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# Sleep Quality and Psychosocial Factors in Liver Transplant Recipients at an Outpatient Follow-Up Clinic in China

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**Background:** Sleep disturbance is a common problem in liver transplant recipients, but few studies have confirmed the psychosocial factors associated with sleep quality in patients after liver transplantation. This study aimed to identify the psychosocial factors related to sleep quality among liver transplant patients during outpatient follow-up.

**Material/Methods:** A retrospective cross-sectional study was performed in 124 liver transplant patients during outpatient follow-up. All participants completed a general demographic questionnaire, the Pittsburgh Sleep Quality Index (PSQI), the Generalized Anxiety Disorder-7 scale (GAD-7), the Patient Health Questionnaire-9 (PHQ-9), and the perceived social support scale (PSSS).

**Results:** The mean global PSQI score was 6.57 (SD, 4.28), which was significantly higher than the mean score for people with normal sleep quality; 50 (40.3%) recipients were classified as having poor sleep quality (PSQI >7). Among the self-reported sleep problems, 62 (50.0%) participants reported that they had to go to the bathroom at night, 58 (43.5%) woke up in the middle of the night or early morning, 84 (67.7%) reported depression symptoms, and 116 (93.5%) had low-level social support. The global PSQI score was positively correlated with anxiety and depression scores, while the global PSSS score was negatively correlated with anxiety and depression scores ( $p < 0.01$ ). Multiple linear regression analysis showed that the length of the post-liver transplant period, the type of residence, BMI, depressive symptoms, and anxiety symptoms were important factors affecting sleep quality among liver transplant patients ( $p < 0.05$ ).

**Conclusions:** Our findings showed high prevalence and incidence of poor sleep quality in liver transplant recipients in outpatient follow-up, with significant correlations with anxiety, depression, and social support, and it was affected by multiple factors. This indicates a need for further research on the follow-up results of sleep and the benefits of comprehensive interventions involving psychosocial factors in liver transplant recipients in China.

**MeSH Keywords:** China • Liver Transplantation • Outpatients • Psychology • Sleep

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## Background

Liver transplantation is considered to be the most effective method for the treatment of end-stage liver disease [1]. In 2017, there were 4733 liver transplants performed in China, ranking second in the world [2], and the survival rates of liver transplant recipients after 1 year and 5 years were 92.0% and 87.5%, respectively [3].

Some studies have demonstrated that liver transplantation improved health-related quality of life and survival rates of patients [4–7]. However, it is surprising that the patients after liver transplantation still have serious sleep disorders, such as sleep latency, sleep disturbances, and daytime dysfunction, and these issues lasted for several years [7–9]. Poor sleep quality can result in poor prognosis in liver transplantation patients [4,10].

It is clear that sleep quality is closely related to psychosocial factors [11]. Although liver transplantation has improved patients' quality of life, it has resulted in little improvement in patients' psychological function [12,13]. Patients still have psychological problems such as anxiety, depression, stress, and insufficient social support after liver transplantation [14–16]. Few studies have linked these psychological factors to the quality of sleep in liver transplant recipients in outpatient follow-up.

Thus, we investigated some psychosocial factors, including social-demographic variables, anxiety, and depression to assess the psychosocial factors related to sleep quality among liver transplant patients in outpatient follow-up.

## Material and Methods

### Design

This cross-sectional survey was conducted at the follow-up clinic of the Organ Transplantation Center of the Third Xiangya Hospital of Central South University, Changsha, Hunan Province. This study passed the ethical review of the Human Subjects Institutional Review Board at the Third Xiangya Hospital of Central South University in July 2018.

### Participants

A total of 124 liver transplant recipients were recruited from the follow-up outpatient clinic between January and June 2019. The inclusion criteria were: age  $\geq 18$  years old, had liver transplant surgery, could speak and read Mandarin, and signed informed consent for voluntary participation in the study. The exclusion criteria were: diagnosed with severe mental illness, cognitive impairment, or physical impermissibility judged by a physician.

### Study procedures

When the patient came to the outpatient clinic, the doctor invited patients who met the inclusion criteria to participate in our study. Participants were invited to complete all questionnaires in different rooms. When the participants completed the questionnaires, a free medicine box was given as a token of appreciation for their participation.

