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WJH mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Intensive care unit readmission in adult Egyptian patients undergoing living donor liver transplant: A single-centre retrospective cohort study

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Abstract

BACKGROUND

Patients who undergo living donor liver transplantation (LDLT) may suffer complications that require intensive care unit (ICU) readmission.

AIM

To identify the incidence, causes, and outcomes of ICU readmission after LDLT.

METHODS

A retrospective cohort study was conducted on patients who underwent LDLT. The collected data included patient demographics, preoperative characteristics, intraoperative details; postoperative stay, complications, causes of ICU readmission, and outcomes. Patients were divided into two groups according to ICU readmission after hospital discharge. Risk factors for ICU readmission were identified in univariate and multivariate analyses.

RESULTS

The present study included 299 patients. Thirty-one (10.4%) patients were readmitted to the ICU after discharge. Patients who were readmitted to the ICU

were older in age (53.0 ± 5.1 *vs* 49.4 ± 8.8, $P = 0.001$) and had a significantly higher percentage of women (29% *vs* 13.4%, $P = 0.032$), diabetics (41.9% *vs* 24.6%, $P = 0.039$), hypertensives (22.6% *vs* 6.3%, $P = 0.006$), and renal (6.5% *vs* 0%, $P = 0.010$) patients as well as a significantly longer initial ICU stay (6 *vs* 4 d, respectively, $P < 0.001$). Logistic regression analysis revealed that significant independent risk factors for ICU readmission included recipient age (OR = 1.048, 95%CI = 1.005-1.094, $P = 0.030$) and length of initial hospital stay (OR = 0.836, 95%CI = 0.789-0.885, $P < 0.001$).

CONCLUSION

The identification of high-risk patients (older age and shorter initial hospital stay) before ICU discharge may help provide optimal care and tailor follow-up to reduce the rate of ICU readmission.

Key Words: Intensive care units; Liver transplantation; Patient readmission; Risk factors

Core Tip: Patients undergoing living donor liver transplantation may suffer complications that require intensive care unit readmission. We retrospectively evaluated 299 patients who underwent living donor liver transplantation. We identified the incidence, causes, and outcomes of intensive care unit readmission after living donor liver transplantation. Older recipient age and longer length of initial hospital stay were recognized as significant independent risk factors for intensive care unit readmission. The identification of high-risk patients before discharge may help provide optimal care and tailor follow-up to reduce the rate of intensive care unit readmission.

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INTRODUCTION

Liver transplantation is the only definitive treatment for end-stage liver disease[1]. As a major abdominal surgery, postoperative complications may occur and might require readmission, which may be serious and life threatening. In general, patients who require intensive care unit (ICU) readmission show higher morbidity, mortality, and prolonged hospital stays than those who do not require readmission[2-5].

Complications following living donor liver transplantation (LDLT) requiring ICU readmission may be serious and life threatening. Identification of the causes of ICU readmission is pivotal to establish effective strategies to reduce the rate of readmission, improve the quality of care and patient outcomes, and reduce health expenditures by medical institutions[6].

Most available reports are on hospital readmission after deceased donor liver transplantation (DDLT). To our knowledge, there are limited published data about hospital readmission of LDLT patients. We hypothesized that ICU readmission after LDLT is due to different reasons. Consequently, this study was conducted to identify the incidence, causes, and outcomes of ICU readmission after LDLT.

MATERIALS AND METHODS

Study design and settings

This retrospective cohort study was conducted by reviewing the hospital files of adult patients who underwent LDLT at Ain Shams University Hospital, Cairo, Egypt, during the period from January 1, 2008, to December 31, 2018.

Ethical considerations

This study was approved by the Ethics Committee of the Faculty of Medicine, Ain Shams University,

Egypt (approval number: IRB/0006379). The confidentiality of the patients' data was maintained by assigning a code number to each patient.

Inclusion criteria

We included adult Egyptian patients (18 years old or above) of either sex who underwent LDLT at our institution during the period from January 1, 2008, to December 31, 2018.

Exclusion criteria

The following patients were excluded from the study: We excluded patients who were less than 18 years old, who died before discharge after LDLT, who underwent retransplantation before discharge from the ICU after the first liver transplant, and who were pregnant patients.

Sampling method

The sample size was calculated using Epi Info™ software (Centers for Disease Control and Prevention, version 7.2.3.0), setting the type-1 error (α) at 0.05, an acceptable margin of error of 5%, and a 95% confidence interval. The results from a previous study[5] showed that the incidence of hospital readmission among cases undergoing liver transplantation was 17.1%. Calculation according to these values produced a minimal sample size of 218 cases.

