Original Article

Fast tracking in adult living donor liver transplantation: A case series of 15 patients

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ABSTRACT

Background and Aims: Fast tracking (FT) for more efficacious use of resources may be difficult after living donor liver transplantation (LDLT) due to a partial liver graft, complex vascular anastomoses and longer operating time. Our study was aimed at reporting our experience with FT (on table extubation) in LDLT recipients. A secondary objective of our study was to look at defining a subgroup of patients who could be prospectively planned for FT. **Methods:** We studied the demographics and outcomes of 15 LDLT recipients extubated immediately in the operating suite based on an uneventful intraoperative course, haemodynamic stability after graft reperfusion and improvement of metabolic parameters post-implantation and vascular anastomoses. **Results:** Twelve recipients were males, and mean age, body mass index (BMI) and Model for End Stage Liver Disease (MELD) score were 43 ± 12 years, 23 ± 3 kg/m^2 and 15.5 ± 6, respectively, most were Child–Turcotte–Pugh Class B. Diabetes and hypothyroidism were present in 1 and 2 patients, respectively. Post-extubation, none required immediate re-intubation and one patient needed non-invasive ventilation for 2 h. **Conclusion:** Fast tracked recipients were young, with a low BMI, low MELD scores, minimal comorbidities and good immediate graft function post-reperfusion.

Key words: Fast tracking, feasibility, living donor liver transplantation, outcomes, criteria for fast tracking

INTRODUCTION

Enhanced skills of transplant surgeons, anaesthetists and intensivists in patient management, and the consequent success with both deceased donor liver transplantation (DDLT) and living donor liver transplantation (LDLT), have led to a steady and consistent increase in the number of liver transplants (LT's) at our centre, in India and globally.[1]

The focus has now shifted from 'successful LT' to 'rapid recovery post-LT'. 'Fast tracking (FT)' aims at rapid progress from pre-operative preparation to surgery and early discharge. FT is a difficult proposition in LT recipients because of pre-existing comorbidities, complex and prolonged surgery with haemodynamic disturbances, large fluid shifts and delayed correction of metabolic derangements by the liver graft.[2] Successful FT has been previously reported, primarily in the DDLT setting, but has been variably defined as immediate extubation in the operating room, or tracheal extubation within 3 h of surgery.[3-5] Factors such as transplantation of a partial graft, complex vascular anastomoses and longer operating times may make FT in the LDLT scenario even more difficult.

Our study was aimed at reporting our experience with FT (on table extubation) in 15 LDLT recipients. A secondary objective of our study was to look

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at defining a subgroup of patients who could be prospectively planned for FT.

METHODS

Between June 2010 and April 2014, 908 LDLTs were performed. Being a retrospective study, the Institute's Ethics Committee waived off the need for a formal written consent for the study.

Intravenous access was secured through a peripheral line in the preoperative ward. In the operating room, the patients were pre-oxygenated with 100% oxygen, pre-medicated with intravenous (IV) midazolam 0.02–0.05 mg/kg, and fentanyl 1–2 mcg/kg, and rapid sequence induction was done with IV thiopentone 3–5 mg/kg and rocuronium 0.6–1.2 mg/kg. Anaesthesia was maintained using isoflurane in an air/oxygen low-flow respiratory mixture, and continuous intravenous (IV) rocuronium infusion was manually adjusted to maintain T1/T0 at 10%. IV infusion of fentanyl 1–2 mcg/kg/h was used for analgesia. Monitoring included electrocardiography, pulse oximetry, invasive left radial arterial pressure, central venous and advanced venous access via right internal jugular vein, and continuous cardiac output through rapid LiDCO™ monitor.

Although there were no prefixed criteria for early extubation, uneventful intraoperative course, haemodynamic stability post-graft reperfusion, improvement of metabolic parameters and decreasing trend of lactates in arterial blood gas guided extubation. The decision was made in consultation with the operating surgeon after confirmation of good flow on Doppler ultrasound on completion of all vascular anastomoses. Isoflurane and fentanyl were stopped, desflurane was started and boluses of rocuronium were given, if required. After completion of surgery, when the TOF (train of four) ratio had recovered to >0.9, residual neuromuscular blockade was antagonised with IV neostigmine and glycopyrrolate and trachea extubated when they met extubation criteria (viz., breathing spontaneously, awake, able to follow simple commands, respiratory rate ≤35 breaths/min, tidal volume ≥5 mL/kg and heart rate ≤20% above baseline). All patients were shifted to Intensive Care Unit (ICU) within 1 h of extubation.

