

Impact of metabolic syndrome on quality of life of liver transplant recipients

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Abstract

Objective: The incidence of metabolic syndrome (MS) increases after liver transplantation. This study was performed to evaluate the impact of MS on patients' quality of life after liver transplantation.

Methods: We collected the medical records of 152 patients during their post-liver transplantation outpatient follow-up. Quality of life was assessed using the Medical Outcomes Study 36-Item Short Form Health Survey. Data on the patients' general condition as well as MS-related indicators were assessed in all patients. Based on the MS diagnostic criteria proposed by the International Diabetes Federation in 2005, the patients were divided into two groups: those with and without MS. We then analyzed the factors influencing MS and their impact on the patients' quality of life.

Results: After liver transplantation, age and underlying liver disease were significantly associated with MS and diabetes, and sex and body mass index were associated with central obesity. Central obesity affected the patients' general health (GH) score and health transition (HT) score, and hypertension affected their GH score and physical component score (PCS).

Conclusions: After liver transplantation, central obesity had a negative impact on patients' GH score and HT score, and hypertension affected their GH score and PCS.

Keywords

Liver transplantation, metabolic syndrome, quality of life, central obesity, hypertension, 36-Item Short Form

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Introduction

Liver transplantation is an effective treatment for patients with end-stage liver disease.^{1,2} As a result of advances in surgical



techniques and the use of new immunosuppressants, the survival time of patients who have undergone liver transplantation has increased; however, numerous post-transplantation complications still threaten the health of patients. Metabolic syndrome (MS) is a common complication of liver transplantation. The established association between MS and cardiovascular disease reflects an important problem for patients undergoing liver transplantation.³ Many studies have been performed to assess post-liver transplantation MS worldwide,⁴⁻⁶ but the impact of MS on the quality of life (QOL) of liver transplant recipients remains unclear.

In this study, the information of liver transplant recipients was collected and used to retrospectively investigate the incidence of MS and relevant influencing factors. The findings of this study will provide a scientific basis for the diagnosis and treatment of MS and improvement of the QOL of these patients.

Patients and methods

Study design

The data for this epidemiological cohort study were obtained through structured interviews. The study protocol was approved by the Ethics Committee of Beijing You An Hospital. The methods were performed in accordance with the guidelines approved by the Ethics Committee of Beijing You An Hospital.

Patients

Patients who underwent liver transplantation from January 2000 to January 2015 and participated in regular medical follow-up at the Liver Transplantation Center in Beijing You An Hospital were enrolled in this study at least 6 months after the surgical procedure. All patients participating

in the study provided written informed consent. Orthotopic liver transplantation was performed in all patients, followed by a standard immunosuppression regimen consisting of tacrolimus or cyclosporine, mycophenolate mofetil (MMF), and steroids. All patients received identical intraoperative and postoperative care. The exclusion criteria were double transplantation and multiple organ transplantation. Weight and height were measured in all patients.

Questionnaire

QOL was assessed using the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36). We collected information regarding the general conditions of patients as well as MS-related indicators. The SF-36 is currently the most widely used questionnaire to assess the QOL of patients after liver transplantation. It contains 36 descriptive items and assesses health in 8 domains associated with physical health [physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP) and general health (GH)] and mental health [vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH)]. The eight scales are summarized by two component summary scores: the physical component score (PCS) and the mental component score. The scores range from 0 to 100 points; a higher score corresponds to a better domain result. This standard questionnaire does not address sociological information; therefore, the respondents' age, sex, address, education level, marital status, and economic situation were obtained through other means.

The following MS diagnostic criteria were proposed by the International Diabetes Federation in 2005⁷: body mass index (BMI) of >30 kg/m², but the waist circumference does not need to be measured; triglyceride level of >150 mg/dL;

reduced high-density lipoprotein cholesterol level of <40 mg/dL for males and <50 mg/dL for females; a high fasting glucose level (≥ 100 mg/dL); and elevated blood pressure ($\geq 130/85$ mmHg or relevant antihypertensive treatment). According to the established definition, MS is diagnosed when patients have central (abdominal) obesity, which is a prerequisite, plus any two of the above criteria.