Study procedures

The hospital files of patients who met the eligibility criteria were thoroughly revised to extract relevant data. The collected data included patient demographics, donor characteristics, preoperative and intraoperative variables, postoperative stay, complications, causes for ICU readmission, and outcomes after ICU readmission.

The studied primary outcome was the incidence of ICU readmission. Readmission was defined as ICU readmission within ≤ 3 mo of initial ICU discharge. Patients were divided into two groups: those who were readmitted to the ICU (the readmission group) and those who were not (the control group). The secondary outcomes included the causes of first hospital readmission after discharge as well as the incidence of ICU readmission for more than one time and two-year survival.

Risk factors for ICU readmission were assessed by examining the contribution of collected patient and donor variables to the probability of ICU readmission.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (IBM SPSS Statistics) for Windows, version 26 (IBM Corp., Armonk, NY, United States). For quantitative data, the Shapiro-Wilk test for normality was performed. For data that followed a normal distribution, values were expressed as the mean ± SD. Comparisons between two groups were carried out using an independent samples T test. For data that did not follow a normal distribution, the median and interquartile range (IQR; expressed as the 25th-75th percentiles) were calculated, and the Mann–Whitney test was used to compare the two groups. For qualitative data, the variables were summarized as frequencies. Pearson's chi square tests for independence, Fisher's exact test or Fisher-Freeman-Halton exact test were used to examine the association between two categorical variables as appropriate. Binomial logistic regression was conducted to identify independent risk factors for ICU readmission, including all variables with a P value < 0.1 in univariant analysis. Kaplan–Meier curves and log rank tests were performed to estimate two-year survival. A P value < 0.05 was adopted to interpret the significance of statistical tests.

The statistical review of this study was performed by a biomedical statistician.

RESULTS

The present study included 299 patients who underwent liver transplantation and were followed up for a median duration of 40 mo (ranging from less than one month to 136 mo) after surgery. Thirty-one (10.4%) patients were readmitted into the ICU within ≤ 3 mo of initial ICU discharge, among whom 7 (2.3% of total cases) had more than one ICU readmission. Hospital readmission was recorded in 10 (3.3%), among whom 5 (1.6% of total cases) were readmitted due to biliary complications and sepsis. Table 1 depicts the causes for ICU readmission.

The preoperative characteristics of the studied patients and donors are shown in Table 2. The mean age of the patients was 49.8 ± 8.6 years. Men outnumbered women (84.9% *vs* 15.1%, respectively). The mean BMI was 28.4 ± 4.3 kgm^2. The median MELD score was 16 (ranging from 6 to 29). Approximately one-third of the patients had one or more comorbidities; the most frequent were diabetes mellitus (26.4%), hypertension (8%), and IHD (1.3%). The most frequent liver disease was HCV (76.6%), followed by HCC (39.1%), PVT (12.4%), and cryptogenic (10.7%). Encephalopathy was diagnosed in 31.8% of patients. Regarding the donors, the mean age was 29.8 ± 6.3 years (ranging from 18 to 48), with a higher percentage of men than women (68.6% *vs* 31.4%, respectively); their mean BMI was 23.7 ± 2.6 kgm^2. The

Table 1 Causes of intensive care unit readmission (total N = 31 out of 299 patients)

	N	%
Sepsis	5	1.6
Pulmonary complications	3	0.9
Cardiovascular complications	3	0.9
HA thrombosis	3	0.9
7Th day syndrome	1	0.3
Acute cellular rejection	1	0.3
Acute Pancreatitis	1	0.3
Cerebrovascular stroke	3	0.9
Graft failure	1	0.3
hemorrhagic shock	1	0.3
Liver infarction	1	0.3
Metabolic disorders	1	0.3
Portal vein thrombosis	1	0.3
Prograf neurotoxicity	2	0.6
PV STENOSIS	1	0.3
Re -transplant[1]	2	0.6
Renal impairment	1	0.3

[1]Re-transplantation for graft failure due to hepatic artery thrombosis in 1 case and small for size in the other case. HA: Hepatic artery; HV: Hepatic vein; LDLT: Living donor liver transplantation; N: Number; PV: Portal vein.

comparison between patients who were readmitted to the ICU and patients who were not readmitted showed that the former group was older in age (53.0 ± 5.1 *vs* 49.4 ± 8.8, $P = 0.001$) and had a significantly higher percentage of women (29% *vs* 13.4%, $P = 0.032$), diabetic patients (41.9% *vs* 24.6%, $P = 0.039$), hypertensive patients (22.6% *vs* 6.3%, $P = 0.006$), and renal patients (6.5% *vs* 0%, $P = 0.010$).

Table 3 summarizes the intraoperative and postoperative details of the studied patients. Synthetic grafts were used in 2.7% of patients. Vascular surgical complications were encountered in 15.7% of patients, mainly in the form of hepatic artery thrombosis (8%). No significant difference was detected between the two groups ($P > 0.05$).