### Instruments

#### *General Demographic Questionnaire*

Information on sex, age, marital status, educational level, career, body mass index (BMI), residence, type of residence, sleep pattern, personal monthly income, family monthly income per capita, length of posttransplant period, and immunosuppressant withdrawal were collected.

#### *Pittsburgh Sleep Quality Index (PSQI)*

The PSQI was used to assess the quality of sleep in the past month [17]. It consists of 19 self-evaluation items, and it is divided into 7 components. Every component ranges from 0 to 3. The total score of the 7 components is the global score of the PSQI, which ranges from 0 to 21. A higher PSQI score indicates worse sleep quality. In China, a global score on the PSQI that was higher than 7 points is considered poor sleep quality, showing good sensitivity (98.3%) and specificity (90.2%) [18].

#### *Generalized Anxiety Disorder-7 scale (GAD-7)*

The GAD-7 is a self-assessment questionnaire based on the DSM-IV, which was published by Spitzer et al. in 2006 [19]. It is used to assess the severity of anxiety in the past 2 weeks. This scale has been used in China and has been proven to have good sensitivity and specificity ( $>85\%$ ) [20]. The scale includes 7 items, with each item score ranging from 0 (not at all) to 3 (almost every day). The severity of anxiety was based on the global score: no anxiety (0–4 points); mild anxiety (5–9 points); moderate anxiety (10–14 points); and severe anxiety ( $\geq 15$  points).

#### *The Patient Health Questionnaire-9 (PHQ-9)*

The PHQ-9 was compiled by Spitzer et al. based on the DSM-IV in 1999 [21]. It is a 9-item self-report instrument used to assess the severity of depressive symptoms over the past 2 weeks [22]. All items have scores ranging from 0 (not at all) to 3 (almost every day), and the total score for the scale ranges from 0 to 21. By calculating the total score of the scale, we can judge the severity of depression: no depression (0–4 points); mild depression (5–9 points); moderate depression (10–14 points);

and severe depression (15–27 points) [23]. In China, the PHQ-9 has been widely used in assessment of depression in the general population [24].

### **Perceived Social Support Scale (PSSS)**

The PSSS used in our study was developed by Zimet (1988) et al. and was revised by Huang Li (2006) et al. [25,26]. The scale consists of 3 dimensions and 12 items. The 7-point Likert scale was used in all items, with “1” indicating “totally disagree” and “7” indicating “totally agree”. The total score for the scale ranges from 7 to 84. Cronbach’s  $\alpha$  for the PSSS was 0.921 [27]. The PSSS emphasizes the individual’s understanding and feeling of social support sources (family, friends, others). The total score reflects the degree of social support felt by the individual, with higher scores indicating better social support.

### **Data analysis**

All questionnaire information was entered into a computer. The data analysis was performed using SPSS 20.0 (SPSS, Inc., Chicago, Ill, United States). Descriptive statistics are expressed in terms of frequency, percentage, mean, and standard deviation. One-way ANOVA and multiple linear regression analyses were used to find the main variables affecting PSQI. Pearson correlation analysis was performed to explore the correlations between PSQI and GAD-7, PHQ-9, and PSSS.

## **Results**

### **General demographic information**

A total of 126 questionnaires were distributed and all were returned (the return rate was 100%); 2 were incomplete and therefore invalid. Information from the remaining 124 patients was included in the analysis. The characteristics of the 124 recipients are shown in Table 1. There were 100 (80.6%) males and 24 (19.4%) females. They were between 24 and 76 years of age, with a mean age of  $48.52 \pm 11.00$  years. Sixty (48.4%) recipients were employed. A total of 114 (91.9%) recipients were married; 42 (33.9%) of the recipients had a middle school education or below. A total of 119 (96%) patients lived with family members, and 63 (50.8%) sleep with others. Regarding residence, 79.8% of the patients lived in urban areas. BMI was available for 98 (79.0%) patients and ranged from 18.5 to 24.9.