The diagnostic criteria for central obesity are based on the waist circumference. According to the International Diabetes Federation, the reference value for waist circumference among Chinese people is >90 cm for males and >80 cm for females. Extensive controversy has surrounded the waist circumference cut-off point for central obesity in recent years. Previous studies have shown that to predict cardiovascular risk, a BMI of ≥ 25.0 kg/m² is more sensitive than a waist-hip ratio of >0.90 (males) and >0.85 (females) as an indicator of overweight/obesity in patients with MS.⁸

In this study, we used the 1999 World Health Organization diagnostic criteria for diabetes (recommended by the 2003 Barcelona International Consensus), which are as follows: diabetic symptoms and random plasma glucose level of ≥ 11.1 mmol/L (200 mg/dL), fasting plasma glucose level of ≥ 7.0 mmol/L (126 mg/dL), or a 2-hour oral glucose tolerance test plasma glucose level of ≥ 11.1 mmol/L; these values must be measured more than twice.

The diagnostic criteria for hypertension are a systolic blood pressure of ≥ 140 mmHg and diastolic blood pressure of <90 mmHg, systolic blood pressure of <140 mmHg and diastolic blood pressure of ≥ 90 mmHg, systolic/diastolic blood pressure of $\geq 140/90$ mmHg, or treatment with antihypertensive drugs after one of the above-mentioned blood pressures was measured prior to medication use.

Statistical analysis

Continuous variables are presented as mean \pm standard deviation. Qualitative variables are presented as percentage and frequency. Statistical analyses were performed using IBM SPSS Statistics, version 19.0 (IBM Corp., Armonk, NY, USA).

Univariate analysis was conducted to evaluate possible associations between patients with and without MS with respect to demographic and clinical characteristics. The independent t-test, chi-square test, and Fisher's exact test were used for data comparisons. Multiple logistic regression analysis was used to determine the independent factors that influence MS and its components. The factors that affected QOL were entered into a multivariate stepwise regression analysis. A P value of <0.05 was considered statistically significant.

Results

Patient sociodemographic characteristics and underlying indications for liver transplantation

In total, 152 patients (125 men, 22 women) were included in this study. The questionnaire response rate was 96.7% (147/152). The patients' sociodemographic characteristics and liver disease data are shown in Table 1. The average age of the patients was 53.96 ± 9.79 years. The mean follow-up time was 52.91 ± 39.29 months. The percentage of patients who were married was 97.28%.

The patients' underlying diseases before liver transplantation were as follows: hepatocellular carcinoma ($n=49$), hepatitis cirrhosis ($n=43$), primary biliary cirrhosis ($n=7$), alcoholic cirrhosis ($n=13$), acute liver failure ($n=26$), and others ($n=9$), including hepatic myelopathy and viral hepatitis combined with alcoholic cirrhosis. The types of immunosuppressants used were

tacrolimus (FK506) (n = 128), cyclosporine A (n = 14), sirolimus (n = 33), MMF (n = 50), and hormone therapy (average dosage of prednisolone = 5 mg/d) (n = 8).

Incidence of MS in patients after liver transplantation

The incidence of MS after liver transplantation was high (46.94%). In the subgroup analysis of MS, central obesity exhibited the highest incidence (53.74%) and dyslipidemia exhibited the lowest incidence (38.78%) among MS components (Table 1).

Comparison of QOL scores between patients with and without MS and its components

Compared with other domains, patients' scores were highest in the PF domain and

lowest in the health transition (HT) domain. The results of our study showed that MS had no specific impact on patients' QOL after liver transplantation. Patients with central obesity had higher GH scores than patients without central obesity. The GH score and PCS of patients with hypertension were lower than those of patients without hypertension (P < 0.05, independent t-test) (Figure 1).

Factors influencing MS

The results of the multiple logistic regression analysis of MS and its components (Table 2) showed that age and underlying liver disease were significantly associated with MS (age, P = 0.001; hepatocellular carcinoma, P = 0.036) and diabetes (age, P = 0.001; hepatocellular carcinoma, P = 0.008; hepatitis cirrhosis, P = 0.009). Sex and BMI were