Table 4 shows the follow-up details of the patients. The median LOS of initial ICU admission was significantly longer in the readmission group (6 *vs* 4 d, respectively, $P < 0.001$). Rejection occurred in 12% of all patients. The mortality rate was 29.8%, with a significantly higher percentage in the readmission group (64.5% *vs* 25.7%, $P < 0.001$).

Logistic regression analysis was conducted to identify risk factors for ICU readmission after discharge (Table 5). Significant independent risk factors included recipient age and length of initial hospital stay after discharge from the ICU. The increase in recipient age by one year was associated with an increased likelihood of ICU readmission by 4.8% (OR = 1.048, 95%CI = 1.005-1.094, $P = 0.030$). A negative relationship existed between the length of initial hospital stay and the probability of ICU readmission, as an increased length of stay resulted in a decreased risk of readmission (OR = 0.836, 95%CI = 0.789-0.885, $P < 0.001$).

Figures 1 and 2 illustrate the survival curve for all studied patients and according to ICU readmission, respectively. The OS rates for all patients at 1 and 2 years were 79.5% ± 2.3% and 75.2% ± 2.5%, respectively. The overall survival (OS) rates for non-ICU readmitted patients were 83.9% ± 2.3% and 79.2% ± 2.5% at 1 and 2 years, respectively. For ICU readmitted patients, the OS rate was 40.6% ± 9.1% at 1 year and persisted until 2 years. The log rank test showed a significant difference between the survival curves of the two groups ($P < 0.001$).

DISCUSSION

Readmission after discharge from the hospital is considered among the important indicators of the quality of delivered health care services. Moreover, readmissions impose an additional considerable

Table 2 Preoperative patients' and donors' characteristics (data were expressed as mean ± SD or number & percentage) (total N = 299)

		Total (N = 299), %		No ICU readmission (N = 268), %		ICU readmission (N = 31), %		Test statistic	*P* value
Age (years); mean ± SD (Range)		49.8 ± 8.6; (19.0 - 67.0)		49.4 ± 8.8; (19.0 - 67.0)		53.0 ± 5.1; (42.0 - 64.0)		3.381[a]	0.001[1]
Gender	Female	45	15.1	36	13.4	9	29.0	FE	0.032[1]
	Male	254	84.9	232	86.6	22	71.0		
BMI (Kg/m^2); mean ± SD (Range)		28.4 ± 4.3; (18.5 - 52.9)		28.2 ± 4.0; (18.5 - 42.0)		29.4 ± 6.5; (20.6 - 52.9)		0.936[a]	0.356
MELD score; Median [IQR] (Range)		16.0; [13.0 – 18.0] (6.0 - 29.0)		16.0; [13.0 -18.0] (6.0 - 29.0)		15.0; [12.0 – 20.0] (7.0 - 28.0)		0.538[b]	0.590
Positive medical history		103	34.4	86	32.1	17	54.8	FE	1.000
	DM	79	26.4	66	24.6	13	41.9	4.282[c]	0.039[1]
	Hypertension	24	8.0	17	6.3	7	22.6	FE	0.006[1]
	Bronchial asthma	3	1.0	2	0.7	1	3.2	FE	0.281
	IHD	4	1.3	4	1.5	0	0.0	FE	1.000
	Renal	2	0.7	0	0.0	2	6.5	FE	0.010[1]
	Bilharziasis	2	0.7	2	0.7	0	0.0	FE	1.000
	Others	9	3.0	8	3.0	1	3.2	FE	1.000
Diagnosis	AIH	10	3.3	10	3.7	0	0.0	FE	0.606
	HCC	117	39.1	107	39.9	10	32.3	0.686[c]	0.408
	PVT	37	12.4	34	12.7	3	9.7	FE	0.780
	Cryptogenic	32	10.7	29	10.8	3	9.7	FE	1.000
	ESLD	10	3.3	8	3.0	2	6.5	FE	0.278
	HCV	229	76.6	204	76.1	25	80.6	0.317[c]	0.573
	HBV	11	3.7	11	4.1	0	0.0	FE	0.612
	BCS	2	0.7	2	0.7	0	0.0	FE	1.000
	PSC	2	0.7	2	0.7	0	0.0	FE	1.000
Encephalopathy		95	31.8	87	32.5	8	25.8	0.568[c]	0.451
Creatinine clearance (mL/min); mean ± SD (Range)		88.7 ± 26.5; (10.0 - 172.0)		88.5 ± 25.8; (10.0 - 170.0)		90.4 ± 32.7; (16.0 - 172.0)		0.384[a]	0.702
Serum creatinine (mg/dL); mean ± SD (Range)		0.97 ± 0.31; (0.30 - 2.40)		0.97 ± 0.32; (0.30 - 2.40)		0.96 ± 0.24; (0.50 - 1.30)		0.255[a]	0.799
Serum Albumin gm/dL; mean ± SD (Range)		3.0 ± 0.5; (1.8 - 4.8)		3.0 ± 0.5; (1.8 - 4.8)		2.8 ± 0.5; (1.8 - 3.8)		1.428[a]	0.154
Na mmol/L; mean ± SD (Range)		135.1 ± 5.2; (117.0 - 147.0)		135.1 ± 5.4; (117.0 - 147.0)		135.0 ± 3.6; (128.0 - 145.0)		0.137[a]	0.891
Total bilirubin mg/dL; Median [IQR] (Range)		1.3; [0.8 - 1.9] (0.2 - 27.0)		1.3; [0.7 - 1.9] (0.2 - 27.0)		1.4; [1.1 - 1.9] (0.6 - 5.6)		1.270[b]	0.204
Alkaline phosphatase IU/L; Median [IQR] (Range)		143.0; [97.0 - 221.0] (6.2 - 2369.0)		144.5; [97.0 - 231.5] (6.2 - 2369.0)		131.0; [98.0 - 167.0] (45.0 - 1410.0)		1.041[b]	0.298
Donor age (years); mean ± SD (Range)		29.8 ± 6.3; (16.0 - 48.0)		30.0 ± 6.3; (16.0 - 48.0)		28.0 ± 5.9; (18.0 - 39.0)		1.731[a]	0.084
Donor gender	Female	94	31.4	83	31.0%	11	35.5	0.263[c]	0.608
	Male	205	68.6	185	69.0%	20	64.5		
Donor BMI (Kg/m^2); mean ± SD (Range)		23.7 ± 2.6; (17.7 - 32.0)		23.8 ± 2.6; (17.7 - 32.0)		23.0 ± 2.3; (18.3 - 29.0)		1.545[a]	0.124