### **Overall evaluation of the PSQI, GAD-7, PHQ-9, and PSSS**

A total of 50 (40.3%) recipients were poor sleepers (global PSQI  $>7$ ). The global PSQI score was 6.57 (SD, 4.28), which exceeded the score of the Chinese general public (3.88 [SD, 2.52]) [18]. In the 7 components, the highest average scores

were subjective sleep quality (1.34 [SD, 1.17]), and the lowest average scores were the use of hypnotic medication (0.13 [SD, 0.42]). The mean sleep time was 6.88 (SD, 1.39), but 37 (29.8%) of patients has sleep inefficiency (sleep efficiency  $<85\%$ , based on PSQI). Only 2 (1.6%) patients reported using sleep medications at least once in the last month. Among self-reported sleep problems, 50.0% of participants reported getting up to use the bathroom, 43.5% reported waking up in the middle of the night or early morning, and 38.7% reported that they could not get to sleep within 30 minutes.

Moreover, 28 (22.6%) liver transplant recipients had anxiety symptoms (GAD-7  $>4$ ), 84 (66.7%) recipients had depression symptoms (PHQ-9  $>4$ ), and 116 (93.5%) participants reported having low levels of social support ( $12 \leq \text{PSSS} \leq 36$ ) (Table 2). Among the PSSS, the average score for each item ranged from 1.44 to 2.02, and the scores of family social support were lowest.

### **Psychological factors affecting PSQI scores in liver transplant patients**

In Table 3, the ANOVA findings showed that there were statistically significant differences in the global PSQI scores among education level, the length of post-liver transplant period, family lifestyle, depressive symptoms, anxious symptoms, and whether immunosuppressant withdrawal occurred ( $p < 0.05$ ). The total score of the PSQI in the depression group was significantly higher than that in the no-depression group. The global PSQI scores of patients with anxiety symptoms were higher than those of patients without anxiety symptoms ( $p < 0.05$ ). The global PSQI scores in the patients who were living with others were higher than the scores of those who were living alone ( $p < 0.05$ ). Although most (93.5%) liver transplant recipients had low levels of social support, there was no significant difference in the global PSQI scores between patients with different social support levels. The PSQI scores of participants with different ages, sexes, careers, family monthly income per capita, personal monthly income, BMI, marriage status, and sleep patterns were not statistically significant ( $p > 0.05$ ).

### **Correlation between the PSQI, GAD-7, PHQ-9 and PSSS**

The global PSQI, GAD-7, PHQ-9, and PSSS scores were introduced in the Pearson correlation analysis equation according to the significance of the variables and researchers’ experience and expertise. There were significant positive correlations among the PSQI scores, GAD-7 scores, and PHQ-9 scores. There was no correlation between the PSQI scores and PSSS scores. The relationships were all in the expected direction: worse sleep quality, more depression, and more anxiety. However, there were significant correlations among the PSSS, GAD-7, and PHQ-9, meaning lower social support, more depression symptoms, and more anxiety symptoms ( $p < 0.01$ ) (Table 4).

**Table 1.** General demographic information of liver transplant recipients.

Characteristic	No.	%	Characteristic	No.	%
Sex		Residence			
Male	100	80.6	City	99	79.8
Female	24	19.4	Countryside	25	20.2
Education level		Length of post-liver transplant period (months)			
Middle school or below	42	33.9	<6	32	25.8
High school	36	29	6–12	25	20.2
Technical school or college	30	24.2	12–36	38	30.6
Undergraduate or above	16	12.9	>36	29	23.4
Age (years)		Career			
18–44	51	41.1	Employed	60	48.4
45–59	53	42.7	Unemployed	64	51.6
≥60	20	16.1	BMI		
Family monthly income per capita (CNY)		<18.5			
1000–4000	13	10.5	18.5–24.9	98	79
4000–7000	32	25.8	≥25	13	10.5
7000–10000	52	41.9	Type of residence		
>10000	27	21.8	Living alone	5	4
Personal monthly income (CNY)		Live with family			
<1000	36	29.0	Sleep pattern		
1000–3000	47	37.9	Sleep alone	61	49.2
>3000	41	33.1	Sleep with others	63	50.8
Marital status		Immunosuppressant withdrawal			
Single/widowed/divorced	10	8.1	No	117	94.4
Married	114	91.9	Yes	7	5.6

