Defining Readmission Risk Factors for Liver Transplantation Recipients

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Abstract: Liver transplantation (LT) is a costly but effective treatment for end-stage liver disease (ESLD). However, there are minimal data on the patterns of and risk factors for hospital readmission after LT. The aim of this study was to determine the frequency of and risk factors for rehospitalization after LT. Consecutive adult patients who underwent LT at a single center (n=208) were prospectively studied over a 30-month period. Within 90 days of LT, 30.3% of LT recipients were readmitted to the hospital. Recipient and donor age, Model for End-Stage Liver Disease score, cold ischemia time, type of hepatic graft, length of hospitalization after LT, and occurrence of operative/postoperative complications had no association with the risk for readmission ($P>.05$). The length of stay in intensive care was negatively correlated with readmission (hazard ratio, 0.92; $P=.028$). ESLD from hepatitis C virus (HCV) infection as an indication for LT was the only factor associated with an increased risk for readmission (hazard ratio, 1.91; $P=.010$). Further studies are needed to explore the reasons for readmission among LT recipients, particularly those with HCV infection, in order to devise cost-savings policies for post-LT care.

Readmission to the hospital after discharge is an important metric for evaluating the cost-effectiveness and quality of health services.[1] Although readmission does not universally indicate suboptimal quality of care at the time of the initial hospitalization, readmission is costly and sometimes preventable.[2-4] Given the widespread economic constraints currently facing many health systems, much focus is being directed toward strategies that minimize rehospitalizations in inpatient populations.[5] However, there are little data on the frequency of readmission or the risk factors that predispose patients to being readmitted to the hospital following liver transplantation (LT).

Although LT is a highly successful, standard-of-care treatment for end-stage liver disease (ESLD), it is often criticized for being

too expensive.[6-9] Given finite resources and competing interests, transplantation programs are increasingly held accountable for healthcare expenditures incurred in the post-transplantation care of recipients. Furthermore, there is speculation that implementation of the Model for End-Stage Liver Disease (MELD) system—which prioritizes LT for patients with the highest estimated 3-month mortality—has resulted in an excess rate of readmission following discharge for LT. In actuality, there are limited cost-effectiveness data to support the MELD system for liver organ allocation, despite its proven effectiveness for decreasing mortality among patients with ESLD who are awaiting organ transplantation from a deceased donor.[10]

Previous studies have assessed the impact of the MELD system on various aspects of healthcare resource utilization (including the length of stay [LOS] in the hospital) and costs associated with inpatient services such as pharmacy, laboratory medicine, radiology, hemodialysis, and physical therapy. Washburn and associates examined the cost of post-LT care among 222 individuals who underwent LT at a single center and found that the recipient's MELD score was significantly associated with post-LT costs, but not with survival.[11] The researchers concluded that sicker LT recipients consume a disparate amount of resources.

In contrast, in a study of 193 consecutive adult LT recipients at a single center, Nair and colleagues found that patients with risk factors that predict poorer surgical outcomes—obesity, diabetes, and previous abdominal surgery—did not utilize more resources and, specifically, did not have higher rates of readmission within 90 days of discharge.[12]

Likewise, in a study from the Cleveland Clinic that examined 112 subjects who underwent LT, those who were in the intensive care unit (ICU) prior to LT (and were, thus, assumed to be more medically compromised) did not consume excess healthcare resources postoperatively. The authors found that patients from the hospital ward, but not the ICU, had the greatest LOS after LT, but there was no difference in overall postoperative costs based on the patient's location before LT. Readmission after LT was not specifically assessed in their analysis.[13]

While the frequency and predictors of rehospitalization after LT have not been thoroughly studied, data currently available in the literature are conflicting as to whether disease severity in patients with cirrhosis correlates with healthcare resource consumption, specifically readmission after LT. A better understanding of why and how often readmissions occur after LT could help to shape policies in transplantation medicine that would promote cost containment. The aim of this study was to determine the frequency of and risk factors for rehospitalization within 90 days of primary LT among adult patients.

Methods

Patient Population

Consecutive patients who were at least 18 years of age and who underwent primary LT between January 1, 2007 and September 1, 2010 at London Health Sciences Center in London, Ontario were prospectively followed. Patients were excluded if they did not survive a minimum of 90 days after LT. For the purposes of this study, survival data on all subjects were verified in January 2011.