[a]Independent samples T-test.
[b]Mann-Whitney test.
[c]Pearson's Chi square test for independence.

[1]Significant at $P < 0.05$. AIH: Autoimmune hepatitis; BMI: Body mass index; DM: Diabetes mellitus; FE: Fisher's exact test; IQR: Interquartile range; N: Number; SD: Standard deviation; ICU: Intensive care unit; IHD: Ischemic heart disease; HCC: Hepatocellular carcinoma; PVT: Portal vein thrombosis; ESLD: End-stage liver disease; HCV: Hepatitis C virus; HBV: Hepatitis B virus; BCS: Budd-Chiari syndrome; PSC: Primary sclerosing cholangitis.

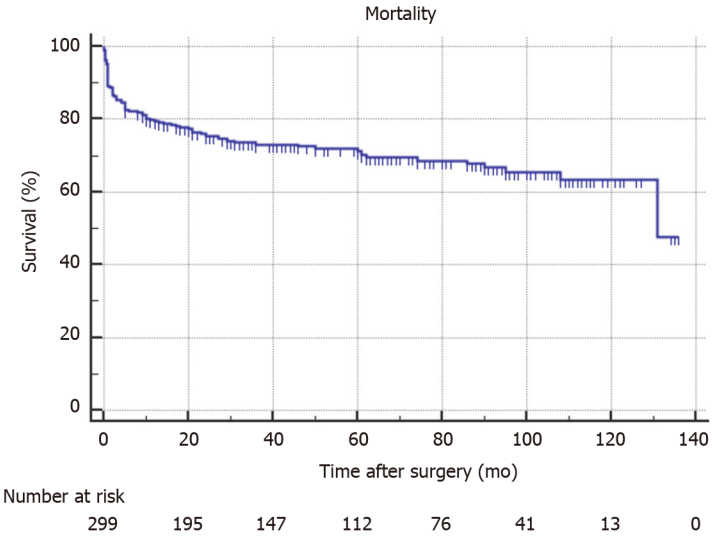

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Figure 1 Kaplan-Meier curve showing survival after surgery in all patients.