**Table 2.** Overall evaluation of the PSQI, GAD-7, PHQ-9, and PSSS among liver transplant patients.

Variables	Minimum	Maximum	Mean (SD)
Subjective sleep quality	0	3	1.34 (1.17)
Sleep onset latency	0	3	1.19 (1.03)
Sleep duration	0	3	1.04 (0.90)
Sleep efficiency	0	3	0.55 (0.97)
Sleep disturbance	0	2	1.04 (0.52)
Use of hypnotic medication	0	3	0.13 (0.42)
Daytime dysfunction	0	3	1.29 (1.05)
PSQI	0	20	6.57 (4.28)
GAD-7	0	17	2.30 (3.35)
PHQ-9	0	16	2.84 (3.84)
PSSS	12	50	20.48 (8.38)

**Table 3.** Psychological factors affecting PSQI scores in liver transplant patients.

Items	Global PSQI Score	Subjective sleep quality	Sleep onset latency	Sleep duration	Sleep efficiency	Sleep disturbance	Use of hypnotic medication	Daytime dysfunction
<b>Education level</b>								
Middle school or below	7.83 (4.91)	1.81 (1.15)	1.40 (1.15)	1.14 (0.93)	0.79 (1.07)	1.02 (0.52)	0.17 (0.54)	1.50 (1.13)
High school	5.19 (3.56)	0.97 (1.06)	1.00 (1.04)	0.78 (0.80)	0.25 (0.69)	1.08 (0.60)	0.03 (0.17)	1.08 (1.00)
Technical school or college	5.93 (3.90)	1.20 (1.22)	1.07 (0.91)	0.93 (0.94)	0.33 (0.80)	0.90 (0.40)	0.17 (0.38)	1.33 (1.12)
Undergraduate or above	7.56 (3.85)	1.19 (1.05)	1.25 (0.86)	1.56 (0.73)	1.00 (1.27)	1.25 (0.45)	0.19 (0.54)	1.13 (0.72)
F	3.116	3.953	75.000	3.347	98.847	1.747	120.032	71.36
p	0.029	0.010	0.000	0.021	0.000	0.161	0.000	0.000
<b>Length of post-liver transplant period (months)</b>								
<6	9.44 (4.27)	2.28 (1.02)	1.72 (0.99)	1.31 (0.90)	0.81 (1.03)	1.16 (0.52)	0.25 (0.62)	1.91 (1.06)
6–12	6.96 (3.88)	1.72 (1.17)	1.08 (0.91)	0.80 (0.82)	0.68 (1.15)	1.12 (0.44)	0.04 (0.20)	1.52 (0.92)
12–26	5.68 (3.91)	0.89 (0.80)	1.18 (1.04)	1.11 (0.95)	0.45 (0.95)	0.92 (0.59)	0.16 (0.44)	0.97 (1.03)
>36	4.24 (3.32)	0.55 (0.87)	0.69 (0.93)	0.86 (0.83)	0.28 (0.70)	1.00 (0.46)	0.03 (0.19)	0.83 (0.81)
F	10.075	17.92	5.781	2.086	69.143	1.488	115.034	8.380
p	0.000	0.000	0.001	0.106	0.000	0.221	0.000	0.000
<b>Type of residence</b>								
Live alone	2.00 (1.87)	0.40 (0.55)	0.00 (0.00)	0.20 (0.45)	0.20 (0.45)	0.60 (0.55)	0.00 (0.00)	0.60 (0.89)
Live with family	6.76 (4.25)	1.38 (1.17)	1.24 (1.02)	1.08 (0.89)	0.56 (0.99)	1.06 (0.51)	0.13 (0.43)	1.32 (1.05)
t	-2.488	-3.657	-13.177	-2.172	-0.815	-1.969	-0.696	-1.509
p	0.014	0.012	0.000	0.032	0.417	0.051	0.488	0.134
<b>GAD-7</b>								
≤4	5.76 (3.82)	1.19 (1.11)	1.05 (1.01)	0.97 (0.86)	0.46 (0.88)	0.93 (0.44)	0.08 (0.31)	1.08 (0.96)
>5	9.36 (4.67)	1.86 (1.24)	1.64 (0.99)	1.29 (0.98)	0.86 (1.21)	1.43 (0.57)	0.29 (0.66)	2.00 (1.05)
t	-4.161	-2.739	-2.732	-1.658	-1.625	-4.278	-1.575	-4.352
p	0.000	0.007	0.007	0.100	0.113	0.000	0.126	0.000
<b>PHQ-9</b>								
≤4	4.97 (3.61)	0.93 (1.00)	0.93 (0.92)	0.80 (0.82)	0.40 (0.87)	0.95 (0.50)	0.05 (0.22)	0.93 (1.00)
>5	7.33 (4.39)	1.54 (1.20)	1.31 (1.06)	1.15 (0.91)	0.62 (1.02)	1.08 (0.52)	0.17 (0.49)	1.46 (1.04)
t	-2.955	-2.983	-2.071	-2.088	-1.172	-1.349	-1.836	-2.744
p	0.004	0.004	0.041	0.039	0.243	0.180	0.069	0.007
<b>Immunosuppressant withdrawal</b>								
No	6.38 (4.19)	1.32 (1.16)	1.15 (1.03)	1.02 (0.89)	0.53 (0.96)	1.00 (0.49)	0.10 (0.38)	1.26 (1.04)
Yes	9.86 (4.88)	1.71 (1.38)	1.86 (0.90)	1.43 (0.98)	0.86 (1.22)	1.71 (0.49)	0.57 (0.79)	1.71 (1.25)
t	-2.118	-0.875	-1.790	-1.182	-0.862	-3.738	-1.566	-1.101
p	0.036	0.383	0.076	0.240	0.390	0.000	0.167	0.273

