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Factors that may affect early extubation after liver transplantation

Shaima Elnour, Zoka Milan

ABSTRACT

It has been suggested that early extubation following liver transplantation (LT) contributes to increased patient and graft survival, shortened hospital stay, and reduced treatment costs. However, few studies have been performed on the clinical criteria for early extubation. Although early extubation criteria are the same as those for any other surgical patient, it is a complex decision for patients who have undergone LT, and there is a learning curve, as it can take some time to increase the early extubation success rate. We summarized and discussed all of the factors reported in the literature that could influence the decision to fast-track patients scheduled for LT. We suggest that the planning process should start earlier, and that potential candidates for early extubation be determined during a pre-assessment session. We divided clinical factors into pre-operative, intra-operative, and post-operative. Intra-operative factors were further divided into factors related to the patient, anesthesia, and graft or surgery quality. We suggest an early extubation strategy following LT that supports the decision-making process and helps accelerate the learning curve for early extubation. Our results may help clinicians with decision-making and can be a platform for additional large, retrospective studies or randomized controlled trials.

Keywords: Liver transplant, Pre-assessment, Fast track

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INTRODUCTION

Improvements in preoperative workups, surgical techniques, and perioperative and postoperative care have made early extubation following liver transplantation (LT) a feasible and safe procedure for a significant proportion of patients. Early extubation has physiological advantages over prolonged mechanical ventilation, including increased venous return to the heart, increased cardiac output, and increased hepatic blood flow [1]. All of these factors contribute to increasing patient and graft survival, shortening hospital stay, and reducing treatment costs [2–5].

Most studies about fast tracking are retrospective, and have analyzed the advantages and disadvantages of fast tracking. Very few studies have been performed on how and when to extubate a patient in the operating theatre who have undergone LT, and which factors affect that

decision. Although early extubation criteria are the same as those for any other surgical patient, it is a complex decision for patients who have undergone LT, and there is a learning curve, as it can take some time to increase the early extubation success rate.

The focus of this study was to review all of the factors that may affect early extubation, and to review the evidence for this procedure. We suggest an early extubation strategy following LT that supports the decision-making process and helps accelerate the learning curve for early extubation.

METHODS

We performed a literature search of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1946–Jun 2015), EMBASE (1980–Jun 2015), CINAHL (1981–Jun 2015), HMIC (1979–Jun 2015), and ISI Web of Knowledge databases, using the search terms 'LT' 'early extubation' and 'fast-track'. This yielded 24 relevant articles. Then, we searched the reference lists from these articles and trials, which yielded an additional eight articles. Of the 32 articles, 9 contained factors that may affect early extubation [2, 3, 6–12].

We found a variety of definitions for fast tracking and early extubation following LT, ranging from removing the endotracheal tube immediately in the operating room to removing it within the first few postoperative hours [13, 14]. We added our long clinical experience at several very different LT centers to suggest an early extubation strategy.

RESULTS

We found that different authors investigated different variables that could potentially become excluding or including criteria for early extubation after LT. We included all of the factors that could affect early extubation. We present our initial findings with absolute contraindications and then with the decision-making process. We classified all of the factors chronologically, and divided them into preoperative and intraoperative stages. We further divided the preoperative period into the time the patients were first placed on the transplantation list, and the time just before their planned LT when the patients were in the hospital.

Preoperative decision

Which patients should be excluded from early extubation attempts? Absolute contraindications for attempting an operating room extubation are intuitive, and seem to be based on the likely clinical course of a critically ill patient with acute or end-stage liver failure. No single study has stated all of the exclusion criteria. We summarized the current contraindications for early extubation in Table 1. After excluding ineligible patients, the next step was to identify patients with characteristics that predict successful early extubation.

Table 1: Exclusion criteria for fast-tracking following liver transplantation

Acute liver failure and multi-organ failure [2, 4, 6, 11, 12]
Multi-organ transplantation [2, 4, 6, 11, 12]
Combined cardiac and liver transplant surgery [11]
Dialysis dependence, acute renal failure [8]
Mechanically ventilated patients [2, 4, 6, 11, 12]
Re-transplantation for primary non-functioning graft [2, 4]
Pulmonary hypertension (MPAP >35 mmHg) [11]
Hepato-pulmonary syndrome if shunt fraction >20% [11]
Encephalopathy grade 3 or 4 [2, 4, 6, 11, 12]

What characteristics (or recipient characteristics) are important at the time of listing? The process of planning an early extubation should start at the time of enlisting patients for LT. The factors that influence such a decision are the patient's condition, including primary liver disease, age, sex, body mass index (BMI), and co-morbidities.

Liver disease: Several studies have failed to prove a correlation between diagnosis and fast tracking [2, 7]. There is only evidence that the absence of a hepatic cellular carcinoma/cholangiocarcinoma diagnosis is a significant predictor of intensive care unit (ICU) admission [7].