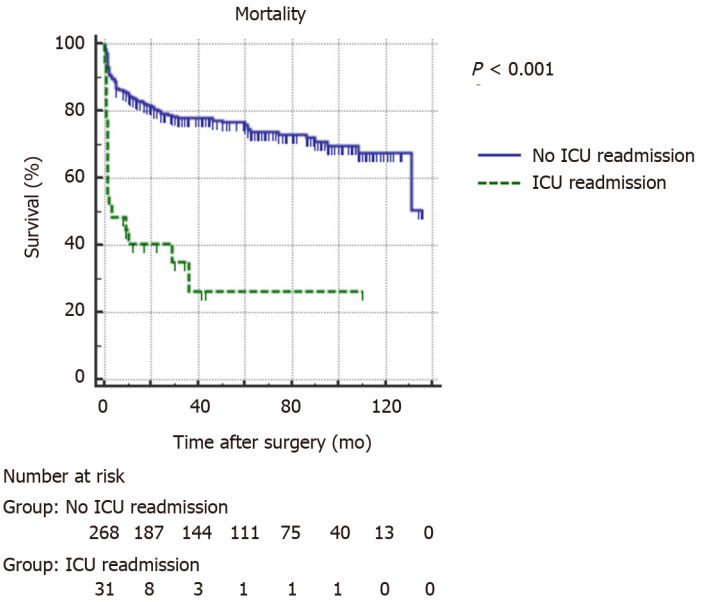

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Figure 2 Kaplan-Meier curve showing survival after surgery in the studied groups. Log rank test: $X^2 = 44.426$, $P < 0.001$. ICU: Intensive care unit.

burden on health care expenditure and on hospital resources[7]. Recipients of liver transplantation are susceptible to the administration of multiple drug regimens, and they endure metabolic changes in addition to the complications that may arise from surgery[5]. All of these factors increase the risk of hospital and ICU readmission in this group of patients[8,9]. The current study aimed to identify the incidence, causes, and outcomes of ICU readmission after LDLT. Our cohort consisted of 299 patients who underwent LDLT and were followed up for a median duration of 40 mo.

In the present study, the incidence of ICU readmission within the first 3 mo after discharge was 10.4% and that of multiple ICU readmissions was 2.3% of the total cases. The incidence of hospital readmission after discharge was 3.3%. In agreement with this low rate of readmission, Chen *et al*[5] reported a 3-mo hospital readmission rate of 9.4% in 791 patients who underwent either LDLT or DDLT. On the other

Table 3 Intraoperative and postoperative data of the studied patients (total N = 299)

		Total (N = 299), %		No ICU readmission (N = 268), %		ICU readmission (N = 31), %		Test statistic	*P* value
Waiting Time (days); Median [IQR] (Range)		86.0; [59.0 - 120.0] (20.0 - 546.0)		86.5; [56.5 - 120.0] (20.0 - 462.0)		74.0; [65.0 - 119.0] (29.0 - 546.0)		0.034[a]	0.973
Warm ischemia time (min); mean ± SD (Range)		48.6 ± 19.4; (20.0 - 145.0)		48.7 ± 19.0; (20.0 - 145.0)		47.9 ± 22.7; (20.0 - 145.0)		0.222[b]	0.274
Graft weight/GRWR; mean ± SD (Range)		1.06 ± 0.47; (0.01 - 6.30)		1.08 ± 0.49; (0.01 - 6.30)		0.98 ± 0.23; (0.01 - 1.30)		1.095[b]	0.825
Cold ischemia time (min); Median [IQR] (Range)		45.0; [30.0 - 60.0] (10.0 - 180.0)		45.0; [31.0 - 60.0] (10.0 - 180.0)		45.0; [30.0 - 50.0] (20.0 - 125.0)		0.864[a]	0.387
Packed red blood cells (units); Median [IQR] (Range)		4.0; [2.0 - 7.0] (1.0 - 28.0)		4.0; [2.0 - 7.0] (1.0 - 28.0)		3.0; [2.0 - 6.0] (1.0 - 17.0)		0.957[a]	0.339
PV Anastomosis	RPV/MPV	255	85.3	230	85.8	25	80.6	FE	0.426
	RPV/CPV	34	11.4	29	10.8	5	16.1	FE	0.372
	RPV/RPV	4	1.3	4	1.5	0	0.0	FE	1.000
	LPV/LPV	1	0.3	1	0.4	0	0.0		
	LPV/MPV	2	0.7	2	0.7	0	0.0		
	RPH/CHV	2	0.7	2	0.7	0	0.0		
	RPV/CBV	1	0.3	0	0.0	1	3.2		
	RPV/CHV	1	0.3	1	0.4	0	0.0		
HA Anastomosis	RHA/RHA	280	93.6	252	94.0	28	90.3	FE	0.708
	RHA/LHA	18	6.0	15	5.6	3	9.7	FE	0.606
	RHA/SPA	1	0.3	1	0.4	0	0.0		
HVs Anastomosis	RHV/RHV	278	93.0	248	92.5	30	96.8	FE	0.708
	RHV/IVC	10	3.3	10	3.7	0	0.0	FE	0.606
	LMHV/LMHV	9	3.0	8	3.0	1	3.2	FE	1.000
	RHV/MHV	2	0.7	2	0.7	0	0.0		
Synthetic graft		8	2.7	7	2.6	1	3.2	FE	0.588
Surgical vascular complications		47	15.7	39	14.6	8	25.8	FE	0.118
	HA stenosis	6	2.0	5	1.9	1	3.2		
	HA thrombosis	24	8.0	19	7.1	5	16.1		
	HV stenosis	3	1.0	3	1.1	0	0.0		
	HVT	2	0.6	2	0.8	0	0.0		
	PV stenosis	4	1.3	3	1.1	1	3.2		
	PV thrombosis	7	2.3	6	2.2	1	3.2		
	Sub-diaphragmatic hematoma	1	0.3	1	0.4	0	0.0		

[a]Mann-Whitney test.

