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Avoiding ICU Admission by Using a Fast-Track Protocol Is Safe in Selected Adult-to-Adult Live Donor Liver Transplant Recipients

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Background. We evaluated patient characteristics of live donor liver transplant (LDLT) recipients undergoing a fast-track protocol without intensive care unit (ICU) admission versus LDLT patients receiving posttransplant ICU care. **Methods.** Of the 153 LDLT recipients, 46 patients were included in our fast-track protocol without ICU admission. Both, fast-tracked patients and ICU-admitted patients were compared regarding donor and patient characteristics, perioperative characteristics, and postoperative outcomes and complications. In a subgroup analysis, we compared fast-tracked patients with patients who were admitted in the ICU for less than 24 hours. **Results.** Fast-tracked versus ICU patients had a lower model for end-stage liver disease score (13 ± 4 vs 18 ± 7; $P < 0.0001$), lower preoperative bilirubin levels (51 ± 50 μmol/L vs 119.4 ± 137.3 μmol/L; $P < 0.001$), required fewer units of packed red blood cells (1.7 ± 1.78 vs 4.4 ± 4; $P < 0.0001$), and less fresh-frozen plasma (2.7 ± 2 vs 5.8 ± 5; $P < 0.0001$) during transplantation. Regarding postoperative outcomes, fast-tracked patients presented fewer bacterial infections within 30 days (6.5% [3] vs 29% [28]; $P = 0.002$), no episodes of pneumonia (0% vs 11.3% [11]; $P = 0.02$), and less biliary complications within the first year (6% [3] vs 26% [25]; $P = 0.001$). Also, fast-tracked patients had a shorter posttransplant hospital stay (10.8 ± 5 vs 21.3 ± 29; $P = 0.002$). In the subgroup analysis, fast-tracked vs ICU patients admitted for less than 24 hours had lower requirements of packed red blood cells (1.7 ± 1.78 vs 3.9 ± 4; $P = 0.001$) and fresh-frozen plasma (2.7 ± 2 vs 5.8 ± 4.5; $P = 0.0001$). **Conclusions.** Fast-track of selected patients after LDLT is safe and feasible. An objective score to perioperatively select LDLT recipients amenable to fast track is yet to be determined.

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The techniques of perioperative surgery and anesthesia management have significantly evolved over the past decades.[1,2] As a result of the improved outcome, fast-track protocols have been developed for many surgical procedures allowing complex surgical interventions, without the need for postoperative intensive care unit (ICU) admission.[3-5] Avoiding ICU care within a fast-track protocol has triggered great interest in the surgical community because it minimizes ICU related morbidity, shortens hospital stay, and reduces the costs of postoperative care.[6]

Recently, it has been demonstrated that fast-track protocols can be applied safely for a selected group of patients undergoing deceased donor liver transplantation (LT).[5] The definition of fast tracking in LT still lacks consensus among different institutions, ranging from early postoperative extubation in the operating room once surgery is completed, to strategies that reduce postoperative ventilation time.[7-9] Generally, however, this term is reserved for early extubation, recovery in a postanesthesia care unit (PACU), and direct transfer to the surgical ward avoiding an ICU stay.

Live donor LT (LDLT) has become a widely accepted technique for the expansion of the donor pool with excellent outcomes.[10,11] Specific considerations apply for LDLT in contrast to deceased donor LT, because the recipient remains with a partial graft that contains a large cut surface, and a risk for small for size syndrome. In addition, the LDLT is most often performed electively, and the time point for transplantation can be optimized. It is unknown if fast-track protocols can be applied safely to patients undergoing LDLT.

In 2009, we started a fast-track protocol for adult-to-adult living related LT. In this study, we aim to determine the safety, feasibility, and outcomes of fast-tracking LDLT recipients by comparing fast-tracked patients to those requiring postoperative ICU care. We investigated if LDLT recipients can undergo safely a fast-track protocol by comparing fast-tracked patients to those requiring postoperative ICU care.

MATERIALS AND METHODS

Patients and Data Collection

We retrospectively identified all LDLT recipients who underwent fast-tracking protocol. Fast tracking was defined as early extubation after LDLT in the operating room or in the PACU, followed by transfer to the stepdown unit, and posteriorly to the surgical ward without the need to be admitted to the ICU. The first LDLT recipient being fast -tracked to the surgical ward dated from October 2009, from that time point onward, we evaluated all LDLT recipients (fast-tracked and nonfast-tracked) for identification of variables and characteristics. All LDLT recipients from October 2009 to December 2013 were analyzed. Chart revision and analysis were approved by the clinical review board at the Toronto General Hospital.

Exclusion criteria included patients admitted in the ICU immediately before LDLT, those undergoing multiorgan transplantation or patients in need of renal replacement therapy before transplantation.

