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A prospective longitudinal cohort study for quality of life in patients undergoing fourth level liver surgery

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Performing fourth-level liver surgery is an exceptionally demanding procedure, fraught with significant risks and technical complexities. Patients undergoing such operations face elevated surgical hazards, substantial physical trauma, prolonged recovery periods, and a multitude of factors that can profoundly impact their postoperative quality of life (QoL). Despite these challenges, there remains a notable gap in the literature regarding the long-term QoL outcomes for these individuals. This study seeks to evaluate the QoL of patients who have undergone fourth-level liver surgery and to identify key factors influencing their recovery. The findings aim to offer clinical insights that can enhance postoperative care and improve patient outcomes. Employing a prospective longitudinal cohort design, this study enrolled patients who received fourth-level liver surgery at a major tertiary hospital in Chengdu, affiliated with a university. QoL assessments were conducted using the EQ-5D-5L scale at three intervals post-discharge: one week, one month, and three months. This study enrolled 125 participants and tracked their health-related QoL using the EQ-5D-5L Utility Index (UI) (health utility values). Initially, 1 week post-discharge, most patients' UI scores fell within the range of - 0.2 to 0.6. These values improved significantly over time, rising to 0.7–1.0 after 1 month and stabilizing between 0.8 and 1.0 by the 3 month mark. On average, patients reported experiencing pain for 4.18 days (±9.72) following discharge. Statistical analyses—both univariate and multivariate—were performed to identify factors influencing QoL at different recovery stages. The findings revealed that admission method was a key determinant of QoL during the 1–3 month period post-discharge. Marital status emerged as a significant factor in the first week, while post-discharge pain levels primarily impacted QoL at the 1 month mark. After fourth-level liver surgery, the vast majority of patients regain their mobility, the ability to care for themselves, and their typical daily activities by 3 months post-discharge. Patients who are admitted to the emergency department tend to experience a lower QoL from 1 to 3 months following their discharge, compared to those who are admitted to the regular department. The persistent pain is a major culprit in diminishing a patient's overall well-being. Consequently, prompt pain management and rehabilitation workouts are essential for expediting recovery and enhancing the patient's QoL.

Keywords Liver surgery, Fourth-level surgery, Quality of life, EQ-5D-5L

In the ASA's (American Society of Anesthesiology, ASA) surgical grading scale, patients are categorized into six tiers, reflecting their physical state and the surgery's potential risks¹. The outcomes can differ greatly across these categories. In 2022, China's National Health Commission overhauled the "Management Measures for Surgical Grading in Medical Institutions," now dividing surgeries into four tiers based on the risk level, complexity, resource usage, or ethical considerations². A fourth-level surgery encompasses those with high risk, intricate procedures, immense difficulty, significant resource demands, or substantial ethical concerns³. This includes high-risk liver surgeries such as liver transplants, partial liver removals, live donor liver resections, and pancreatic transplants. These patients face substantial surgical risks, severe trauma, and a lengthy recovery period. The factors impacting their postoperative quality of life (QoL) are multifaceted^{4,5}. By concentrating on postoperative

¹Liver Transplant Center, Transplant Center, West China Hospital, Sichuan University, Chengdu 610041, China. ²West China School of Nursing, Sichuan University, Chengdu 610041, China. ³Laboratory of Liver Transplantation, Institute of Organ Transplantation, Key Laboratory of Transplant Engineering and Immunology, NHC, West China Hospital of Sichuan University, Chengdu 610041, China. ^{Sem}email: gangxu@wchscu.cn; doctoryjy@163.com QoL and its determinants, and by intervening in modifiable factors during their hospital stay, we can enhance both the QoL and patient satisfaction.

As medical tech advances, the success rates and safety of liver surgeries are on the upswing. QoL is a vital gauge of a patient's overall health, playing a pivotal role in their recovery and outlook after liver surgery. A multitude of factors, such as the surgery's results, the patient's age, gender, and any pre-existing conditions, can impact the QoL of those undergoing advanced liver procedures^{6,7}. The two go-to QoL assessment tools in liver surgery are the SF-36 and the QLQ-C30^{8,9}. A review of the literature reveals that the EuroQol-5 Dimensions (EQ-5D) can boost the sensitivity of health status measurements and mitigate the ceiling effect in chronic liver disease cases¹⁰. There's a gap in research focusing on the QoL of fourth-level liver surgery patients, which is what this study aims to fill. We plan to utilize the Chinese version of the EQ-5D scale to delve into a follow-up study of these patients' QoL and examine the factors that influence it, ultimately aiming to offer clinical insights for enhancing their postoperative QoL.