[b]Independent samples T-test. Significant at $P < 0.05$. FE: Fisher's exact test; IQR: interquartile range; N: Number; SD: Standard deviation; GRWR: Graft to recipient weight ratio; HA: Hepatic artery; HV: Hepatic vein; PV: Portal vein; RPV: Right portal vein; MPV: Main portal vein; CPV: Common portal vein; LPV: Left portal vein; CHV: Central hepatic vein; RHA: Right hepatic artery; LHA: Left hepatic artery; SPA: Splenic artery; RHV: Right hepatic vein; IVC: Inferior vena cava; LMHV: Left and middle hepatic veins; MHV: Middle hepatic vein; HVT: Hepatic vein thrombosis; ICU: Intensive care unit.

hand, much higher incidence rates of hospital readmission were reported by earlier studies[6,8-10].

Shankar *et al*[9] assessed risk factors for rehospitalization in 208 patients who underwent liver transplantation (among whom 8 patients only underwent LDLT) over a duration of 4 years. They reported a hospital readmission rate of 30.3% within 3 mo. Pereira *et al*[8] conducted an assessment of

Table 4 Outcome of the studied patients (total N = 299)

	Total (N = 299)		No ICU readmission (N = 268)		ICU readmission (N = 31)		Test statistic	*P* value
Initial Hospital length of stay (days); Median [IQR] (Range)	21.0; [18.0 - 26.0](1.0 - 150.0)		22.0; [19.0 - 26.0] (5.0 - 120.0)		3.0; [2.0 - 9.0] (1.0 - 150.0)		8.003[a]	< 0.001[1]
Length of stay in initial ICU (days); Median [IQR] (Range)	4.0; [3.0 - 5.0] (2.0 - 45.0)		4.0; [3.0 - 5.0] (2.0 - 45.0)		6.0; [5.0 - 7.0] (4.0 - 9.0)		6.676[a]	< 0.001[1]
Rejection (N, %)	36	12.0	34	12.7	2	6.5	FE	0.557
Mortality(N, %)	89	29.8	69	25.7	20	64.5	19.978[b]	< 0.001[1]

[a]Mann-Whitney test.

[b]Pearson's Chi square test for independence.

[1]Significant at $P < 0.05$. IQR: Interquartile range; N: Number; ICU: Intensive care unit.

Table 5 Logistic regression analysis for risk factors of intensive care unit readmission

	Wald	*P* value	OR	95%CI for OR	
				Lower	Upper
Patients' age (years)	4.707	0.030[1]	1.048	1.005	1.094
Gender (male compared to female)	2.722	0.099	0.399	0.134	1.188
DM	1.257	0.262	1.828	0.637	5.244
Hypertension	0.462	0.497	1.641	0.394	6.842
Donors' age (years)	1.700	0.192	0.954	0.888	1.024
Length of initial ICU stay (days)	1.255	0.263	1.055	0.960	1.159
Length of initial hospital stay (days)	37.306	< 0.001[1]	0.836	0.789	0.885

[1]Significant at $P < 0.05$. CI: Confidence interval; DM: Diabetes mellitus; OR: Odds ratio; ICU: Intensive care unit.

766 patients undergoing DDLT over an 8-year period. They found a 30-d readmission rate of 45%. Patel *et al*[10] evaluated 325 patients with DDLT over a 10-year period, with an overall 90-d readmission rate of 46%. Yataco *et al*[6] studied hospital readmission in 445 patients who underwent either DDLT or LDLT, with a 90-d hospital readmission rate of 42%. All of these studies included patients who underwent either DDLT only or a mixed sample of DDLT and LDLT. Nagaraja *et al*[11] assessed 140 LDLT patients and found the rate of readmission within 3 mo after discharge to be lower than reported in DDLT or a mixed sample (27.1%).

The wide variation in the reported readmission rates among studies may be explained by the difference in preoperative patient characteristics, as only 16.7% of studies included patients undergoing LDLT and had MELD scores above 19. In addition, institutional policies for patient selection before transplant and the criteria for readmission differ among the centres, potentially impacting the reported rates of readmission.

