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Fast tracking in liver transplantation. Immediate postoperative tracheal extubation: feasibility and clinical impact

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Summary

Increased survival rates after orthotopic liver transplantation (OLT) in patients with end-stage liver disease have become possible due to an advanced understanding of the pathophysiology of liver disease, the establishment of multiorgan procurement and preservation techniques, and the development of safer and more potent immunosuppressive drugs. In addition, standardisation of surgical techniques and advances in anaesthetic management have contributed significantly to this development. The up-to-date concept of improving patient outcome following OLT includes a fast track approach in selected patient populations, which may shorten ICU and/or hospital stay and reduce costs. In particular, immediate postoperative extubation has been identified as an excellent tool to achieve both improved clinical results and a reduced drain on financial resources.

Studies on fast tracking protocols have shown clearly that prolonged mechanical ventilation following surgery is no longer justified in the majority of patients. On current evidence at least 70–80% of transplant recipients can be extubated immediately following surgery. The incidence of reintubation is not increased hereafter when compared to patients extubated later. However, special attention should be focused on liver transplant recipients in poor clinical condition at the time of OLT, undergoing complicated surgery, or receiving liver grafts with severe preservation injury. These patients might not be eligible for fast tracking protocols and may be at increased risk of prolonged postoperative mechanical ventilation.

Key words: surgery; postoperative period; postoperative ventilation; liver transplantation

Introduction

Since the first successful human liver transplantation was performed in 1963 this procedure has become an accepted therapy for acute and chronic end-stage liver disease [4]. Several improvements with regard to pre-, intra-, and postoperative management of liver transplant recipients have had a markedly favourable effect on patient outcome and resulted in 1-year survival rates of more than 90% in experienced transplant centres.

In recent years, fast tracking has been implemented in clinical pathways aiming at more efficient use of medical resources. Fast tracking, a term once used to characterise rapid career advancement, now describes a procedure to (i) improve quality of care, (ii) to shorten surgical patients' ICU and hospital length of stay (LOS) and (iii) to reduce total treatment costs. A fast track approach to liver transplantation can theoretically be defined as a process aiming at rapid progress from preoperative preparation of the transplant recipient throughout surgery and at early discharge from hospital. Due to the nature of liver disease in patients awaiting a cadaver liver donor graft, fast tracking clinically refers to specific intra- and postoperative surgical and anaesthesiological strategies once a donor liver becomes available. In liver transplantation, fast tracking essentially means a reduction in postoperative ventilation time.

Today, new drugs and techniques, advanced monitoring and improved perioperative patient care mean rapid and uneventful recovery from surgery, fewer postoperative complications, shorter hospitalisation, increased patient satisfaction and a better overall outcome. As a prerequisite for fast track strategies patients should be free from postoperative complications or these should be minimised.

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Fast tracking uses tools such as short-acting medication and early enteral feeding protocols. Previous anaesthetic regimens for fast track in OLT were characterised by balanced anaesthesia with reduced doses of fentanyl combined with isoflurane [7]. The use of desflurane in current approaches further contributes to shortening anaesthesia action time (Table 1). Mechanical ventilation should be terminated as early as possible if extubation criteria are fulfilled (Table 2). Several investigators have documented a reduction in resource utilisation in coronary artery bypass patients extubated at an early stage after surgery. Thus early extubation, even performed immediately after an invasive procedure such as liver transplantation, appears to be an important component of fast tracking, though the two are not synonymous [7, 21].

Table 1

Current protocol for fast track anaesthesia in OLT, Charité – University Medical Centre, Berlin.

Premedication with midazolam (1 mg iv.)
Fentanyl (1–3 µg/kg iv.)
Thiopental (3–5 mg/kg)
Succinylcholine (1–2 mg/kg iv.)
Desflurane (2–6 Vol%, not in ALF)
Cisatracurium (0.15–0.25 mg/kg, repetition using TOF guidance), no nitrous oxide

Table 2

Criteria for immediate extubation after OLT [9].

When patients are awake and responsive, appropriate criteria for extubation in fast track anaesthesia are:
a) Haemodynamic stability
b) Normoxia
c) Normothermia
d) Sufficient tidal volume [VT 5–8 ml/kg]
e) Respiratory rate (RR) of less than 20 breaths/min
f) Adequate minute ventilation (VE)
g) Positive gag reflexes
After tracheal extubation, oxygen should be given in the intensive care unit by nasal mask in order to maintain oxygen saturation >92%.

Although clinical acceptance is now increasing, fast tracking is still incompletely implemented as a standard procedure for OLT. Recently published results from a survey among departments of anaesthesiology cooperating with transplantation centres in Germany show that 87% of these aimed at early extubation of OLT patients in the ICU. Only one department, however, routinely performed immediate postoperative extubation in the operating theatre [19], documenting a widespread lack of confidence in the success of fast extubation in most transplantation centres. This review therefore focuses on current evidence for the feasibility and effects of immediate postoperative extubation for fast tracking in liver transplantation.