Study Design

First, we compared all fast-tracked and ICU patients and defined donor and recipient characteristics in both groups. We performed a subanalysis between patients that were fast-tracked, with patients that had an ICU stay of less than 24 hours. Both groups were compared regarding patient and perioperative characteristics, as well as postoperative outcomes.

Recipient Data

Preoperative patient characteristics included the following; age, sex, body mass index (BMI), model for end-stage liver disease (MELD) score, time on the waitlist, liver disease etiology, and biochemical profile.

Donor and Perioperative Data

Donor characteristics included age, sex, BMI, sex, and graft versus body weight ratio (GBWR). Perioperative information included the following: blood loss, surgical time, intraoperative transfusion of blood-derived products, cold ischemia time (CIT), warm ischemia time (WIT), and type of immunosuppressive induction therapy. Also, time to extubation after the end of surgery was considered. Information regarding morphologic assessment of the graft included number of bile ducts encountered at procurement and the need for a Roux en Y anastomosis for bile duct reconstruction.

Postoperative Outcomes

Postoperative graft injury was assessed by peak aspartate aminotransferase (AST) and alanine aminotransferase (ALT) within 24 hours. Graft function was determined by international normalized ratio (INR) and bilirubin levels at 1 week and 3 months. Complications related to surgery were classified with the Dindo-Clavien score, accounting for all major complications over grade 3b. Postoperative hospitalization included whole hospitalization stay, ICU stay, and stepdown unit stay for both fast-tracked and nonfast-tracked patients. Other variables analyzed included bile duct complications, rejection, and hepatitis C virus (HCV) recurrence within the first year. The need for retransplantation and 30-day mortality was also assessed.

Surgical and Anesthetic Techniques

All recipients received right hepatic lobe grafts (segment V-VIII) with inclusion of the middle hepatic vein. In the occurrence of residual volume issues in the donor, then the middle hepatic vein is spared. Segment V and VIII tributaries are reconstructed if they are greater than 8 mm in size, as previously described.[12] In patients with 2 or more bile ducts, a Roux en Y bile duct reconstruction was performed. In patients with only 1 bile duct, a duct-to-duct anastomosis was the reconstruction method of choice. Detailed donor and recipient surgical techniques have been described in previous communications.[12,13]

Anesthetic induction and maintenance was performed with a combination of midazolam, fentanyl, propofol, and rocuronium. Patients were ventilated with an oxygen-air mixture of isoflurane or sevoflurane. Hemodynamic monitoring consisted of an arterial line, central venous catheter, and a pulmonary artery catheter. Body temperature was maintained with warming blankets and intravenous fluid warmers with a target temperature of 36°C to 37°C. Cell salvage was used in all cases not involving hepatocellular carcinoma (HCC) or sepsis. Transfusion of packed red blood cells (PRBC) was based on clinical assessment, hemodynamic monitoring, and laboratory measurement of hemoglobin and hematocrit. The target hemoglobin concentration was 8.0-10.0 g/dL (hematocrit 25-30%). Fresh frozen plasma (FFP) (2 units) was indicated for an INR activity between 1.5 and 2.0 during the preanhepatic phase if

associated with blood loss. If the INR exceeded 2.0, 4 units of FFP were administered before repeating a coagulation profile. Platelets (5 units) were transfused when needed to keep the platelet count above 80×10^9/L. Cryoprecipitate was given for fibrinogen level below 1.5 g/L in the bleeding patient. Crystalloids (normal saline, plasmalyte and Ringer's lactate) and albumin 5% were used for volume replacement and to maintain adequate urine output (0.5 mL/kg per hour). Cyclokapron was given for suspected massive transfusion antifibrinolytic therapy, and from 2013 onward, the use was guided by the ROTEM results. When given, tranexamic acid was administered as a 1-g bolus followed by a 10-mg/kg per hour infusion until 2 hours after reperfusion.

Fast track was defined as early extubation of LDLT recipients, with subsequent recovery in the PACU, transfer to the stepdown unit, and final transfer to the surgical ward without the need to be admitted to the ICU. Fast-tracking failure was defined as initial fast tracking to the stepdown unit or surgical ward with posterior transfer to the ICU within 72 hours after completion of the surgical procedure.

The decision to fast track was made by the transplanting surgeon and the anesthesiologist most responsible for the case shortly before skin closure. The patient was either extubated in the operating room or in the PACU per our institutions early extubation guidelines. Early extubation was done only if the following parameters were achieved: the patient followed verbal commands with nearly complete reversal of neuromuscular blockade as determined by nerve stimulation or bedside clinical assessment; satisfactory respiratory parameters including FiO_2 requirements less than 50%, oxygen saturation greater than 96%, and normocarbia (PCO_2 < 60 mm Hg with a pH >7.25); hemodynamic stability, and core body temperature between 36.5°C and 37.5°C. Once transferred to the PACU, the patient was assessed by registered nursing staff on a 1:1 nurse to patient ratio. If the patient was eligible for fast tracking to the surgical ward, a previous transfer to the stepdown unit was required at our institution. The decision to fast track and avoid transfer to the ICU was based on disease severity, transfusion requirements of PRBC, and estimated blood loss during surgery.