The most common causes of ICU readmission among our patients included sepsis (5/31 patients), followed by pulmonary and cardiac causes (3/31 each). Previous studies reported sepsis as the most common cause for hospital readmission, followed by biliary complications[6,11]. Meanwhile, sepsis due to biliary complications were reported among the causes for hospital readmission (1.6% of total cases) in our cohort.

We proceeded in the current study to identify potential risk factors that increase the likelihood of ICU readmission within 3 mo after discharge. Several variables were assessed in the literature as potential predictors of rehospitalization after liver transplantation.

The recipient's age was found on univariate and multivariate analyses in the current study to be significantly associated with an increased probability of ICU readmission. This association is supported by the results of Levy *et al*[12] and Patel *et al*[10]. However, several studies showed a lack of significant association with rehospitalization[5,6,8,9,11].

Regarding the recipient's sex, univariate analysis showed that women were significantly more likely to be readmitted to the ICU, but this association was not significant in multivariate analysis. Patel *et al*[10] reported a lower risk for men and an increased risk for women. Other previous studies reported the

lack of a significant effect of recipient sex on rehospitalization[5,6,8,9,11,12].

The presence of comorbidities was assessed in the present study. A higher percentage of ICU readmission was associated with diabetes, hypertension, and renal disease in univariate analysis, while multivariate analysis showed the lack of a significant effect on ICU readmission. The increased risk of rehospitalization with the presence of chronic illnesses was stated in the literature in patients undergoing surgery[13,14]. Our results are in line with previous studies assessing rehospitalization after liver transplantation, which did not show this significant association[5,8,11]. On the other hand, other preoperative morbid conditions, such as preoperative HCV infection[9] and PVT[8], were reported to increase the risk of hospital readmission, although such an association was not detected in our cohort.

While the current study results revealed a significantly longer initial ICU stay in ICU readmitted patients using univariate analysis, the association was not found to be significant on multivariate analysis. Similarly, Nagaraja *et al*[11] and Yataco *et al*[6] reported the lack of a significant difference between readmitted and non readmitted groups. In contrast, Levy *et al*[12] found that a higher percentage of non readmitted patients had an ICU stay less than 3 d than readmitted patients (67.8% *vs* 56.3%, $P = 0.0231$). Shankar *et al*[9] reported that a longer LOS in the ICU had a lower risk ratio.

Numerous other factors were identified by some researchers as predictors of rehospitalization but were nonsignificant in the current study, including the MELD score and postoperative complications.

We found that the initial hospital stay correlated negatively with the probability of ICU readmission (OR = 0.836, 95%CI = 0.789-0.885, $P < 0.001$), indicating an increased risk with shorter stays. The literature shows controversial reports concerning the relationship between the length of initial hospital stay and rehospitalization. A negative correlation was also observed by Kassin *et al*[13], Ladner *et al*[15], Pereira *et al*[8], and Chen *et al*[5]. Contradictory results were stated by Yataco *et al*[6], who found that an initial hospital stay longer than 7 d was significantly associated with hospital readmission. Prolonged hospital stay can potentially exert two contradictory effects on the probability of hospital readmission, which may depend largely on the range of stay. On the one hand, a longer stay can prevent discharge before full assessment, optimization of the patient, and adequate management of postoperative complications. Some postoperative complications, such as rejection, may not manifest within the first days after transplantation, and their detection after discharge leads to early hospital readmission. On the other hand, prolonged stay predisposes the patient to an increased risk of contracting nosocomial infection with a negative impact on the patient's health and outcomes.

A higher MELD score has been associated with higher health care costs and increased utilization of hospital resources[16,17]. Nevertheless, the MELD score was not found to be significantly associated with ICU readmission in this study, a finding shared by several previous studies assessing risk factors for hospital readmission[5,6,8-11]. The calculation of the MELD score is based on a limited set of laboratory measurements that are not able to capture all aspects of the patient's functional status.

We did not find a significant difference in the rate of postoperative complications between readmitted and nonreadmitted groups, a finding shared by Nagaraja *et al*[11]. However, Chen *et al*[5] found that the risk of readmission correlated positively with the number and severity of complications after liver transplantation. An increased risk in patients suffering postoperative complications was also observed by Pereira *et al*[8].

The mortality rate in our series was 29.8%. The OS rates for all patients at 1 and 2 years were 79.5% ± 2.3% and 75.2% ± 2.5%, respectively. Patients with ICU readmission had a significantly higher mortality rate than those without readmission (64.5% *vs* 25.7%, $P < 0.001$). The OS rates for ICU readmitted patients were significantly reduced compared to the non readmission group at one year (40.6% ± 9.1% *vs* 83.9% ± 2.3%) and two years (40.6% ± 9.1% *vs* 79.2% ± 2.5%) post transplantation. This association between readmission and mortality could be explained by the worsened health status of readmitted patients, which requires readmission and at the same time increases the risk of mortality. Moreover, ICU readmission may expose the patient to nosocomial infections, and the use of multiple medications may negatively affect renal function and result in further deterioration of the patient's health status.