**Table 4.** Correlation between the PSQI, GAD-7, PHQ-9, and PSSS.

Variables	PSQI	GAD-7	PHQ-9	PSSS
PSQI	1			
GAD-7	0.344**	1		
PHQ-9	0.482**	0.815**	1	
PSSS	-0.135	-0.235**	-0.238**	1

\*\*  $p < 0.01$ .**Table 5.** Multivariable logistic regression analysis of the psychosocial factors affecting sleep quality in liver transplant recipients.

variable	B	SB	t	p
Constant	-9.020		-2.340	0.021*
Age	0.674	0.113	1.505	0.135
Education level	0.384	0.093	1.141	0.256
Length of post-liver transplant period	-1.984	-0.517	-6.582	0.000**
Type of residence	4.097	0.189	2.532	0.013*
GAD-7	2.776	0.272	3.568	0.001**
PHQ-9	1.830	0.201	2.505	0.014*
PSSS	0.518	0.030	0.392	0.695
Immunosuppressant withdrawal	0.391	0.021	0.274	0.784
Sex	1.454	0.135	1.862	0.065
BMI	2.221	0.198	2.552	0.012*
Family monthly income per capita	-0.405	-0.087	-1.067	0.288

95% CI,  $R^2=0.388$ ,  $F=12.350$ ,  $p < 0.001$ . \*  $p < 0.05$ ; \*\*  $p < 0.01$ .

### Multivariate analysis of PSQI scores in liver transplant patients

Although BMI, age, education level, sex, and family monthly income per capita were not significant in the ANOVA, they were also included in the multiple linear regression analysis based on the literature and professional experience. Multivariate linear regression analysis showed that the length of the post-liver transplant period, type of residence, BMI, depressive symptoms, and anxiety symptoms were factors influencing global PSQI scores ( $p < 0.05$ ) (Table 5).

### Discussion

This study describes the frequency of self-reported sleep disturbances and also identified the significant sociodemographic and psychosocial determinants of sleep quality in liver transplant recipients surveyed at the follow-up clinic. The sleep quality of liver transplant recipients was worse than that of

the Chinese general public ( $t: 4.387$ ,  $p < 0.05$ ) [18], and the incidence of poor sleep quality reported by participants (40.2%, poor sleep quality, PSQI score  $> 7$ ) was lower than the rates reported by Akahoshi et al. (68%, poor sleep quality, PSQI  $> 7$ ) and Mendes et al. (71.11%, poor sleep quality, PSQI  $> 5$ ) [8,15]. While total sleep time was adequate on average, it still revealed that recipients had sleep interruption. It was worth noting that 50.0% of recipients had excessive urination at night, about half of the recipients woke up in the middle of the night or early in the morning, and over one-third took more than 30 minutes to fall asleep. Recent studies have confirmed that waking up in the middle of the night, nocturia (excessive urination at night), and difficulty falling asleep were common issues for liver transplant recipients [4,28], but the causes and details of these symptoms have not been studied. In addition, it should be emphasized that only 10.48% of patients reported the use of hypnotic medication in the past month, which is less than that reported by Rodrigue (62.1%) [4]. This may be because the sedatives and hypnotic drugs are prescribed drugs that are strictly regulated, and the patients have to request them from



designated medical institutions in China [29]; some patients may be concerned about drug adverse effects such as memory damage, cognitive impairment, and drug addiction [30,31].