Stepdown Unit Characteristics and Assessment

Patients recovering in the stepdown unit must be stable and with no need of vasopressors or ventilatory support before transfer. Stepdown unit beds are contiguous to the ICU ward and near the surgical ward. All clinical decisions during stepdown unit stay relied on the physician on call from the surgical multi organ transplant unit, and no assistance was given by nurses or by ICU staff. Patients could initiate oral intake and physical activity with assistance. Once on the stepdown unit, patients were assessed by registered nursing staff on a 1:2 nurse to patient ratio. Removal of the nasogastric (NG) tube is encouraged in first 24 to 48 hours posttransplant if there is no abdominal distension or overt signs of postoperative ileus. Once the NG tube is discontinued, the patient is started on clear fluids. If the patient tolerates well clear fluids, then diet is progressed to a full fluids diet in the next 24 hours. The full fluids diet is comprised of juice, soups, and gelatins. Once the patient is tolerating a full fluid diet, they are upgraded to diet as tolerated, comprised mainly of solid foods. Urinary catheter removal is encouraged in the first 24 hours if the urinary output is above 0.5 to 1 mL/kg per hour plus a descending value of creatinine on laboratory control. Patients are encouraged to use incentive spirometry once they are extubated, working closely with respiratory therapy educators. Physical therapy staff are in charge of early physical activity with isometric exercises on the bed and aerobic dynamic exercises once tolerated.

If any issues were encountered during PACU or stepdown unit observation, responsibility relied on the surgical LT staff in charge of the patient. Before transfer to the surgical ward, hemodynamic stability and spontaneous breathing was confirmed, ensuing a safe removal of invasive monitoring devices such as arterial lines and pulmonary artery catheters.

Statistical Analysis

The SPSS 22 statistical package (IBM, Chicago, IL) was used for the analysis. Categorical variables were compared using χ^2 or Fischer exact test.

Continuous variables were compared using student-t test and Wilcoxon rank-sum test when required. A *P* value of 0.05 or less was considered statistically significant.

RESULTS

Between October 2009 and December 2013, 153 adult-to-adult LDLT were performed at our institution with right hemilivers as grafts (SV-VIII). The first fast-tracked patient was dated from October 2009. To reduce confounding bias regarding decision-making before the start of the fast-track protocol, we decided to use this time frame as our inclusion starting point. Ten patients were excluded from the study for the following reasons: ICU admission immediately before LDLT (n = 3), multiorgan transplantation (n = 1), need for renal replacement therapy before LDLT (n = 6). One hundred forty-three patients were included in the final analysis. Forty-six patients (32%) were successfully fast-tracked to the surgical ward, and 97 (68%) were admitted to the ICU.

Preoperative Characteristics of all LDLT

ICU-admitted patients had higher medical MELD scores compared with fast-tracked patients (mean of 18 ± 7 vs 13 ± 4, *P* = 0.0001), respectively (Table 1). Demographic characteristics, such as age, sex, BMI, and time on the waitlist, showed no differences between groups (Table 1). Biochemical preoperative profile showed no differences regarding creatinine

TABLE 1.

Preoperative characteristics of LDLT recipients

Variables	Fast track, N = 46 Mean ± SD, % (number)	ICU admitted, N = 97 Mean ± SD, % (number)	*P*
Ag, y	51.6 ± 11.66	52.4 ± 11.95	0.69[a]
Sex (male)	63 % (29)	60% (58)	0.71[b]
BMI, kg/m^2	26.04 ± 4.63	26.15 ± 5.66	0.9[a]
MELD	13 ± 4	18 ± 7	0.0001[a]
Bilirubin, mg/dL	51 ± 50	119.4 ± 137.3	0.001[a]
INR	1.6 ± 0.66	1.95 ± 1.29	0.06[a]
Creatinine, mg/dL	77.72 ± 22.22	83.36 ± 36.23	0.33[a]
Time waitlist, d	202.48 ± 406.93	171.92 ± 222.06	0.56[a]
HCC diagnosis	34% (15)	27% (26)	0.33[b]
HCV diagnosis	28% (13)	22% (21)	0.38[b]

[a] Student *t* test.

[b] χ^2 test.

and INR values. Bilirubin levels were higher in ICU-admitted patients compared with fast-tracked patients (119.4 ± 137.3 mg/dL vs 51 ± 50 mg/dL, $P = 0.001$), respectively. End-stage liver disease etiology had the same distribution between both groups. HCC diagnosis accounted for 34% in the fast-tracked group and 27% in the ICU-admitted group. HCV diagnosis was the second most common indication for LDLT, accounting for 28% of fast-tracked patients and 22% of ICU-admitted patients (Table 1).