Data Collection

Following approval by the Institutional Review Board, data were collected on clinicodemographic factors, donor graft characteristics, medical and surgical complications after LT, number of consultative services used in postoperative care, LOS after LT, LOS in the ICU, readmission within 90 days of LT, and survival. The United Network for Organ Sharing (UNOS)'s modification of the MELD score was calculated using the formula on the Mayo Clinic's website; scores were based on laboratory parameters collected within 24 hours of LT. For the purposes of this study, MELD exception points were not given to patients with hepatocellular carcinoma. Only consultative services other than the core services that comprise the transplant team were quantified; core services were considered to be hepatology, hepatobiliary surgery, intensive care, nutrition, and physical therapy. Severe debility as a postoperative medical complication was defined as physical deconditioning that required extensive physical therapy and contributed to LOS. Malnutrition was included as a medical complication if patients required enteral or parenteral feeding, and diabetes mellitus was included as a medical complication if patients required insulin with regular monitoring and insulin dosage adjustments. All patients received regular follow-up care in the post-transplantation ambulatory facility and were managed by a group of 3 transplant hepatologists. If patients resided outside the clinic's jurisdiction after LT, complete follow-up data, including information on readmission and death, were captured by the clinic's LT coordinators. Surgical complications pertaining to the index admission for the primary LT procedure included hepatic artery thrombosis, hepatic artery stenosis, portal vein thrombosis, bile leak, and wound infection requiring surgical intervention. For the purposes of this analysis, survival data were updated in January 2011.

Statistical Analysis

Continuous variables were reported as means with standard deviations, and frequencies with percentages were reported for categorical variables. Cox proportional

Table 1. Baseline Clinicodemographic Factors

Factor	Mean or frequency	Standard deviation or percentage
Demographics		
Age	53.1 years	9.8 years
Male gender	164	78.8%
Underlying liver disease		
Hepatitis C virus infection with or without alcoholic liver disease	53	25.5%
Autoimmune liver disease*	33	15.9%
Alcoholic liver disease	22	10.6%
Nonalcoholic fatty liver disease	20	9.6%
Other liver diseases, including combinations	80	38.5%
Hepatocellular carcinoma	33	14.9%
Patient's location before undergoing liver transplantation		
Home	113	54.2%
Hospital ward	60	29.1%
Intensive care unit (without ventilation)	20	9.4%
Intensive care unit (with ventilation)	15	7.4%
Donor/graft factors		
Deceased donor (brain death)	172	82.7%
Deceased donor (cardiac death)	28	13.4%
Live donor	8	3.8%
Cold ischemia time	403.2 minutes	161.9 minutes
Length of stay		
Total hospitalization post–liver transplantation	25.0 days	27.9 days
Stay in intensive care post–liver transplantation	6.4 days	12.7 days

*Autoimmune hepatitis, primary biliary cirrhosis, or primary sclerosing cholangitis.

hazards regression analysis was performed to assess factors associated with readmission within 90 days of discharge. Statistical significance was set at less than 5% for all analyses. Statistical analysis was performed using SAS version 9.1.2 software (SAS, Inc).

Results

A total of 208 LT recipients fulfilled the inclusion criteria. Baseline clinicodemographic factors of the patients are shown in Table 1. The mean age of the patients was 53.1 years, and 164 (78.8%) patients were male. The most common etiologies of ESLD were hepatitis C virus (HCV) infection with or without distant alcohol misuse, which occurred in 53 (25.5%) patients; distant alcohol misuse, in 22 (10.6%) patients; nonalcoholic fatty liver disease, in 20 (9.6%) patients; and autoimmune liver disease (autoimmune hepatitis, primary sclerosing cholangitis, or primary biliary cirrhosis), in 33 (15.9%) patients. Patients' mean calculated MELD score was 20.4. The majority of LT

Table 2. Postoperative Complications and Readmission Rate

	Frequency	Percentage
Malnutrition requiring enteral or parenteral feeding	29	13.9%
Diabetes mellitus requiring insulin	22	10.6%
Severe debility	19	9.1%
Infection	16	7.7%
Surgical complications*	59	28.4%
Readmission within 90 days	63	30.3%

*Hepatic artery thrombosis, hepatic artery stenosis, bile leak, portal vein thrombosis, wound infection.