Age: Several studies have shown that younger age is a significant co-factor for early extubation, but there is no age limit [2, 7]. A study by Taner [7] used age <65 years as one of the factors contributing to early extubation.

Sex: Male sex was significantly associated with an increased likelihood of successful fast tracking in a multivariate analysis of retrospective data collected from 1,296 patients who underwent LT, of whom 54.3% were successfully extubated [2].

BMI: A very high and very low BMI can negatively affect fast tracking. A higher BMI has been associated with prolonged mechanical ventilation [2, 6]. In a study by Mandell [4], a BMI >34 kg/m^2 and a BMI >35 kg/m^2 in the study by Taner [7] were significant factors that contributed to prolonged mechanical ventilation. Low BMI, which is characteristic of patients with advanced liver disease, is more prevalent in patients requiring prolonged ventilation, suggesting that malnutrition may be an important factor impacting the postoperative course [6].

Co-morbidities: Patients with minimal or no co-morbidities are more likely to be extubated early. No easy way to quantify co-morbidities exists. Some studies have suggested that patients with cardiac and pulmonary disease should not be extubated early. However, there is no evidence to support this statement. Although patients

with coronary artery disease are considered unsuitable for early extubation, there are case reports of successful early extubation in patients with coronary artery disease [15] . If the preoperative cardiorespiratory reserve, as defined by cardiopulmonary exercise testing (CPET), is a sensitive and specific predictor of early survival after LT [16], it would be interesting to determine whether patients with better cardiorespiratory reserve, as shown by better CPET performance, would be more likely to be extubated after LT.

Other factors

Although previous abdominal surgery and the presence of encephalopathy grades I and II are not included in any early extubation scoring system, they can both delay extubation following LT [7].

Preoperative assessment

The clinical picture of patients and their symptoms can change significantly because the period between enlisting and actual LT may be several days to several years. The second stage of decision-making starts with the preoperative visit. Normal clotting (assessed by INR, platelets count and fibrinogen level) or corrected clotting abnormalities make early extubation a greater possibility, because they usually lead to lower intraoperative blood loss, which has a favorable impact on early extubation [2, 4]. The model for end-stage liver disease (MELD), as an indicator of liver disease severity, has significant predictive power for identifying subjects with a higher likelihood of immediate extubation [2]. In a prospective analysis of 354 patients by Biancofiore [17], a MELD score of 11 had significant predictive power for identifying subjects with a higher likelihood of immediate extubation, whereas a MELD score <12 in the study by Bulatao increased the probability of fast tracking. Patients who are already in the hospital before LT are also less likely to be extubated early after LT [2].

Intraoperative

Decision about early extubation is best made after reperfusion, after hepatic artery reconstruction or between hepatic artery reconstruction and abdominal closure [15].

Donor organ characteristics: The main difference between other major surgeries and LT is that patients receive a new organ that influences recovery during LT. A good-quality graft certainly contributes to a fast recovery, but deciding whether the graft is of good or bad quality is not straightforward. The donor risk index (DRI), a scoring system that assesses donor liver quality for organ allocation purposes, failed as a factor to predict early extubation in the study by Bulato [2]. Donation after cardiac death also has no significant impact on fast tracking [2]. Live related donors have been considered unsuitable for fast tracking in the past, but Cammu [12] reported the successful fast tracking of four patients who received grafts from a live related donor. No evidence suggests that cold or warm graft ischemia time influence fast tracking following LT [2]. Severe reperfusion injury is a risk factor for prolonged mechanical ventilation [2, 6, 7] . We must rely on clinical markers of graft dysfunction, such as severe acidosis, high lactate level, persistent coagulopathy, and hemodynamic instability that require high inotropic support when planning fast tracking [6] .

Surgical characteristics: Several studies have shown that a shorter operating time leads to early extubation [2, 4]. A multi-centre study by Mandel [18] found that the use of veno-venous bypass and the piggyback technique is associated with a higher risk of complications. The author questioned whether they directly affected the outcome or were surrogate variables for other practices not examined in the study. Active bleeding requiring abdominal packing at the end of surgery is a good reason not to extubate a patient postoperatively [2, 4].