Donor and Perioperative Characteristics

Donor age, BMI, and GBWR showed no differences between both groups (Table 2). Donors of ICU-admitted recipients had a male gender preponderance compared with donors of the fast-tracked recipient group (48% vs 30%, $P = 0.04$), respectively (Table 2).

Regarding the surgical procedure, estimated blood loss was higher in those patients admitted to the ICU compared to fast-tracked patients (2489±2060 mL vs 1834 ± 1069 mL, $P = 0.05$), respectively. CIT and WIT were the same for both study groups. Operative time was longer in ICU patients compared to fast-tracked patients (535.51 ± 108.97 minutes vs 497 ± 79.44 minutes, $P = 0.04$), respectively. Transfusion of blood-derived products was lower in fast-tracked patients; PRBC transfusion rates were lower (mean 1.7 ± 1.78 Units vs 4.4 ± 4 Units; $P = 0.0001$), as well as FFP transfusions (2.7 ± 2 Units vs 5.8 ± 5; $P = 0.0001$). No difference was seen in vasopressor requirements. Time to extubation after skin closure was shorter in fast-tracked patients compared to ICU group (mean 127 ± 202 minutes vs 1059 ± 3005; $P = 0.08$). Variables such as immunosuppressive induction therapy were similar in both groups. Bile duct reconstruction did not show any statistically significant differences between fast-tracked patients and ICU-admitted patients (Table 2).

Two patients failed to fast-track and needed ICU admission after initiation of the fast-track protocol. One patient required a splenectomy within 72 hours post-LDLT due to small for size syndrome and the patient was transferred to the ICU posteriorly. The other patient presented with a bile leak and sepsis on the third postoperative day. A Roux-en-Y construction and placement of drains was performed. The patient was admitted to the ICU postoperatively due to biliary sepsis. None of the 2 patients needed mechanical ventilation during ICU admission.

TABLE 2.

Donor and recipient perioperative characteristics

Variables	Fast Track, n = 46 Mean ± SD, % (number)	ICU admitted, n = 97 Mean ± SD, % (number)	*P*
Donor characteristics			
Donor age, y	37.9 ± 10.65	36.85 ± 11.73	0.6[a]
Donor male sex	30% (14)	48% (46)	0.04[b]
Donor BMI, kg/m^2	26 ± 4	27 ± 5	0.06[a]
GBWR	1.02 ± 0.23	1.16 ± 0.38	0.2[a]
Recipient characteristics			
Estimated blood loss, mL	1834 ± 1069	2489 ± 2060	0.05[a]
PRBC, Units	1.7 ± 1.78	4.4 ± 4	<0.0001[a]
FFP, Units	2.7 ± 2	5.8 ± 5	<0.0001[a]
Platelets, Units	1.71 ± 3	2.8 ± 4	0.10[a]
Operative time, min	497 ± 79.44	535.51 ± 108.97	0.04[a]
CIT, min	99.25 ± 42.37	99.15 ± 63.63	0.99[a]
WIT, min	45 ± 11.72	45.19 ± 16.20	0.95[a]
Time to extubation, min	127 ± 202	1059 ± 3005	0.08[a]
Vasopressor during surgery	63% (29)	79% (77)	0.17[c]
Antibody induction therapy	87% (40)	91% (88)	0.56[c]
Simulect induction	87% (40)	90% (87)	0.56[c]
Timoglobulin induction	0% (0)	2% (2)	1.00[c]
Tacrolimus induction	76% (35)	80% (77)	0.66[b]
Cyclosporine induction	35% (16)	27% (26)	0.33[b]
No. bile ducts	1.28 ± 0.07	1.30 ± 0.05	0.86[a]
No. bile ducts >2	26% (12)	28% (27)	0.83[b]
Hepaticoyeyunostomy	46% (21)	64% (29)	0.06[b]

[a] Student *t* test.
[b] χ^2 test.
[c] Fisher exact test.

Postoperative Outcome of Fast-Tracked Versus ICU-Admitted Patients

Patients admitted to the ICU had a mean stay of 4.25 ± 9 days; of these, 47 patients (48%) required an ICU stay for less than 24 hours. The mean posttransplant hospital stay for ICU-admitted patients was longer than for those avoiding the ICU (21.3 ± 29 days vs 10.8 ± 5 days, $P = 0.002$), respectively (Table 3).

Ischemia reperfusion injury and graft function was assessed by biochemical analyses such as AST, ALT, Bilirubin, and INR peak levels. Also, the difference between these variables from pre-LDLT settings and those seen on the seventh postoperative day was considered. INR and bilirubin peak levels showed statistically significant differences between both groups (Table 3). Also, decrease in INR and bilirubin levels from the pretransplant scenario to the seventh postoperative day was different amongst both groups (Table 3).

