sleep medicine, may be necessary and helpful.

## LIMITATIONS AND RECOMMENDATIONS

This study has certain limitations such as being a single-centre cross-sectional survey. Additional longitudinal studies of fatigue in liver transplant recipients are needed. We only measured LT recipients' BMI, and other indices of their nutritional and sarcopenic status were not assessed and measured. Also, we did not report LT recipients' indications, MELD scores and post-transplant status which might be associated with their fatigue. More influencing factors, such as recipients' nutritional status, sarcopenic status, renal function, cardiorespiratory fitness, anaemia, primary disease diagnosis, and pretransplant and post-transplant status, should be considered and explored in future research.

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**Contributors** X-HL participated in the data collection and data analysis and drafted the manuscript. H-XL designed the study and revised the manuscript. Y-JZ, LW and JZ participated in the data collection. JZ provided suggestions for the manuscript. ST and Y-BS executed the scheme and collected data. All authors read and approved the final manuscript.

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