Blood loss and red blood cells (RBC) replacement is one of the most important factors in the decision making process. Different studies have found different numbers of transfused blood units as a cut-off point for not proceeding with early extubation. It was 12 units in the study by Biancofiore [8], 10 units in the study by Cammu [12], 7 units in the study by Surzak [6], and 6 units in the study by Glanemann [9]. The varying significance of RBCs and blood product replacement may also be the result of differences in transfusion practices and triggers between centers, as well as the efficiency and prevalence of cell salvage use. Moreover, it is important to recognize the difference in the significance of blood transfusion volume relative to patient weight. For example, 12 units of blood is equivalent to a circulating blood volume of a 50 kg woman, but is approximately 50% that of a 100 kg man. The volume of blood transfused during LT is a measure of several events. Transfusion may be required due to coagulopathy or surgical bleeding. Coagulopathy is a marker of underlying liver disease severity, as well as a surrogate graft function marker. Surgical bleeding is correctable, but can lead to coagulopathy if not resolved quickly. In contrast, several studies have demonstrated a significant difference in the number of fresh frozen plasma, platelets, cryoprecipitate, and red blood cell units between recipients successfully extubated in the operating room and those requiring prolonged ICU ventilation [6, 17].

Body temperature: There is only one study so far that has shown that LT patients who were extubated in the operating room had significantly higher body temperature than patients who were not extubated immediately following surgery [10].

Anesthesia: Short-acting anesthetics, analgesia, and muscle relaxants contribute significantly to early extubation. Centers that cannot afford these or that prefer to ration the use of anesthesia, switch to short-acting agents after hepatic artery reconstruction [15].

Postoperative factors: Post-LT facilities play a significant role in decision-making for early extubation. Patients being treated in more advanced LT centers are transferred to post-anesthetic care units for recovery and extubation, and are then transferred to a ward, which completely eliminates an ICU stay [2].

All factors affecting early extubation following liver transplant are summarized in Table 2.

Table 2: Factors contributing to the decision to extubate early following a liver transplant (LT)

At the time of listing patients for liver transplant:
Primary liver disease (no evidence so far/absence of HCC, HCA)
Age (<65/>65 years)
Gender (M/F)
BMI (<30/>30)
Co-morbidities (None/Diabetes, hypertension, ischemic heart disease, hepatopulmonary syndrome, hepatorenal syndrome)
On the day of liver transplant:
MELD score (<12/>12)
Patient in hospital at the time of call for LT (no/yes)
Encephalopathy grade I or II (no/yes)
Previous abdominal surgery (no/yes)
Intraoperative data:
Graft type (DBD,LRD/DCD)
CIT (short/long)
WIT (short/long)
Anhepatic phase (short/long)
Intraoperative blood replacement (<1500/>1500 ml)
Duration of surgery (<330/>330 min)
Inotropes at the end of surgery (low/high dose)
Lactate at the end of surgery (<3.5/>3.5)
Temperature (<36°C />36°C)

HCC-HCC, hepatocellular carcinoma; CCA, cholangiocarcinoma; MELD, model of end-stage liver disease; DBD, donation after brain death; LRD, live related donation; DCD, donation after cardiac death; CIT, cold ischaemia time; WIT, warm ischaemia time.

DISCUSSION

Immediate extubation of patients following LT is a safe and feasible component of cost-saving fast-track pathways. However, it is not feasible in all patients who have undergone LT, because multiple factors determine whether it is feasible for a particular patient to be fast tracked, the decision has been based mainly on the individual anesthetist's experience. There is a learning curve for every anesthetist involved. Other factors that contribute to decision-making are two scoring systems, suggested by Skurzak and Bulatao [2, 7], that remain to be validated , and studies that address early extubation criteria [3–5, 8–14, 17, 18].

We summarized and discussed all of the factors reported in literature that could influence the decisions to fast-track patients who have undergone LT. We suggest that the planning process should begin earlier, and that potential candidates could be determined even in a pre-assessment session. We gathered all of the criteria reported in literature. We divided factors into preoperative, intraoperative, and postoperative. The intra-operative factors were further divided into factors related to the patient, anesthesia, and graft or surgery quality.

There are factors that we did not consider because they are not easily measurable, but may have important role, such as the medical centres' experience, the quality of the teamwork, local protocols, and supporting services and facilities, such as nutritionists, social workers, physiotherapists and recovery room/high dependency unit/ICU settings. Therefore, clinical judgement remains an important factor in decision-making. Our study can help clinicians with their decision-making, and may also be a platform for additional larger retrospective studies or randomized controlled trials.

Table 2 summarizes all the factors that, according to the current literature, can contribute to the fast track decision. It shows how complex this issue is. This paper brings us a step closer to the objective decision making, but we are still some way off creating a flow chart that can guide us when bringing clinical decisions for early extubation.

CONCLUSION

We summarized all the factors that were present in the current literature and we concluded that: (a) are absolute contraindication and (b) can contribute to the decision of early extubation following liver transplantation. We created a table that can be used as a checklist to help clinicians to include all contributing factors in consideration for early extubation. If most factors are affirmative, the chance for early extubation is greater. However, we still need to validate a cut-off point in terms of the number of factors that determine our ability to early extubate patients with history of liver transplantation.

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Shaima Elnour – Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Zoka Milan – Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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