Patients whom were not candidates to fast-track had more postoperative complications. Major complications classified as greater or equal to grade 3B in the Dindo and Clavien classification score were more common in the ICU-admitted patient group compared to the non-ICU group (33 % vs 6.5 %, $P = 0.002$), respectively. Also, bacterial infections within 30 days post-LDLT were more common in this group (29 % vs 6.5%, $P = 0.002$), respectively. Pneumonia was only encountered in patients that went to the ICU, compared to those who avoided an ICU stay (11.3 % vs 0%, $P = 0.02$). Although there were no differences between groups regarding the number of bile ducts encountered and the need for a hepaticoyeyunostomy, patients in the ICU group had more biliary complications within the first year compared to fast-tracked patients (26% vs 6%, $P = 0.001$). Hepatic artery thrombosis was more common in the ICU group. Rejection and HCV recurrence within the first-year post-LDLT showed no differences between groups. Outcomes regarding 30-day mortality and retransplantation rates were the same in both groups (Table 3). Detailed description of minor and major complications encountered within 30 days of LDLT for both groups is shown on Table 4.

Patient and graft survival showed no statistical significant differences on Kaplan Meier log rank test (Figure 1 and Figure 2). One-, 3 -, and 5-year patient survival was 98%, 88%, and 76% for fast-tracked patients, and 87%, 79% and 77% for ICU patients, respectively, $P = 0.16$. Graft survival at 1,

TABLE 3.

Hospitalization stay, graft outcomes, and postoperative complications of fast tracked patients versus ICU patients

Variables	Fast track, n = 46 Mean ± SD, % (number)	ICU admitted, n = 97 Mean ± SD, % (number)	*P*
Hospitalization stay			
ICU stay, d	0	4.25 ± 9	0.0001[a]
Stepdown unit stay, d	4.16 ± 2.56	5.42 ± 9	0.36[a]
Hospital stay after LT, d	10.8 ± 5	21.3 ± 29	0.002[a]
Graft outcomes			
AST peak, U/L	678.3 ± 468.6	648.7 ± 435.4	0.71[a]
ALT peak, U/L	536.4 ± 406.2	540.4 ± 384.1	0.95[a]
INR peak	2.17 ± 0.37	2.49 ± 0.7	0.002[a]
Bilirrubin peak, mg/dL	95.6 ± 70	174.6 ± 124.2	0.001[a]
Creatinine peak, µmol/dL	109.37 ± 40.63	113.1 ± 61.6	0.59[a]
Bilirubin decrease (pre-LT day 7), mg/dL	2.5 ± 63.4	30.6 ± 127.7	0.001[a]
INR decrease (pre-LT day 7)	0.37 ± 0.72	0.6 ± 1.4	0.02[a]
Major complications—Dindo Clavien >3B	6.5% (3)	33% (32)	0.002[b]
Early postoperative complications			
Bacterial infections within 30 d	6.5% (3)	29 % (28)	0.002[b]
Pneumonia	0% (0)	11.3 % (11)	0.02[b]
Hepatic artery thrombosis	2 % (1)	7.2 % (7)	0.01[b]
30-d Mortality	2 % (1)	3 % (3)	1.00[b]
Late postoperative complications			
Biliary complications within the first year	6 % (3)	26 % (25)	0.001[b]
Rejection within the first year	17% (8)	21 % (20)	0.65[b]
HCV recurrence within the first year—methavir >2	4 % (2)	4.1 % (4)	1.00[b]
Re-LT	2% (1)	7.2 % (7)	0.44[b]

[a] Student *t* test.
[b] X^2 test.

3, and 5 years for fast-tracked patients was 98%, 88%, and 88%, versus 91%, 84%, and 82% for ICU patients, respectively (*P* = 0.23) (Table 4).

TABLE 4.

Minor and major complications within 30 days

	Fast track, n = 46	ICU admitted, n = 97
Dindo and Clavien <3b		
Rejection	8	10
Fluid collection	1	9
Atrial fibrillation	1	0
Hepatic vein thrombosis	2	0
Pneumonia	0	11
Seizures	0	2
Portal vein thrombosis	0	3
Pulmonary embolism	0	1
Urinary tract infection	0	2
Dindo and Clavien >3b		
Bile leak	1	6
HA thrombosis	1	7
Small for size syndrome	1	5

HA, hepatic artery.

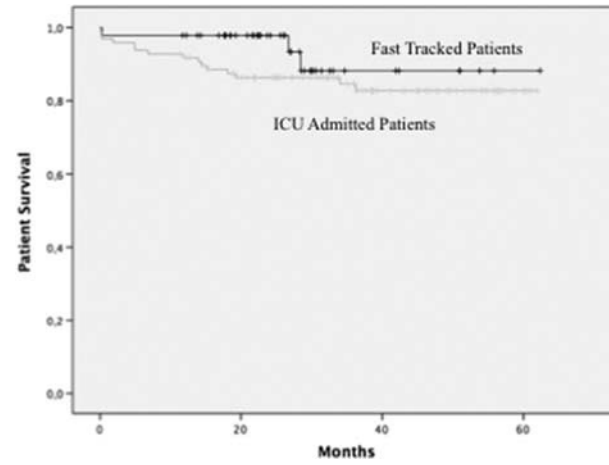

FIGURE 1. One-, 3 -, and 5-year patient survival of fast-tracked patients and ICU requiring patients.