recipients were residing at home and underwent elective LT (n=113; 54.2%); in addition, 60 (29.1%) patients were in the hospital ward, 20 (9.4%) patients were in the ICU (but were not intubated), and 15 (7.4%) patients were in the ICU and on mechanical ventilation. The mean donor age was 44.8 years, and the mean cold ischemia time was 403.2 minutes. The majority of grafts were from deceased donors after brain death (n=172; 82.7%), but 28 (13.4%) grafts were from deceased donors after cardiac death, and 8 (3.8%) recipients received live-donor grafts. The mean LOS after LT was 25.0 days, and the mean LOS in the ICU after LT was 6.4 days.

Table 2 summarizes postoperative complications and readmissions: 29 (13.9%) patients had malnutrition, 22 (10.6%) patients had diabetes mellitus requiring insulin, 19 (9.1%) patients had severe debility, and 16 (7.7%) patients had infectious complications. Overall, 63 (30.3%) patients were readmitted to the hospital within 90 days of discharge following LT. The mean time to readmission was 27.8 days (standard deviation, 25.7).

Table 3 summarizes the results of Cox proportional hazards regression analyses. Recipient age, MELD score, donor age, cold ischemia time, type of donor graft, length of hospitalization, postoperative medical and surgical complications, and recipient location prior to LT had no association with readmission. LOS in the ICU had a hazard ratio (HR) of 0.92 (95% confidence interval [CI], 0.85–0.99; *P*=.028), indicating a negative correlation with risk for readmission. An underlying diagnosis of HCV infection was significantly associated with readmission (HR, 1.91; 95% CI, 1.17–3.14; *P*=.010). MELD score was not associated with risk for readmission (HR, 0.97; 95% CI, 0.95–1.00; *P*=.050).

Table 4 shows mortality data for the study population. Overall, 19 (9.1%) patients died; deaths occurred a mean of 5.51 months after LT.

Discussion

To date, the frequency of and risk factors for readmission to the hospital after LT have not been well described in the literature. Given that LT centers are increasingly held accountable for resource utilization and costs in post-LT care, studying factors that lead to rehospitalization could yield strategies that reduce readmissions and limit healthcare expenditures after LT.

This prospective study found that 30.3% of LT recipients were readmitted within 90 days of LT. LOS in the ICU was negatively associated with risk for readmission (HR, 0.92; *P*=.028), suggesting that patients who required a prolonged stay in the ICU may have had immediate complications that were definitively managed during the initial hospital admission, making these patients less likely to require rehospitalization. MELD score was not associated with readmission, supporting the notion that well-selected recipients do not consume excess resources following the index admission, regardless of the degree of a LT candidate's decompensation prior to the procedure. As such, our findings support the continued practice of prioritizing liver graft allocation to recipients with the highest MELD scores, and this practice does not affect the risk of readmission post-LT.

Interestingly, HCV infection was associated with readmission (HR, 1.91; *P*=.010). One plausible reason for this association is that HCV-infected patients are at risk for elevated liver enzyme levels that necessitate prompt evaluation in the post-LT period; in addition, a minority of HCV-infected LT recipients develop severe recurrent cholestatic HCV infection, which usually requires initiation of anti-HCV therapies that are difficult to tolerate in the early post-LT period and render patients vulnerable to adverse drug events, graft failure, and death.[14] Further studies are needed to better explore the specific reasons for readmission among HCV-infected recipients.

Surprisingly, recipient age was not associated with readmission. This finding may be due to the fact that LT recipients over 60 years of age are carefully selected at our center. Our selection practice is similar to the one described in a retrospective analysis of the UNOS database conducted by Aloia and coworkers.[15] This study found that older patients with 3 or more preoperative risk factors fared poorly; these risk factors included mechanical ventilation, diabetes mellitus, HCV infection, renal insufficiency, or a combined recipient and donor age of at least 120 years.[15]