Methods

Study design and sampling

This research is a prospective longitudinal cohort study that received the green light from the Biomedical Ethics Review Committee of West China Hospital of Sichuan (Review No. 439, 2024). The study adhered to the Helsinki Declaration. Participants were enrolled following a phone consultation, with all patients giving their consent beforehand. We focused on patients who had liver surgery at a top-tier, university-connected hospital in Chengdu, China, from January to March 2024. The criteria for inclusion were: ^① patients hospitalized with liver conditions aged 14 or older; ^② those who underwent fourth-level liver surgery, which encompasses resection and transplantation; ^③ patients and their families were fully informed and willing to collaborate with the research team. The sample size was set to be at least five to ten times the number of variables. Based on past literature, around a dozen factors are known to impact quality of life. Accounting for a potential dropout rate of 10% to 15%, the ideal sample size was estimated to be between 58 and 118 individuals. Consequently, the final sample size for our survey was set at 100 participants.

Survey tool

In the current research, the go-to instrument for assessing the QoL is the universally applicable EuroQol-5 Dimensions (EQ-5D), a scale rooted in self-reported data from patients and crafted by the European Quality of Life Group. This scale encompasses five key aspects: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression¹¹. Initially, the EQ-5D-3L offered three different levels per dimension but has since been enhanced to include five levels for each, giving rise to the EQ-5D-5L^{12,13}. The state of health for each dimension of the EQ-5D can be translated into utility scores using the Utility Index (UI) (health utility values), which is based on preferences from the target population¹⁴. Calculating the UI isn't a one-size-fits-all scenario; it varies from person to person. As a result, distinct health utility scoring systems have been crafted for diverse nations. For our investigation, we employ the EQ-5D-5L scale that Professor LUO developed in 2017, utilizing the Chinese health utility score framework. The UI, which gauges an individual's quality of life, spans from -0.391 to 1.000, with higher scores denoting a superior quality of life. Notably, a score that's below zero indicates a health status deemed worse than death¹⁵.

Data collection

We conducted an in-depth assessment of the QoL for liver disease patients at the 1 week, 1 month, and 3 month marks following their release from the hospital. The evaluation encompassed a range of details about the participants, such as age, gender, diagnostic information, occupation, educational, and body mass value (BMI). We also utilized the EQ-5D-5L scale as a measure. The research team consists of clinically trained nurses who are all uniformly well-versed in their methodologies.

Statistical analysis

Once the follow-up data were gathered and organized, we dived into the analysis with SPSS 26.0. The numbers were broken down into frequencies and percentages, while the counts were presented as averages with their respective standard deviations. We applied the Friedman test to compare the QoL scores across different timeframes. To pinpoint the factors influencing QoL throughout these periods, we conducted both univariate and multivariate analyses. For the univariate dive, we relied on the rank sum test, also known as the Wilcoxon Mann Whitney test. When comparing UI between two groups, we used the two-sample rank sum test. For three or more groups, the Kruskal Wallis diversity rank sum test took the lead. The multivariate approach was handled through multiple regression analysis. A p-value of less than 0.05 signaled that the differences were indeed statistically meaningful.

Results

Analysis of factors influencing patients' QoL

This research involved 136 individuals who underwent fourth-level liver surgery. During the follow-up period, one patient passed away, while ten others were lost to contact (accounting for 7.35% of participants). The remaining 125 patients successfully completed the study. Among these participants, the average age was 49.92 years (\pm 14.50), with men making up the majority at 67.2% (84 out of 125). Hospital stays averaged 15.01 days (\pm 11.69), and post-discharge pain typically lasted 4.18 days (\pm 9.72). The most prevalent condition was decompensated cirrhosis (29.6% of cases), followed by hepatocellular carcinoma.

The univariate analysis revealed that admission method significantly impacted patients' QoL during the first three months post-discharge, while marital status influenced QoL for 1 week after discharge. Postoperative pain levels were found to affect QoL outcomes for 1 month after discharge (Table 1).

Further analysis through multiple regression demonstrated that marital status continued to play a role in QoL during the first week after discharge. Additionally, both postoperative pain and hospital length of stay (LOS) emerged as significant factors influencing QoL at 1 week and 1 month post-discharge (Table 2).

Patient QoL distribution by EQ-5D-5L dimensions

1 week post-discharge QoL assessments revealed widespread functional challenges among patients: nearly all struggled with mobility (92.8%), self-care tasks (93.6%), and regular activities (98.4%), while persistent pain affected 83.2% of cases. By the 1 month follow-up, marked progress emerged in mobility, self-care, and participation in usual activities. The 3 month evaluation demonstrated even greater recovery, with 95.2% of patients regaining mobility, 90.4% achieving independent self-care, and 89.6% resuming regular activities (Fig. 1).