A subgroup analysis of the 47 patients who remained for less than 24 hours in the ICU was made. These patients had higher MELD scores compared with fast-tracked patients. Also, they had greater PRBC and FFP transfusion requirements. Although there was no statistically significant differences, operative time and time to extubation was longer in the less than 24 hours ICU group compared with fast-tracked patients (Table 5). Patient and graft survival showed no statistical differences in the subgroup analysis regarding Kaplan Meier log rank test (Figure 3 and Figure 4).

DISCUSSION

In this study, we present a cohort of LDLT recipients undergoing fast-tracking protocol in a large LT center. One third of adult-to-adult LDLT recipients were successfully fast-tracked and avoided an ICU stay without complications, demonstrating the feasibility and safety of fast-tracking LDLT recipients. Only 2 patients (4.3%) presented failure to fast-track due to surgical complications. In a subgroup analysis comparing fast-tracked patients to those with an ICU stay of less than 24 hours, ICU patients had higher MELD scores, as well as higher PRBC and FFP requirements.

Taner et al[5] recently presented the results of a fast-track protocol after deceased donor LT. The author compared 523 patients

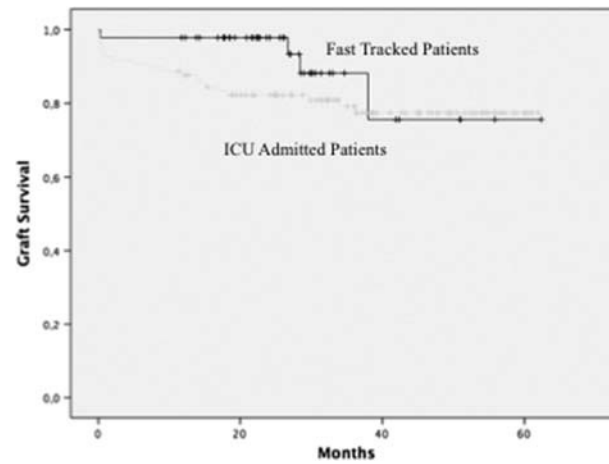

FIGURE 2. One-, 3-, and 5-year Graft survival of fast-tracked patients and ICU requiring patients.

TABLE 5.

Demographic data, perioperative characteristics, and outcomes of LDLT recipients undergoing fast tracking to the surgical ward versus LDLT recipients who were admitted to the ICU for less than 24 hours

Variables	Fast track, n = 46 Mean ± SD, % (number)	ICU admitted, n = 47 Mean ± SD, % (number)	P
Patient characteristics			
Age, y	51.61 ± 11.66	51.1 ± 13.4	0.84[a]
BMI, kg/m^2	26.04 ± 4.63	24.4 ± 5	0.10[a]
Sex (male)	63 %	57.4%	0.3[b]
MELD	13.5 ± 4.36	18.12 ± 7.6	<0.0001[a]
Perioperative characteristics			
Estimated blood loss, mL	1834 ± 1069	2422.7 ± 2040	0.09[a]
PRBC, Units	1.7 ± 1.78	3.9 ± 4	0.001[a]
FFP, Units	2.7 ± 2	5.8 ± 4.5	0.0001[a]
Platelets, Units	1.71 ± 3	2.7 ± 4.26	0.21[a]
Operative time, min	497 ± 79.44	528.5 ± 78	0.07[a]
CIT, min	99.25 ± 42.37	90.25 ± 73.11	0.40[a]
WIT, min	45 ± 11.72	44.6 ± 38.6	0.91[a]
Time to extubation, min	127 ± 202	810 ± 2149.8	0.08[a]
Hospitalization stay			
Stepdown unit stay, d	4.16 ± 2.56	3.6 ± 3	0.35[a]
Hospital stay after LT, d	10.8 ± 5	12.4 ± 6.8	0.20[a]
Postoperative complications			
Bacterial infections within 30 d	6.5 % (3)	14.8 % (7)	0.32[b]
Pneumonia	0 % (0)	4.3 % (2)	0.50[b]
Biliary complications within first year	6 % (3)	21 % (10)	0.07[b]
30-d Mortality	2 % (1)	2.13 % (1)	1.00[b]
Dindo Clavien >3B within 30 d	6.5 % (3)	19.15 % (9)	0.12[b]

[a] Student *t* test.
[b] X^2 test.

who were fast-tracked to the surgical ward versus 347 patients who went to the ICU after transplantation. Fast-tracked patients were younger, had lower MELD scores, lower BMI, less WIT, less surgical time, and less transfusion rates compared to those who went to the ICU. Length of hospital stay was lower in fast-tracked LT recipients. Ten patients (1.9%) that had been fast-tracked initially had to be admitted to the ICU within 72 hours of LT due to complications. Four of these patients had surgical-related complications, the remaining 6 patients had cardiac and renal complications. However, it remained unclear if fast-tracking provided any benefit for the patients or the institution.