Concept of the fast tracking approach in liver transplantation

Historically, liver transplant recipients have been ventilated for up to 48 hours on a routine basis following the operative procedure. As rationale for these protocols, several investigators have claimed that postoperative positive airway pressure ventilation with sedation may decrease surgical stress response, improve haemodynamic stability, and facilitate early postoperative recovery [20, 26].

Meanwhile it has been shown that increased intrathoracic pressures induce elevated pulmonary vascular resistance, increasing right ventricular afterload [5]. Moreover, backward flow into the inferior vena cava and hepatic veins from associated tricuspid regurgitation may induce venous congestion of the liver graft [10]. In contrast, spontaneously breathing patients show reduced intrapleural pressures, thus improving venous return and hepatic blood flow and potentially resulting in better liver graft recovery [11]. Consequently, Rossaint and co-workers combined early postoperative extubation with restrictive intraoperative fluid management in liver transplant recipients [24]. The latter contributes to reduce oedema formation in the lung, thus preventing the need for high airway pressures during mechanical ventilation. This procedure resulted in rapid recovery of hepatic function and favoured early extubation.

Effects on patient outcome

Successful early extubation is now feasible in the majority of patients within 5–6 hours following surgery. Findlay and colleagues demonstrated that using fast track anaesthesia concepts significantly reduced postoperative ventilation time from 1081 minutes to 553 minutes. However, this did not shorten ICU stay in their study [7]. Neelakanta and coworkers reported similar results showing that in a subgroup of patients extubation could be safely performed in the OR at the end of liver transplant surgery [17]. With respect to survival rate, liver transplant recipients undergoing fast tracking in our hospital certainly benefited from this approach. In a retrospective analysis of n = 546 OLT patients, immediate tracheal extubation in the operating theatre was achieved in 19% and extubation within 24 h was possible in a further 70% (median duration of postoperative mechanical

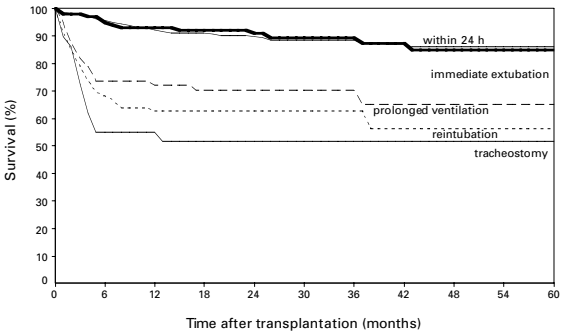

Figure 1

Survival of OLT patients with reference to the time point of postoperative extubation (Charité, 1992–1996, n = 546 patients) [8]. Survival rate was significantly reduced in patients with prolonged ventilation when compared to early extubated patients (P <0.001).

ventilation: 5 h). These patients experienced significantly higher survival rates compared to patients requiring prolonged postoperative mechanical ventilation, i.e. 90 % versus 70% during the first three years (p <.05) (Figure 1) [8]. These findings were confirmed in a recent study by Biancofiore and coworkers, who reported significantly decreased mortality during primary hospitalisation following fast tracking (mortality rates: 1% in transplant recipients with immediate extubation; 4% in patients extubated within 24 h; 42% in patients extubated after 24 h; p <.05) [2]. In addition, fast tracking had been shown to be cost effective, since a reduction in ICU resource utilisation results in lower overall costs [14, 16, 22]. Mandell and coworkers reported that a 13% reduction in total liver transplantation costs had been achieved by a fast track anaesthesia protocol in their institution [14]. Whether fast tracking may have the potential to reduce susceptibility to nosocomial infections or to decrease the incidence of respiratory failure in OLT patients should be addressed in future studies.

Feasibility of immediate postoperative extubation

It has been demonstrated that immediate postoperative extubation in the operating room (OR) could be successfully performed in a large fraction of patients without an increased risk of subsequent reintubation [8, 13, 17]. With regard to possible failure of immediate postoperative extubation, Biancofiore and colleagues reported that variables such as primary graft dysfunction, renal and/or cardiovascular failure, serious neurological impairment, transfusion of more than 12 units of intraoperative red blood cells and pulmonary oedema were predictive for delayed tracheal extubation (more than 3 hours postoperatively), as indicated by logistic regression analysis in 168 patients [1]. Interestingly, neither severity of liver disease, duration of surgery, nor duration of graft cold ischaemia significantly influenced the time of extubation in their analysis. Only a MELD-(Model for End-stage Liver Disease)-score <11 was predictive for successful extubation in the OR [2]. A further statistical analysis in a similar patient population demonstrated that encephalopathy and increased body mass index (>34) were significantly associated with an increased risk of immediate extubation failure (Table 3) [15].