QoL UI at different periods

In the EQ-5D-5L UI distribution charts, taken at 1 week, 1 month, and 3v months post-discharge, the indices failed to exhibit normal distribution (p < 0.05). Consequently, we resorted to reporting the median and quartiles for the data. At 1 week, the median EQ-5D-5L UI was 0.189, with the upper quartile at -0.028 and the lower quartile at 0.459. The minimum value was -0.297, and the maximum reached 1.000, with most patients' UIs hovering around -0.2 to 0.6. One month later, the median UI was 0.907, the upper quartile was 0.663, and the lower quartile was 1.000, with a minimum of -0.030 and a maximum of 1.000. The majority of patients' UIs fell between 0.7 and 1.0. By three months, the median UI was 0.931, while the maximum remained 1.000. For the majority of patients, their UIs were clustered between 0.8 and 1.0 (Fig. 2)..

Friedman test revealed significant variations in EQ-5D-5L UI scores across groups at 1 week, 1 month, and 3 months post-discharge (Table 3).

Discussion

In the current research, a follow-up investigation into the QoL among 125 liver patients was conducted using the EQ-5D-5L questionnaire, and the potential determinants were meticulously examined. The findings revealed that the majority of patients had yet to regain mobility, self-care, and usual activities just one week post-discharge, and they continued to endure discomfort. It typically takes them around three months to reclaim their capabilities. On average, the duration of post-discharge pain was approximately four days. Other studies have indicated that the QoL of liver donors has notably diminished following surgery, and prolonged observation is crucial for enhancing patients' QoL¹⁶. Moreover, the review of the literature revealed that patients who underwent fourthlevel liver surgery demonstrated a superior QoL at 13 to 24 months and beyond three years post-operation compared to those who had less than a year's worth of follow-up. However, the recovery process within the first three months post-surgery significantly impacts the long-term QoL of these patients¹⁷. Consequently, this study delved into a post-surgery QoL follow-up analysis for fourth-level liver surgery patients at the three-month mark. The data suggest that it's imperative to bolster the patient's rehabilitation efforts, focusing on mobility and daily activities during the critical first month following surgery, and to ensure they receive the necessary support to regain their independence promptly.

This research reveals that factors like gender, age, ethnicity, educational background, occupation, and BMI do not impact a patient's QoL following their release from the hospital. Yuan Liao's research delved into the QoL and its determinants for patients post-liver transplant, concluding that age, gender, and education level didn't correlate with their QoL⁷. Similarly, Meimei Liu noted that there was no substantial statistical discrepancy in the EQ-5D UI among various subgroups, including gender, age, nationality, occupation, and education level¹⁸. The study's findings indicate that the method of admission can influence a patient's QoL for up to three months post-discharge, with emergency patients experiencing a lower QoL compared to those admitted through regular channels. Marital status, particularly for those who are divorced or widowed, can boost QoL within a week of discharge. The presence or absence of post-discharge pain affects QoL for a month, with pain-free patients enjoying a notably higher QoL. Previous studies have been sparse on the connection between admission methods and QoL. This study highlights a lower QoL among emergency department patients, which could be attributed to their critical condition and the array of diseases they often face, thus impacting their post-operative QoL. Studies have also shown that emergency surgeries, due to their urgency, are often rushed and have a higher risk of complications and mortality, leading to reduced quality of life post-surgery¹⁹. Moreover, pre-existing conditions such as hypertension, diabetes, lung disease, or heart disease can significantly increase the risk of post-operative complications²⁰. We recommend that healthcare professionals give closer attention to emergency department patients and implement targeted interventions, such as pain management and early rehabilitation exercises. Furthermore, research indicates that marital status does not significantly influence the quality of life for patients undergoing fourth-level liver surgery.

Persistent pain is a major deterrent to the QoL for patients post-discharge, and it can severely hamper their recovery process. If acute pain during the initial phase of the perioperative period is not adequately managed, it may escalate into chronic post-op pain, significantly impacting the disease's progression and outlook. Pain is a crucial factor contributing to the escalation of postoperative complications and mortality rates. Studies indicate that a 10% increase in severe post-op pain can lead to a 24% increase in pain intensity six months post-surgery²¹. Previous research has yet to fully delve into the correlation between pain and patients' QoL. This study, however, offers fresh insights. It suggests that healthcare professionals must prioritize addressing the onset of pain in