In contrast to the study of Taner et al, our patient population included only adult-to-adult right lobe living donor liver transplants. One advantage of the living donor liver transplant setting is that the graft quality is very homogenous since liver abnormalities, such as steatosis, are not present. In addition, donor age and ischemia times have a low variation in LDLT facilitating the comparison of groups by reducing background noise. Furthermore, the same transplant team performed all

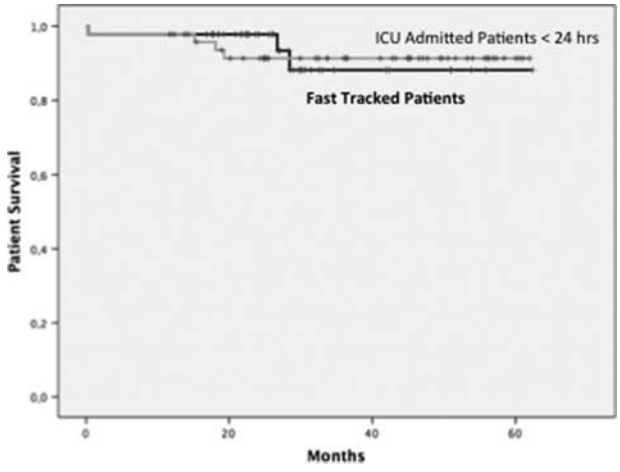

FIGURE 3. One-, 3-, and 5-year patient survival of fast-tracked patients and patients admitted to the ICU for less than 24 hours.

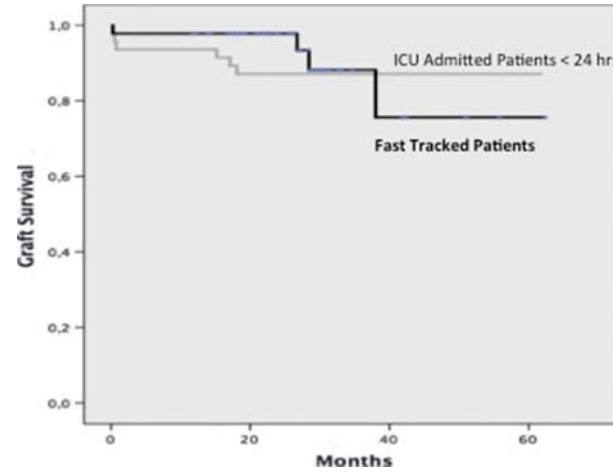

FIGURE 4. One-, 3-, and 5-year graft survival of fast-tracked patients and patients admitted to the ICU for less than 24 hours.

transplants within 5 years, with identical protocols for preoperative and postoperative care, and the homogeneous graft quality and age facilitates the comparison of both groups.

It is important to point out that our fast-track protocol comprises a stepdown unit stay between PACU and surgical ward observation. This may create a slight difference in comparison to Taner et al, where patients were transferred directly from the PACU to the surgical ward. However, Taner et al reports a 1:1 nurse to patient ratio for the first 12 to 24 hrs post-LT once the patient arrives to the surgical ward, as well as continuous monitoring of pulse oximetry, electrocardiography, and central venous pressure. The hemoglobin concentration was measured every 6 hours in the first 24 hours posttransplant if indicated. The surgical ward monitoring protocol resembles our stepdown unit monitoring protocol and patient care responsibility relied entirely on the transplant surgeon and not ICU staff. The difference resides in whether the patient is in a bed embedded on the surgical ward or outside of it, as in our case.

Like the study from Taner et al, our study found that fast-tracked patients also had lower medical MELD scores, lower surgical time, and lower transfusion requirement rates compared to patients who required ICU therapy. GBWR, donor characteristics, CIT, and WIT did not show any significant differences. Only 2 cases of fast-tracking failure were identified, both due to surgical complications.

In our study, from all patients who were admitted to the ICU, nearly half (48%) stayed in the ICU for less than 24 hours. This raises the question of whether more patients could have been fast-tracked, and it highlights the need for identifying objective tools to determine which patients require ICU care. It is possible that LT in the live donor setting places an extra stress on the surgical and anesthesia team resulting in a more conservative approach and seeking secure postoperative assessment in the ICU.

Interestingly, fast-tracked patients presented less major postoperative complications within the Dindo and Clavien score greater than 3B. Hepatic artery thrombosis, as well as biliary complications within the first-year posttransplant was more common in ICU patients. All episodes of pneumonia were encountered only in ICU-treated patients.