Table 3. Factors Associated with Readmission After Liver Transplantation

Factor	Hazard ratio (95% confidence interval)	*P*-value
Demographics		
Age	1.01 (0.98–1.03)	.685
Male gender	1.25 (0.67–2.35)	.483
Underlying liver disease		
Hepatitis C virus infection with or without alcoholic liver disease	1.91 (1.17–3.14)	.010*
Autoimmune liver disease	1.01 (0.46–2.21)	.985
Alcoholic liver disease	1.34 (0.77–2.33)	.307
Patient's location before undergoing liver transplantation		
Home	Reference	
Hospital ward	0.96 (0.55–1.67)	
Intensive care unit (without ventilation)	0.42 (0.13–1.36)	
Intensive care unit (with ventilation)	0.36 (0.09–1.50)	
Donor/graft factors		
Deceased donor (brain death)	Reference	
Deceased donor (cardiac death)	1.50 (0.78–2.89)	
Live donor	1.51 (0.47–4.86)	
Donor age	1.01 (0.99–1.02)	.267
Cold ischemia time	1.00 (0.99–1.00)	.722
Complications		
Malnutrition	0.83 (0.42–1.63)	.586
Diabetes mellitus	1.44 (0.71–2.91)	.317
Debility	0.66 (0.24–1.82)	.424
Infection	0.33 (0.08–1.33)	.118
Surgical complications	0.99 (0.58–1.72)	.981
Length of stay		
Total hospitalization post–liver transplantation	0.99 (0.97–1.00)	.064
Stay in intensive care post–liver transplantation	0.92 (0.85–0.99)	.028*
Other factors		
Model for End-Stage Liver Disease score	0.97 (0.95–1.00)	.050
Additional consultative services	0.97 (0.79–1.19)	.771

*Statistically significant.

Table 4. Mortality After Liver Transplantation

Variable	Mean or frequency	Standard deviation or percentage
Death	19	9.1%
Time to death (months)	5.51	7.03

Similar to recipient age, donor factors such as donor age, cold ischemia time, and the type of donor graft were not associated with readmission. This lack of association is not surprising given the relatively low mean donor age and cold ischemia time in our study. Furthermore, most sequelae from suboptimal grafts occur acutely during the primary admission; occasionally, they are delayed but can be managed conservatively in the ambulatory setting over a prolonged period. Hence, these complications rarely necessitate readmission after discharge.

As hospitalization (particularly ICU admission) prior to LT is a surrogate marker for the sickness of LT recipients, it was expected that recipient location pre-LT would predict readmission. Instead, this study found that recipient location pre-LT did not predict readmission, which suggests that with careful recipient selection, even patients with severely advanced disease may have good outcomes without an excess rate of postoperative readmission; this finding has been corroborated in the literature. Furthermore, given the large catchment area serviced by LT centers such as ours, it is common practice to avoid premature discharge from the hospital, thus minimizing the chances that a patient will need early rehospitalization. This is likely the reason that patients with medical and surgical complications or a longer LOS did not have higher rates of readmission. Moreover, the nature of surgical complications is unlikely to warrant readmission, as effective management typically involves definitive treatment during the initial hospitalization.

This study has several strengths and inherent weaknesses. Its strengths include its prospective design and large sample size. Another strength is its single-center design, which minimizes variables that could impact readmission and would be difficult to ascertain in a multicenter study with variations in LT teams. Additionally, the potential confounder of a patient's insurance coverage was obviated, as all subjects in this study had universal coverage under the single-payer Canadian healthcare system.

The weaknesses inherent in this study's single-center design are its lack of external validity and the poor generalizability of its findings. Another flaw is the study's failure to link the pretransplantation health state of a patient to his or her risk of readmission beyond the data captured by MELD score, serum albumin level, and location of the patient prior to LT. Despite the weaknesses of our study, our results address a deficit in knowledge in the literature on health services utilization, specifically rehospitalization, after LT.

Conclusion

Just as transplant programs should promote the most efficient use of donor grafts, these programs are also obliged to maximize the financial resources bestowed upon them for the betterment of society and the sustainability of LT activity in their center. Understanding the patterns and risk factors for rehospitalization after LT is the first step toward creating internal strategies and overarching regional policies to reduce readmission in high-risk patients. Although not all rehospitalizations are avoidable, minimizing readmissions could result in significant cost savings over time for healthcare systems that finance LT programs. Further studies are needed to explore the reasons for higher readmission rates following LT among the HCV-infected population. It is our belief that without drastic efforts to halt costs in a myriad of inpatient services (including transplantation medicine), healthcare systems will ultimately fail to fulfill their mandate for providing timely and appropriate care for patients.

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