				1 week after dis	scharge		1 month after d	lischarge		3 months after	discharge	
Project	Category	Number	Proportion	EQ-5D-5L UI	H/Z	Ρ	EQ-5D-5L UI	H/Z	Ρ	EQ-5D-5L UI	H/Z	P
	≤ 20	6	4.8%	0.380			0.892			0.975		
Are (vears old)	21-45	34	27.2%	0.148	3716	1020	0.764	1 673	0.643	0.900	2 500	0.475
11ge (Jeans out)	46-65	68	54.4%	0.216	01 //2	F/7.0	0.720	C /0.1	CEO.0	0.882	000.7	C/E-0
	> 65	17	13.6%	0.212			0.829			0.943		
Con dou	Male	84	67.20%	0.200	0.360	0 712	0.766	0.227	0740	0.911	0.320	CF 2 0
Celluer	Female	41	32.80%	0.214	600.0	c1/.0	0.731	700.0 -	0./40	0.876	ncc.n -	0./42
	Hepatic echinococcosis	10	8.00%	0.198			0.732			0.891		
	Liver occupying lesions	13	10.40%	0.213			0.721			0.913		
	Hepatocellular carcinoma	35	28.00%	0.175		1000	0.793	2 407		0.895	000 6	002 0
Diagnose	Decompensated cirrhosis	37	29.60%	0.218	0.0/	0.984	0.743	5.480	070.0	0.919	<i>3.000</i>	0./00
	Cholangiopathy	13	10.40%	0.183			0.860			0.960		
	Other related diseases of the liver	17	13.60%	0.249			0.659			0.817		
Mathed of admission	Regular admission	65	52.00%	0.237	C1 C 1	0 1 00	0.814	002 0	*0000	0.934	0 1 E O	*000
Method of admission	Emergency admission	60	48.00%	0.170	710.1 -	- 601.0	0.691	07/77 -	. /00.0	0.862	061.2 -	.70.0
Ethnicity	Han nationality	103	82.30%	0.198	- 0.681	907.0	0.742	0.085	0 374	0.893	- 1 254	0 210
Tumury	Minority nationality	22	17.50%	0.238	100.0 -	0/1-0	0.817		E70.0	0.931	FC2.1 -	017.0
	Unmarried	10	800.00%	0.231			0.828			0.979		
Marital status	Married	110	88.00%	0.181	11 112	*1100	0.739	1 567	200.0	0.889	2745	000 1
INTALILAL STATUS	Dissociation	2	1.60%	0.622	<i>c</i> 11.11	110.0	1.000	100.1	007.0	1.000	0.42.0	000.1
	Bereft of ones spouse	3	2.40%	0.723			0.950			0.965		
	Illiterate	15	12.00%	0.225			0.759			0.930		
	Primary school	17	13.60%	0.164			0.779			0.928		
Education land	Junior high school	40	32.00%	0.159	1 530	0 675	0.701	1 31 3	902.0	0.886	1 321	CC2 0
Education level	High school	20	16.00%	0.253	0001	c/0.0	0.813	710.1	07/.0	0.873	100.1	0.722
	Undergraduate	32	25.00%	0.233			0.767			0.902		
	Postgraduate	1	0.80%	0.532			0.907			1.000		
	Company employee	20	16.00%	0.216			0.789			0.901		
	Student	4	3.20%	0.118			0.650			0.901		
	Public functionary	3	2.40%	0.389		(1.000			1.000		
Occupation	Farmer	22	17.50%	0.275	3.941	0.685	0.772	7.0221	0.319	0.927	8.017	0.237
	Retired	20	16.00%	0.195			0.724			0.819		
	Other	24	19.20%	0.147			0.747			0.933		
	Unemployed	32	25.60%	0.192			0.737			0.897		
	< 18.5	5	4.00%	0.241			0.661			0.831		
BMT	18.5-23.9	80	64.00%	0.200	7 602	0 112	0.749	2 010	0.300	0.894	0 754	0 860
TIMO	24.0-27.9	33	26.40%	0.243	C00.7	CEE.0	0.830	010.0	00000	0.929	EC / 0	
	≥ 28.0	7	5.60%	0.046			0.540			0.873		
Dain	Yes	75	60.00%	0.259			0.800			0.900		
1 ann	No	45	40.00%	0.123	- 2.450	0.014^{*}	0.687	- 3.800	•000.0	0.900	- 8.999	0.369
Table 1. Univariat	e analysis outcomes for QoI	across v	arious time	intervals. *I	ndicates	P<0.0!	iç.					