Table 3

Risk factors for prolonged mechanical ventilation after OLT; results from multivariate logistic regression analyses.

No extubation in the OR (147 patients) [15]
– Encephalopathy
– Body mass index (>34)
No extubation within 3 h (168 patients) [1]
– Primary graft dysfunction
– Renal failure
– Cardiovascular failure
– Neurological impairment
– Use of >12 units red blood cells
– Pulmonary oedema
No extubation within 24 h (546 patients) [8]
– Acute liver failure
– Retransplantation
– Severe preservation injury
– Mechanical ventilation prior to transplantation
– Use of >15 units red blood cells and fresh frozen plasma

Prolonged mechanical ventilation in liver transplant recipients is still required in some patients, though the criteria predictive of post-transplant ventilation time are still incompletely understood. It was suggested that a history of encephalopathy and poor graft function are contraindications for early extubation [13]. In a recent study Mandell et al. demonstrated that immediate postoperative extubation may succed in up to 75% of patients after liver transplantation, though this excludes patients with retransplantation, donor graft dysfunction, living donation liver transplant, multiorgan transplants, or United Network for Organ Sharing (UNOS) status 1 [14].

Using a multivariate descriptive regression analysis, the indications of acute liver failure and retransplantation, as well as mechanical ventilation prior to OLT, massive intraoperative bleeding (transfusion of >15 units red blood cells and fresh frozen plasma, and severe reperfusion injury of the liver graft were identified as risk factors for prolonged postoperative mechanical ventilation (>24 hours postoperatively) [8].

Pulmonary complications requiring reintubation include aspiration, atelectasis, pulmonary oedema and pneumonia [12, 23]. Surgical complications are primarily associated with acute postoperative bleeding or severe peritonitis in cases of bile duct insufficiency. With respect to cerebral complications, drug-induced seizures or immunosuppressant (tacrolimus/cyclosporine) overdose have also been reported [9]. To avoid these complications frequent drug monitoring is strongly

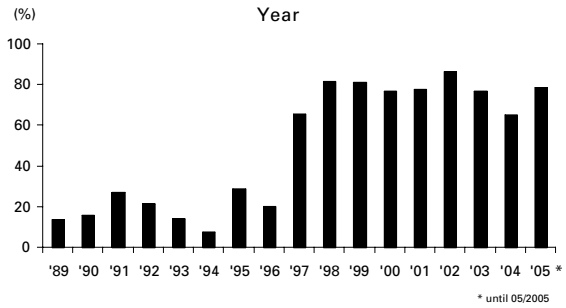

Figure 2

Percentage of patients (%) with successful immediate postoperative extubation in the operating room after liver transplantation during the last decade (Charité, 1989–2005, n = 1483 patients). The data demonstrate that immediate extubation has become feasible in 70–80% of OLT patients since fast track was implemented in 1997.

recommended. In this context, cardiac complications such as heart failure, myocardial infarction or cardiac arrest are rare events, since preoperative evaluation makes it possible in most cases to identify patients with preexisting cardiovascular diseases [1, 9]. Accordingly, in a subset of patients in which factors such as retransplant, donor graft dysfunction, living-related liver transplantation, multiorgan transplantation, or United Network for Organ Sharing (UNOS) status 1 were excluded, the reintubation rate after immediate extubation in the OR was as low as 1–2% [2, 14]. This underlines the feasibility and safety of immediate postoperative extubation as part of fast tracking in otherwise stable liver transplant recipients. Consequently, the reported number of immediately extubated patients has markedly increased in recent years and now approximates 70–80% of all recipients [2, 6, 18, 25]. In accordance with studies from Biancofiore et al. and Salizzoni et al. [2, 25], we currently extubate up to 80% of all OLT patients in the OR (Figure 2). This finding also applies to paediatric and living-related liver transplant recipients [3, 27, 28]. Noteworthy is that patients in our own study who were immediately extubated in the OR following liver transplantation had the lowest reintubation rate (8%) when compared to patients extubated on average 5 h postoperatively (13%), or those requiring prolonged mechanical ventilation of more than 24 h (36%) [8].

Conclusion

In conclusion, early extubation has become the desirable goal for the transplant team, since early liver graft recovery is significantly associated with early patient recovery. Postoperative mechanical ventilation after OLT is no longer required in the majority of patients, since immediate postoperative extubation is usually feasible, safe and well tolerated. However, in liver transplant recipients in poor clinical condition at the time of OLT, or receiving liver grafts with severe preservation injury, special attention is required. These patients may not be eligible for fast tracking protocols and may be at increased risk of prolonged postoperative mechanical ventilation. Future prospective controlled clinical trials should aim to confirm the advantages of fast tracking with respect to duration of mechanical ventilation, length of ICU stay and a possible reduction in the incidence of postoperative nosocomial infections in OLT.

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