We found that 67.7% of recipients had depression, which was higher than that reported by others. Some scholars have found that the incidence of depression after liver transplantation was 30~40% [32,33]. In the present study, we found strong relationships between sleep quality and depression symptoms, and these findings were consistent with others [16]. Meller et al. reported that liver transplant patients who experienced depression had lower survival rates than in nondepressed patients [34]. Depression symptoms have been confirmed to have a negative effect on liver transplant survival rates [34,35]. Among liver transplant recipients, symptom levels of 6% to 35% had been described for anxiety [36–38]. In our study, 28 (22.6%) participants reported anxiety symptoms, and these symptoms were still strongly correlated with sleep quality. This may be related to adverse effects of immunosuppressants, family financial burdens, inability to participate in work and normal social activities, and worries about hepatitis or tumor recurrence [39]. Our findings suggest that to improve the sleep quality of patients, we should pay attention to patients' negative emotions. Psychological symptoms such as stress and anxiety can have a negative impact on the course of the disease, can impair adherence to treatment, and can affect the quality of life of patients [14].

Social support was an important predictor of mortality after liver transplantation [40]. In our study, 116 (93.55%) patients had low-level support status, and none of the patients had high-level support status, and the family support score was lowest among family, friends, and others. These results all indicate that most liver transplant patients had difficulty in getting social support from family, friends, and others, especially their family members, who provide the least support as their closest companions. Our results are supported by the findings of Langenbach et al. (2008), who reported that low social support scores among patients with liver transplantation and social support had positive significance for the improvement of patients' mental health and quality of life [41]. The findings reported by Gao et al. revealed that high social support had a positive effect on reducing patients' anxiety level, which was the same as reported in our study [42]. In our study, social support level was negatively correlated with anxiety and depression. This finding suggested that families, society, and the government, and especially family members, should be mobilized

to pay attention to this special group, provide them with more social support, alleviate anxiety and depression, and improve the patients' long-term quality of life.

Table 4 shows 4 factors that affect sleep quality. The patients who had a post-liver transplant period length of less than 6 months exhibited anxiety, and patients who were living with others had higher global PSQI scores. Some of our findings are supported by those of previous studies. Mendes et al. indicated that patients with high anxiety levels had an increased incidence of poor sleep quality. A study performed in Swiss patients confirmed that post-liver transplant patients within 6 months of transplant had the highest incidence (36.21%) of poor sleep quality [9]. In addition, patients with a higher BMI, depressive symptoms, and lower family monthly income per capita had a higher risk of sleep disturbances. These findings are supported previous research by Rodrigue et al. (2010) [4]. It was surprising that patients who lived with others had a higher risk of sleep disturbances. This could be because living with others can affect sleep patterns and thus affect sleep quality.

Some limitations of our study need to be mentioned: (1) This study was a single-center, cross-sectional survey, and all of the participants were recruited from an organ transplantation center in Changsha City, Hunan Province; (2) We had a limited number of patients for this study; and (3) We investigated only the effects of some psychological variables on sleep quality, while other psychological variables, such as personality, stress, and self-efficacy, were not considered. In the future, multicenter studies with large samples are needed to confirm our conclusions, and more psychological variables should be included in these studies.

## Conclusions

In conclusion, the present study found that sleep problems were common in liver transplant recipients. Difficulty falling asleep, sleep disruption, and nocturia were major sleep problems. The length of the post-liver transplant period, type of residence, BMI, depressive symptoms, and anxiety symptoms were the main factors affecting sleep quality. The vast majority of patients had low levels of social support. In addition, we found that anxiety and depression symptoms were negatively correlated with sleep quality and social support. Psychosocial interventions are crucial to improve quality of sleep in Chinese liver transplant recipients.

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