Table 1. Patients' demographic and clinical characteristics

Characteristics	Patients (n = 147)
Body mass index, kg/m ²	24.21 ± 0.28
Age, years	53.96 ± 9.79
Mean postoperative follow-up time, months	52.91 ± 39.29
Sex	
Female	22
Male	125
Marriage status	
Married	143 (97.28)
Single	4 (2.72)
Immunosuppressant regimen	
Tacrolimus	128 (87.07)
Cyclosporine A	14 (9.52)
Sirolimus	33 (22.45)
Mycophenolate mofetil	50 (34.01)
Hormone	8 (5.44)
Underlying liver disease	
Hepatocellular carcinoma	49 (33.33)
Hepatitis cirrhosis	43 (29.25)
Primary biliary cirrhosis	7 (4.76)
Alcoholic cirrhosis	13 (8.84)
Acute liver failure	26 (17.69)
Others	9 (6.12)
Metabolic syndrome and its components	
Metabolic syndrome	69 (46.94)
Central obesity	79 (53.74)
Diabetes	76 (51.70)
Hypertension	72 (48.97)
Dyslipidemia	57 (38.78)

Data are presented as n, n (%), or mean ± standard deviation.

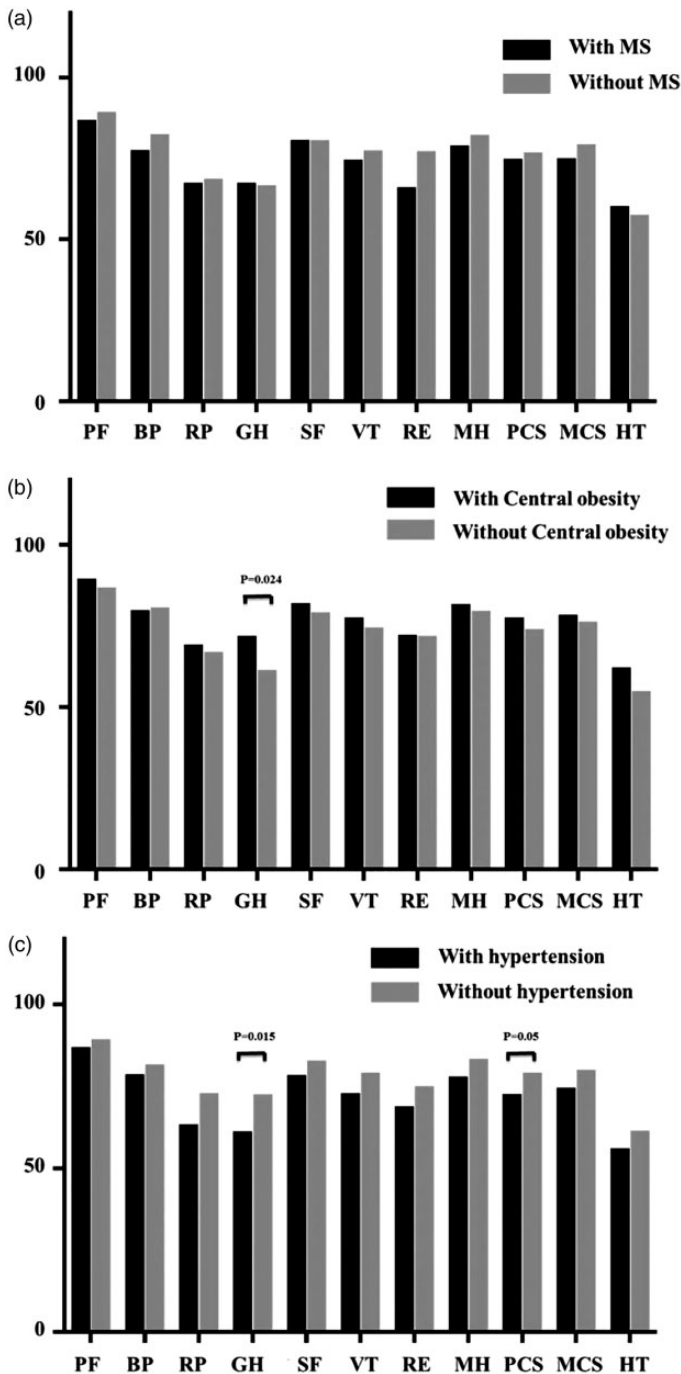


Figure 1. (a) Comparison of quality of life (QOL) scores (8 domains) between patients with and without metabolic syndrome (MS). (b) Comparison of QOL scores (8 domains) between patients with and without central obesity. (c) Comparison of QOL scores (8 domains) between patients with and without hypertension. PF, physical functioning; BP, bodily pain; RP, role limitations due to physical problems; GH, general health; SF, social functioning; VT, vitality; RE, role limitations due to emotional problems; MH, mental health; PCS, physical component score; MCS, mental component score; HT, health transition.