	1 week after discharge			1 month after discharge				3 months after discharge				
	В	SE	t	р	В	SE	t	p	В	SE	t	p
Diagnose	0.025	0.021	1.220	0.225	0.019	0.023	0.809	0.42	0.006	0.013	0.467	0.641
Age	- 0.04	0.041	- 0.966	0.336	- 0.028	0.045	- 0.613	0.541	- 0.01	0.026	0.395	0.694
Gender	- 0.036	0.058	- 0.608	0.544	- 0.086	0.064	- 1.346	0.181	- 0.053	0.036	- 1.457	0.148
Method of admission	- 0.075	0.058	- 1.295	0.198	- 0.112	0.064	- 1.758	0.081	- 0.071	0.036	- 1.965	0.052
Ethnicity	0.078	0.077	1.011	0.314	0.084	0.085	0.987	0.326	0.021	0.048	0.446	0.657
Marital status	0.142	0.065	2.196	0.030*	0.019	0.071	0.269	0.788	- 0.004	0.040	- 0.097	0.923
Education level	0.008	0.013	0.561	0.576	0.006	0.015	0.403	0.688	0.001	0.008	0.124	0.902
Occupation	- 0.001	0.013	- 0.083	0.934	- 0.001	0.014	- 0.073	0.942	0.000	0.008	0.042	0.966
BMI	- 0.040	0.041	- 0.972	0.333	- 0.027	0.045	- 0.608	0.545	0.009	0.025	0.352	0.726
Pain	- 1.131	0.054	- 2.451	0.016*	- 0.126	0.059	- 2.138	0.035*	- 0.005	0.033	- 1.191	0.882
length of stay (LOS)	- 0.006	0.002	- 2.731	0.007*	- 0.008	0.003	- 2.999	0.003*	- 0.002	0.001	- 0.148	0.236

 $\label{eq:constraint} \textbf{Table 2.} \ \ \textbf{Multivariate regression outcomes for patient QoL across time intervals. Note: * indicates P < 0.05.$





Fig. 1. Distribution of QoL in different dimensions of EQ-5D-5L.



	Test statistic	Standard error	Standard test statistic	Р
1 week VS 1 month	- 1.192	0.126	- 9.424	0.000
1 week VS 3 months	- 1.724	0.126	- 13.629	0.000
1 month VS 3 months	- 0.532	0.126	- 4.206	0.000

 Table 3. Comparison of QoL UI among patients in various time intervals.

patients who undergo liver surgery and implement essential measures to mitigate their discomfort to prevent the onset of persistent pain upon discharge. For effective pain management in liver surgery patients, we recommend employing preoperative preemptive analgesia, such as the use of nonsteroidal anti-inflammatory drugs, in combination with postoperative multimodal analgesia, which involves a sequential approach to analgesics, complemented by non-pharmacological methods²².

Conclusion

This research examined shifts in patients' QoL and identified key influencing factors by tracking individuals who underwent stage fourth-level liver surgery over a three-month period. The findings indicate that a majority of patients regained their mobility, self-care, and usual activities within three months post-discharge. However, those admitted through emergency departments reported notably poorer QoL during the first three months compared to elective admission patients. The persistent pain emerged as a significant barrier to recovery, substantially diminishing patients' overall well-being. Consequently, healthcare providers must prioritize prompt intervention through early pain management strategies and structured rehabilitation programs to optimize patient outcomes.

Limitations

This research was confined by the constraints of location and time, thus it was confined to a single hospital setting. Consequently, the results could be somewhat constrained. Nonetheless, the hospital chosen was a university-affiliated, high-level care facility, which helped somewhat in mitigating the sample size limitations by enrolling patients from various regions across southwestern China. One notable gap in our study, however, was the absence of baseline EQ-5D data from the patients, which left us without a comprehensive dataset to compare pre- and postoperative quality of life outcomes. Moving forward, we aim to conduct a multicenter study involving a broader sample size, thereby offering a richer body of reference evidence.

Data availability

The datasets used or analysed during the current study are available from the corresponding author upon reasonable request.

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Author contributions

All authors helped to perform the research. All authors have read and approved the manuscript. XXF participated in the conception and design of the work, the collection and interpretation of data, conducted the statistical analysis, and drafting of the manuscript. JX participated in the collection and interpretation of data. XXF and JX are co-first authors. YJY and TL participated in the conception and design of the work. GX participated in the conception and design of the work, and revision of manuscript for important intellectual content.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

This study had been approved by the Biomedical Ethics Review Committee of West China Hospital of Sichuan University (2024 Review No. 439) and reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement for cross-sectional studies. This study had been performed in accordance with the Declaration of Helsinki. And no organs/tissues were procured from prisoners.

Informed consent

All participants provided informed consent before participating in this study, and they all agreed to participate in the study.

Additional information

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