We analyzed a group of patients who stayed for less than 24 hours in the ICU despite being allocated as candidates requiring postoperative intensive therapy. Analysis of fast-tracked patients versus those staying in the ICU for less than 24 hours showed more transfusion requirements of PRBC and FFP as a main difference. Also, these patients allocated to ICU therapy had higher MELD scores when compared to fast-tracked patients. This indicates that some patients that could have been fast-tracked underwent ICU surveillance, and emphasizes the need for identifying objective tools to determine which patients really need to go to the ICU in the perioperative setting. LDLT carries an important burden regarding outcomes. This may shift decision-making in the transplant team towards a more conservative approach by seeking secure postoperative assessment in the ICU.

The study was not designed to evaluate possible benefits of fast-track protocols over ICU admission after LDLT. The different patient characteristics of both groups do not allow the comparison of outcomes between fast-tracked and ICU-treated patients. However, it is possible that fast-tracking LDLT recipients offer medical advantages. ICU admission with prolonged intubation could have deleterious effects on some LDLT recipients. First, the longer intubation time associated with ICU admission could lead to ventilation-associated pneumonias. Second, positive pressure ventilation, particularly with positive end-expiratory pressure, reduces splanchnic blood flow which could have a negative impact on partial graft function.[14,15] Third, contact with other critically ill patients may increase the risk of nosocomial infections. A randomized controlled trial comparing fast-track and ICU-treated patients might be difficult to perform. In our experience, some patients who were fast-track eligible were admitted to the ICU instead for logistic reasons, such as unavailability of stepdown beds or PACU space. Future studies should capture these patients prospectively to better compare the effects of fast-track versus ICU stay on outcome of liver transplant recipients.

This study has several shortcomings. It used a retrospective study design and has a small sample size. In addition, as highlighted above, selection biases may have had an impact on the different outcomes in the comparison groups. In addition, we only included LDLT within the same time period.

In conclusion, fast-tracking of selected adult-to-adult LDLT recipients is safe and feasible. Criteria need to be developed to better define the patient population that can benefit from fast-track protocols. Possible benefits for fast-tracking versus ICU care need to be investigated in prospective studies to avoid selection bias.

REFERENCES

1. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth*. 1997;78:606–617.
2. Hawkes CA, Dhileepan S, Foxcroft D. Early extubation for adult cardiac surgical patients. *Cochrane Database Syst Rev*. 2003:CD003587.
3. Razonable RR, Findlay JY, O'Riordan A, et al. Critical care issues in patients after liver transplantation. *Liver Transpl*. 2011;17:511–527.
4. Niemann CU, Kramer DJ. Transplant critical care: standards for intensive care of the patient with liver failure before and after transplantation. *Liver Transpl*. 2011;17:485–487.
5. Taner CB, Willingham DL, Bulatao IG, et al. Is a mandatory intensive care unit stay needed after liver transplantation? Feasibility of fast-tracking to the surgical ward after liver transplantation. *Liver Transpl*. 2012;18:361–369.
6. Bulatao IG, Heckman MG, Rawal B, et al. Avoiding stay in the intensive care unit after liver transplantation: a score to assign location of care. *Am J Transplant*. 2014;14:2088–2096.
7. Mandell MS, Stoner TJ, Barnett R, et al. A multicenter evaluation of safety of early extubation in liver transplant recipients. *Liver Transpl*. 2007;13:1557–1563.
8. Glanemann M, Busch T, Neuhaus P, et al. Fast tracking in liver transplantation. Immediate postoperative tracheal extubation: feasibility and clinical impact. *Swiss Med Wkly*. 2007;137:187–191.
9. Glanemann M, Hoffmeister R, Neumann U, et al. Fast tracking in liver transplantation: which patient benefits from this approach? *Transplant Proc*. 2007;39:535–536.
10. Adcock L, Macleod C, Dubay D, et al. Adult living liver donors have excellent long-term medical outcomes: the University of Toronto liver transplant experience. *Am J Transplant*. 2010;10:364–371.
11. Abt PL, Mange KC, Olthoff KM, et al. Allograft survival following adult-to-adult living donor liver transplantation. *Am J Transplant*. 2004;4:1302–1307.
12. Cattral MS, Molinari M, Vollmer CM, et al. Living-donor right hepatectomy with or without inclusion of middle hepatic vein: comparison of morbidity and outcome in 56 patients. *Am J Transplant*. 2004;4:751–757.
13. Shah SA, Grant DR, Greig PD, et al. Analysis and outcomes of right lobe hepatectomy in 101 consecutive living donors. *Am J Transplant*. 2005;5:2764–2769.
14. Mandell MS, Hang Y. Pro: early extubation after liver transplantation. *J Cardiothorac Vasc Anesth*. 2007;21:752–755.
15. Steadman RH. Con: immediate extubation for liver transplantation. *J Cardiothorac Vasc Anesth*. 2007;21:756–757.