Table 2. Results of multiple logistic regression analysis of metabolic syndrome and its components

Factor	Patients (n = 147)		Multiple logistic regression analysis ^a					
	With MS (n = 69)	Without MS (n = 78)	P	MS	Central obesity	Dyslipidemia	Hypertension	Diabetes
Age, years	56.84 ± 8.34	51.41 ± 10.31	0.001 ^a	1.077 ^{**}	-	-	-	1.068 ^{**}
				(1.035-1.121)				(1.026-1.112)
Sex (male/female)	61/8	64/14	0.001 ^c	-	0.246 [*]	-	-	0.35
					(0.065-0.928)			(0.118-1.038)
Body mass index, kg/m ²	24.87 ± 3.27	23.62 ± 3.32	0.024 ^a	-	2.057 ^{**}	-	-	-
					(1.649-2.565)			
Postoperative follow-up time	56.95 ± 41.56	49.40 ± 37.10	0.248 ^a	-	-	-	-	-
Hepatocellular carcinoma (yes/no)	19/50	30/48	0.161 ^c	2.432 [*]	-	-	-	3.494 ^{**}
				(1.131-5.230)				(1.392-8.771)
Hepatitis cirrhosis (yes/no)	25/44	18/60	0.08 ^c	-	-	-	-	3.445 ^{**}
								(1.343-8.832)
Primary biliary cirrhosis (yes/no)	1/68	6/72	0.121 ^d	8.399	-	-	-	7.116
				(0.950-74.275)				(0.982-51.572)
Alcoholic cirrhosis (yes/no)	6/63	7/71	0.953 ^c	-	-	-	-	-
Acute liver failure (yes/no)	12/57	14/64	0.93 ^c	-	-	-	-	-
Smoking (yes/no)	11/58	7/71	0.198 ^c	-	-	-	-	-
Current alcohol consumption (yes/no)	1/68	4/74	0.371 ^d	-	-	-	-	-
Tacrolimus (yes/no)	63/6	65/13	0.151 ^c	-	-	-	-	-
Cyclosporine A (yes/no)	5/64	9/69	0.376 ^c	-	-	-	-	-
Sirolimus (yes/no)	12/57	21/57	0.167 ^c	-	-	-	-	-
Mycophenolate mofetil (yes/no)	22/47	28/50	0.608 ^c	-	-	-	-	-
Hormone (yes/no)	4/65	4/74	0.57 ^c	-	-	-	-	0.200
								(0.037-1.082)-

Data are presented as n, mean ± standard deviation, or odds ratio (95% confidence interval) unless otherwise indicated.

Methods: ^abackward stepwise (Wald), ^bindependent t test, ^cchi-square test, ^dFisher's exact test.

*P < 0.05, **P < 0.01

MS, metabolic syndrome

associated with central obesity (sex, $P=0.038$; BMI, $P=0.001$). However, immunosuppressant agents did not affect MS or its components in our study.

Impact of MS on patients' QOL after liver transplantation

The results of our analysis (Table 3) showed that MS had no specific impact on patients' QOL after liver transplantation. However, central obesity affected the GH score and HT score, and hypertension affected the GH score and PCS. Diabetes and dyslipidemia had no significant impact on any aspect of QOL. Age was significantly associated with the PF score ($P<0.01$), VT score ($P=0.025$), PCS ($P=0.025$), and HT score ($P=0.036$), and the postoperative follow-up time was associated with the HT score ($P=0.001$). Immunosuppressants, especially cyclosporine A, affected the BP score ($P=0.036$), GH score ($P=0.045$), and HT score ($P=0.003$) of transplant recipients.

Discussion

QOL is an important factor with which to assess the value of liver transplantation. QOL is a multifaceted construct that includes both physical and mental domains. Previous studies have proven a significant improvement in QOL (both mental and physical components) after transplantation.⁹ More than 80% of studies have shown improvements in physical functioning, and 60% of studies have shown improvements in mental and social functioning.¹⁰ In the present study, patients' scores were highest in the PF domain and lowest in the HT domain. Many factors might affect QOL after liver transplantation, such as age, immunosuppressant use, and postoperative complications (Table 3).