Additional detailed protocol-based post-operative monitoring included echocardiogram, pulse oximetry, invasive blood pressure monitoring, urine output, biochemical analysis, regular chest X-rays, transthoracic echocardiography and Doppler ultrasonography. Perioperative antibiotic and antifungal prophylaxis and meticulous physiotherapy and pulmonary toilet regimens were followed.

In the 15 patients who were successfully fast tracked, we reviewed patient demographics (age, sex, body mass index [BMI], co-morbidities, METs [metabolic equivalent], presence of ascites or hepatorenal syndrome, Child–Turcotte–Pugh [CTP] and Model for End Stage Liver Disease [MELD] score); intraoperative parameters (packed red blood cell transfusions [BTs], anhepatic, warm ischaemia time [WIT] and cold ischaemia time [CIT], inferior vena cava [IVC] clamp duration and total surgical duration); post-operative course and ICU and hospital stay.

RESULTS

Patient demographics are summarised in Table 1.

Compared to patients who were not fast tracked, we found that fast-tracked patients were younger (mean age, 43 ± 12 years vs. 49 ± 11 years), had a lower BMI (mean, 23.2 ± 3 kg/m^2 vs. 25 ± 3 kg/m^2), and had a low MELD (15 ± 6 vs. 17 ± 7) compared to non-fast-tracked recipients. Most fast-tracked recipients were CTP class A or B. They had a METs' score of 4–6, and no significant co-morbidities.

Mean graft-to-recipient body weight ratio was 1.08 (range, 0.71–1.39). Mean duration of surgery was 660 ± 100 min.

Table 1: Patient demographics in the 15 fast-tracked recipients

Parameter	Value
Age (mean±SD) years	43±12
Sex (male:female)	12:3
BMI (kg/m^2) mean±SD	23.2±3
Aetiology of underlying CLD	
Hepatitis C/Hepatitis B	7/3
Primary sclerosing cholangitis	2
Ethanol	2
Cryptogenic	1
CTP score	
CTP A/B/C	3/9/3
MELD (mean±SD)	15±6
Significant co-morbidities	
Diabetes mellitus	1
Hypothyroidism	2
Suprasellar saccular aneurysm	1
History of	
Ascites/hepatic encephalopathy	4/3

BMI – Body mass index; CLD – Chronic liver disease;
CTP – Child–Turcotte–Pugh; MELD – Model for End Stage Liver Disease

Piggyback technique with full IVC clamp (mean, 50 ± 11 min) was used for graft implantation. The mean anhepatic phase, CIT and WIT were 140 ± 53 min, 70 ± 41 min and 41 ± 8 min, respectively. In all the 15 recipients, single-arterial anastomosis was performed; in one patient, an autologous vein graft was used to extend donor portal vein on the bench.

Five patients did not require any BTs and eight patients needed <4 units of leucocyte-depleted packed red blood cell. Two patients required four and one required five BTs.

In the 15 patients, mean lactate level during the anhepatic phase was 5 ± 2 mmol/L and before extubation, it was 4 ± 2 mmol/L. Mean vasopressor requirement (nor adrenaline) was 0.08 ± 0.06 mcg/kg/min. Only two patients were receiving noradrenaline at the time of extubation (at 0.03 mcg/kg/min and 0.01 mcg/kg/min, respectively).

Regarding post-operative respiratory function, none of the patients required immediate re-intubation. One patient had mild respiratory distress and was managed with non-invasive ventilation for 2 h on the 1st post-operative day. Another had a biliary complication (bile leak) and was re-intubated on the 15th post-operative day for re-exploration. All the other patients had an uneventful post-operative course in the ICU. Mean ICU stay was 4 ± 1 days and mean hospital stay was 17 ± 2 days.

DISCUSSION

To our knowledge, this is probably the largest series of patients from a single centre fast tracked after LDLT. While most of our LDLT recipients (90%) are extubated within 8–12 h in the ICU, we could safely fast-track 15 patients with on-table extubation. Due attention to pre-operative performance status, intraoperative course and a mutual discussion with the operating surgeon are essential when taking a call on possible FT. A competent critical care team helps ensure safe and successful FT. Teamwork is thus of essence if we envisage increasing the proportion of fast-tracked patients.