In accordance with these findings, Pereira *et al*[8] found decreased OS at one year after transplantation in readmitted patients compared to nonreadmitted patients (88.2% *vs* 95.6%, $P < 0.05$). Nagaraja *et al*[11] reported that readmitted patients had a significantly higher mortality rate than nonreadmitted patients (8% *vs* 0%; $P = 0.01$). Chen *et al*[5] reported reduced OS in readmitted patients at 1 year (81.2% *vs* 94.1%) and 2 years (68.1% *vs* 88.2%). Patel *et al*[10] stated that readmitted patients had a significantly lower 5-year survival (75% *vs* 88%, $P = 0.008$). Nevertheless, Yataco *et al*[6] reported the lack of a significant difference in the 1-year survival rate between readmitted and nonreadmitted recipients.

The present study differs from previous studies by investigating ICU readmission and not all rehospitalizations, which may explain differences in results from those studies. We believe that ICU readmission imposes more negative effects on both patients and the resources of health care systems than rehospitalization into other hospital wards or units. Considering that the resources of the ICU are limited and the cost of care is higher than that encountered with hospital ward admission, the identification of specific causes and risk factors for ICU readmission is crucial. However, the present study bears some points of limitation. The retrospective nature of the study predisposes the collected data to inaccuracies. Moreover, patients may have been readmitted to other health care facilities, and such data may not be recorded in our institution's files. Being a single-centre experience hinders the generalization

of our results.

CONCLUSION

Older recipient age and shorter initial hospital stay were significantly associated with ICU readmission. The overall survival rate for ICU readmitted patients was significantly lower than that for non-ICU readmitted patients. The identification of high-risk patients with these factors before discharge may help provide optimal care and tailor follow-up to reduce the rate of ICU readmission.

ARTICLE HIGHLIGHTS

Research background

Intensive care unit (ICU) admission and readmission following liver transplantation is important field in liver transplantation operation. Readmission causes and effect on prognosis in terms of morbidity and mortality are still needed to be further investigated

Research motivation

To identify causes and outcome in recipients post living donor liver transplantation (LDLT) who required ICU readmission after initial discharge from ICU and to compare them with patients who did not require readmission

Research objectives

A retrospective cohort study carried on recipients who had LDLT in single Egyptian center in the period betwenn 2008 and 2018. Patients were divided into two groups according to ICU readmission after initial hospital discharge. Risk factors for ICU readmission were identified in univariate and multivariate analyses.

Research methods

Retrospective cohort study was conducted by reviewing the hospital files and records of adult patients who underwent LDLT at Ain Shams University Hospital, Cairo, Egypt, during the period from January 1, 2008, to December 31, 2018. Causes and outcome of ICU readmission were compared between both groups (Readmission group and non readmission group). Risk factors for ICU readmission were also assessed including donor and recipient factors. Binomial logistic regression was conducted to identify independent risk factors for ICU readmission, including all variables with a P value < 0.1 in univariant analysis.

Research results

Thirty-one (10.4%) patients were readmitted into the ICU within ≤ 3 mo of initial ICU discharge, among whom 7 (2.3% of total cases) had more than one ICU readmission. Biliary complication and sepsis was the most common cause of ICU readmission. Significant independent risk factors included recipient age and length of initial hospital stay after discharge from the ICU.

Research conclusions

The study concluded that older recipient age and duration of hospital stay (word stay) before ICU readmission were significant risk factors for ICU readmission. The overall survival rate for ICU readmitted patients was significantly lower than that for non-ICU readmitted patients.

Research perspectives

Further study are warranted to identity how to improve management of the risky patients and hence improve their survival.

FOOTNOTES

Author contributions: Korraa AA, Elewa GM, and El Gendy HA designed the research; Montasser IF, Salah M, and Labib HA performed the research, wrote the paper, contributed analytical tools and analysed the data; Abdelrahman M and Goda MH contributed in data collection and analysis; Dabbous H, Bahaa M, and El-Meteini M revised the manuscript; All authors have read and approved the final manuscript.

Institutional review board statement: This study was approved by the Ethics Committee of the Faculty of Medicine, Ain Shams University, Egypt (approval number: IRB/0006379). The confidentiality of the patients' data was

maintained by assigning a code number to each patient.

Clinical trial registration statement: The trial is registered in clinical trial.gov (NCT04067739).

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