Similar to our study, previous studies have shown that MS is a common complication and has a higher incidence after liver

transplantation^{6,11} (35.6%–58.0%) than in the general population in both the United States¹² (23.7%) and China¹³ (12%–14%). Our study also showed high incidences of the components of MS, including hypertension, central obesity, diabetes, and dyslipidemia, which is consistent with similar findings reported previously.^{14,15} The impact of MS on patients' QOL after liver transplantation is multifaceted: long-term diabetes can lead to vascular lesions, dyslipidemia is a high-risk factor for atherosclerosis, hypertension can lead to a high incidence of cerebral vascular accidents, and central obesity can facilitate the emergence of cardiovascular disease risk factors. These complications not only increase patients' medical expenses but may also be life-threatening in severe cases. However, very few studies have been performed to assess the impact of MS on long-term survival of patients after liver transplantation.

Few studies have investigated the impact of MS on QOL of liver transplantation recipients. Notably, the present study is the first to analyze the impact of MS on QOL of liver transplantation recipients. This study showed that MS has no significant impact on patients' QOL. Nevertheless, we found that central obesity affected the GH and HT scores and that hypertension affected the GH score and PCS of transplant recipients, and the differences were statistically significant. These results are theoretically and practically important to adjust immunosuppressive agents when patients develop MS.

Various factors affect the incidence of MS, including many preoperative factors. For example, underlying diseases, obesity, advanced age, and donor gene polymorphisms are risk factors for metabolic diseases after liver transplantation.¹⁶ However, long-term immunosuppressive therapy is a well-known and important cause of MS. In recent years, the results of studies on hormone reduction or removal and minimal calcineurin inhibitor

Table 3. Results of multivariate linear regression analysis of quality of life

Factor		Multivariate linear regression analysis ^a (n = 147)											
		PF	BP	RP	GH	SF	VT	RE	MH	PCS	MCS	HT	
		t	P	t	P	t	P	t	P	t	P	t	P
Age		-4.200	0.000**	-	-	-	-	-	-	-	-	-2.118	0.036**
Postoperative follow-up time		-	-	-	-	-	-	-	-	-	-	-3.420	0.001**
Cyclosporine A		-	-	-	-	-	-	-	-	-	-	-	-
Central obesity		2.115	0.036*	-	-	2.019	0.045*	-	-	-	-	3.018	0.003**
Dyslipidemia		-	-	-	-	2.801	0.006**	-	-	-	-	2.911	0.004**
Hypertension		-	-	-	-	-2.814	0.006**	-	-	-	-	-	-
		-	-	-	-	-	-	-	-	-2.024	0.045*	-	-

^aStepwise analysis'

*P < 0.05, **P < 0.01

PF, physical functioning; BP, bodily pain; RP, role limitations due to physical problems; GH, general health; SF, social functioning; VT, vitality; RE, role limitations due to emotional problems; MH, mental health; PCS, physical component score; MCS, mental component score; HT, health transition.

immunosuppressive regimens have shown that hormone-free MMF or a combination of MMF and reduced calcineurin inhibitor treatment can reduce the adverse effects of other immunosuppressants on metabolic diseases while ensuring the efficacy of immunosuppression in patients after liver transplantation. Although the present study showed no direct correlation between any immunosuppressant and MS, hormones are generally considered to be related to MS after liver transplantation.¹⁷⁻¹⁹ However, hormone therapy was withdrawn during the early postoperative period in our patients. Accordingly, the impact of long-term hormone use on MS requires further study.

Many recent studies have shown that cardiovascular disease is one of the most common late causes of death, accounting for 12% to 16% of deaths (primary or major contributing causes) among liver transplant recipients.²⁰⁻²² Due to the established association between MS and cardiovascular disease, additional attention should be directed toward the management of MS.

In summary, MS is a common complication after liver transplantation and has a significantly higher incidence in post-liver transplant patients than in the general population. Additionally, central obesity exhibits the highest incidence among MS components and shows an upward trend with time. MS has no significant impact on patients' QOL after liver transplantation. However, central obesity affected the GH and HT scores and hypertension affected the GH scores and PCS of transplant recipients in the present study.

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