Historically, LT recipients have been electively ventilated for 48 h with the rationale that positive pressure ventilation with sedation may decrease surgical stress, improve haemodynamic stability and facilitate early recovery.[6] Immunosuppressed post-LT recipients may also be particularly vulnerable to ventilator-associated pneumonia with prolonged ventilation. Prolonged mechanical ventilation may also increase right ventricular afterload and even induce venous congestion of the liver graft, especially in those with pre-existing tricuspid regurgitation and raised pulmonary artery pressures (which is not uncommon in end-stage liver disease patients). Further, hepatic venous drainage is better in spontaneously breathing patients as it reduces intrapleural pressure, thereby increasing cardiac end-diastolic volume, which in turn increases cardiac output and hepatic blood flow. Improved donor graft circulation could aid in early liver graft recovery and regeneration. In addition, cost benefits of FT in LDLT recipients are due to reduced ventilator requirement and ICU and hospital stay.[7]

In the DDLT setting, some authors have demonstrated safe FT and also proposed predictors of possible early extubation (FT).[1,8-10] There is a difference though between the DDLT and LDLT recipients. In adult-to-adult LDLT, the partial graft (right or left lobe) usually takes time to regenerate and attain optimal function. Higher incidence of vascular complications leading to re-exploration is a possibility owing to small size and stumps of vessels in the harvested graft. In addition, surgical duration, and consequently total anaesthesia time for the recipient, is also more in LDLT compared to DDLT. Hence, experience with only a few cases of FT LDLT recipients has been published so far.[11,12] The small proportion of FT recipients in our high-volume centre confirms this difficulty with LDLT recipients.

As mentioned in the results, fast-tracked patients were young, had a low BMI, most were CTP class A or B, had a low MELD score, METs' score of 4–6, and no significant co-morbidities. Most fast-tracked patients had no need for major BT. None of the patients in this subgroup required immediate re-intubation, all recovered well with short ICU and hospital stay and there were no major complications. Based on our experience, we have tried to develop an algorithm, which can aid in deciding on FT LDLT recipients [Table 2].

Advances in balanced anaesthesia techniques and monitoring systems allowing rapid arousal from anaesthesia, like use of remifentanil (due to its rapid elimination), may aid in FT. Another option is to use fentanyl-free periods intermittently during the surgery, instead of continuous fentanyl since it has a long context-sensitive time.

Our study does have some drawbacks. This is a retrospective review of a small number of fast-tracked

Table 2: Proposed criteria to consider patients for fast tracking after living donor liver transplantation

Pre-operative criteria
Inclusion criteria
Age <50 years
Patient BMI <22-26 kg/m^2
Good performance status METS >4
Admission from home
Well-controlled co-morbid condition (diabetes mellitus, hypertension, thyroid disease)
MELD score <20, CTP class A, B (only selected CTP Class C patients)
Exclusion criteria
Patients with hepatic encephalopathy
Patients on renal replacement therapy (SLED, CRRT)
Fulminant hepatic failure patients
Morbidly obese patients
Patients with co-existing HPS or POPH
Intraoperative criteria
Use of <5 units of packed red blood cells during surgery
Low inotropic requirement at the end of surgery (single inotrope, noradrenaline dose <0.05 mcg/kg/min)
Lactates on the downward trend on arterial blood gas after reperfusion
Short duration of surgery (<12 h)
Actual GRWR ratio >0.7
Low-risk vascular anastomoses (especially hepatic artery anastomosis, no multiple arterial anastomoses, no size mismatch)

BMI – Body mass index; METS – Metabolic equivalent; MELD – Model for End Stage Liver Disease; CTP – Child–Turcotte–Pugh; CRRT – Continuous renal replacement therapy; SLED – Sustained low-efficiency dialysis; HPS – Hepatopulmonary syndrome; POPH – Portopulmonary hypertension; GRWR – Graft-to-recipient body weight

patients. Proposing on-table extubation criteria based on a small proportion of patients (15) may be considered inappropriate; however, no other criteria exist as of now, and we structured the criteria based on our cumulative experience with more than 2500 LDLTs (and currently 250–300 LTs every year). This proposed algorithm will have to be validated in a larger subset of patients. Before this, we also plan to perform a prospective study in FT patients meeting these criteria after LDLT which could help in not only further refining the proposed algorithm, but also in initiating the validation process.

CONCLUSION

Although FT is safe and feasible in the LDLT setting, only a small proportion of recipients could be safely fast-tracked. Patients were younger, with a low BMI and MELD, had minimal comorbidities and had an uneventful intraoperative course with good immediate graft function. Defining such a subgroup could guide us to increase on-table extubation, with its subsequent benefits in patient recovery and cost-effectiveness.

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Conflicts of interest

There are no conflicts of interest.

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