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Predictors of Success of Immediate Tracheal Extubation in Living Donor Liver Transplantation Recipients

Thesis

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Douaa Galal

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List of Abbreviations

Abb.	Full term
ASCOT	Ain Shams Center for Organ Transplant
ASUSH	Ain Shams University Specialized Hospital
BMI	Body mass index
CVP	Central venous pressure
EOS	End of surgery
ESLD	End stage liver disease
FFP	Fresh frozen plasma
HAART	Highly active antiretroviral therapy
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HPS	Hepatopulmonary syndrome
HR	Heart rate
ICU	Intensive Care Unit
INR	International normalized ratio
IQR	Interquartile range
LDLT	Living donor liver transplantation
LT	Liver transplantation
MABP	Mean arterial blood pressure
MELD	Model for end stage liver disease
OR	Operating room
PSC	Primary sclerosing cholangitis
PVT	Portal vein thrombosis

Abb.	Full term
RBCs	Red blood cells
ROC	Receiver operating characteristic
SaO_2	Oxygen saturation
SORELT	Safe Operating Room Extubation after Liver transplantation
TIPS	Trans-jugular intrahepatic portosystemic shunt
TOF	Train-of-four
UCSF	University of California San Francisco

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Predictors of Success of Immediate Tracheal Extubation in Living Donor Liver Transplantation Recipients

ABSTRACT

Background: Early tracheal extubation of recipients following liver transplantation (LT) has been promoted and gradually replacing standard postoperative prolonged mechanical ventilation, possibly contributing to better graft and patient survival and reduced costs. There are no universally accepted predictors of success of immediate extubation in LT recipients. We hypothesized a number of factors as predictors of successful immediate tracheal extubation in living donor liver transplantation (LDLT) recipients.

Aim: The aim of this study was to evaluate the validity of the following hypothesized factors: Model for end stage liver disease (MELD) score, duration of surgery, number of intraoperatively transfused packed red blood cells (RBCs) units and end of surgery (EOS) serum lactate, as predictors of success of immediate tracheal extubation in living donor liver transplantation (LDLT) recipients.

Methods: In this prospective clinical trial, perioperative data of adult LDLT recipients were recorded. "Immediate extubation" was defined as tracheal extubation immediately and up to 1 hour postransplant in the operating room. Patients were divided into; extubated group who were successfully extubated with no need for reintubation, and non-extubated group who failed to meet criteria of extubation or were re-intubated within 4 hours of extubation.

Results: Of 64 patients, 50 (76.9%) were extubated early after LDLT while 14 (23.07%) were transported to the intensive care unit (ICU) intubated. After data analysis, it was found that EOS serum lactate, duration of surgery and number of packed RBCs units transfused intraoperatively, were good predictors of success of immediate extubation, while MELD scores had no statistically significant impact on the results. In addition, other factors such as EOS urine output and *p*H were shown to have significantly affected the results.

Conclusions: EOS serum lactate, duration of surgery and number of packed RBCs units transfused were predictors of post-transplant early extubation.

Key Words: Living donors, Liver transplantation, Tracheal extubation

Introduction

Orthotopic liver transplantation (LT) is an established therapy for acute liver failure, end stage liver disease (ESLD), advanced liver cirrhosis and liver tumors ***(Hoffmeister et al., 2008)***.

Increased survival rates after orthotopic LT have become possible due to an advanced understanding of the pathophysiology of liver disease, the establishment of multi-organ procurement and preservation techniques, and the development of safer and more potent immunosuppressive drugs. In addition, standardization of surgical techniques and advances in anesthetic management have contributed significantly to this development ***(Glanemann et al., 2007).***

Standard postoperative care after LT includes mechanical ventilation and admission to the intensive care unit (ICU). Clinicians believe this type of clinical management improves outcome by providing a smooth transition into the recovery phase and reducing physiological stress caused by awakening and spontaneous ventilation. This has remained common practice despite a lack of evidence that routine postoperative ventilation or ICU admission prevents perioperative complications or

benefits donor organ function. Rather, improvements in intraoperative medical management and technical surgical advances probably explain the recent trend toward fewer perioperative complications and improved patient survival ***(Strong, 2001).***

It thus is reasonable to question whether physicians who use routine postoperative ventilation may be using unnecessary resources and incurring additional costs that do not enhance patient or donor organ outcome ***(Mandell et al., 2002).***

Improvements in preoperative workups, surgical techniques, and perioperative and postoperative care have made early extubation following LT a feasible and safe procedure for a significant proportion of patients ***(Elnour & Milan, 2015).***

"Early" extubation in LT is defined as immediate tracheal extubation in the operating room (OR) within 1 hour post-transplant ***(Mandell et al., 2007)***.

Early extubation has physiological advantages over prolonged mechanical ventilation, including increased venous return to the heart, increased cardiac output, and increased hepatic blood flow and improvement of hepatic drainage. All of these factors contribute to increasing

patient and graft survival, shortening hospital stay, and reducing treatment costs ***(Bulatao et al., 2014)***.

Early extubation in LT recipients was reported in the early nineties. At present, early extubation after LT has been successful in many patients and is gradually being adopted in more and more hospitals ***(Wu et al., 2012).***

However, determination of the appropriate tracheal extubation timing and conditions remains important in securing safe and reasonable patient recovery after LT. No definitive or universal criteria have yet been established regarding predictors for early tracheal extubation in LT patients ***(Lee et al., 2014).***

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 ***(Elnour & Milan, 2015).***

Aim of the Work

The aim of this study was to evaluate the validity of the following hypothesized factors as predictors of success of immediate tracheal extubation in living donor liver transplantation (LDLT) recipients:

1. Model for end stage liver disease (MELD) score.
2. Duration of surgery.
3. Number of intraoperatively transfused blood products {(units of packed red blood cells (RBCs)}.
4. End of surgery (EOS) Serum lactate.

Review of Literature

History of Liver Transplantation

The history of solid organ transplantation dates back several decades. However, it was not until the advent of more aggressive surgical techniques, immunosuppressive agents, and improved organ preservation that the field became successful. The earliest attempts at LT occurred in canine models and were initially unsuccessful with respect to survival. *In 1952, Vittorio Staudacher from Milan, Italy* published the first description of a canine LT ***(Busuttil et al., 2012).***

In USA, C. Stewart Welch at Albany Medical College described the first attempts at canine transplants *in 1955* ***(Welch, 1955)*** followed by *Jack Cannon at the University of California, Los Angeles in 1956* ***(Cannon, 1956)***. These initial transplants resulted in rapid recipient death, but ultimately set the stage for future trials. Shortly thereafter *in 1958*, teams led by *Thomas Starzl in Denver, Colorado* (***Starzl et al., 1961)*** and *Francis Moore in Boston, Massachusetts* ***(Moore et al., 1959)*** were able to perform technically successful canine LT, but these were plagued by poor organ preservation and rapid organ rejection eventually leading to death ***(Fox & Brown, 2016)***.

Starzl performed the first human LT *in Colorado in 1963* on a pediatric patient with biliary atresia. Unfortunately, the patient suffered intraoperative bleeding complications resulting in death. For the next few years there were other unsuccessful attempts by Starzl's team and others around the world. Ultimately, *in 1967, in Colorado, Starzl* performed the first successful LT in an 18-month-old child with hepatoblastoma. The patient survived just over 1 year post transplant and died due to recurrent malignancy. This single transplant provided the proof of concept that LT could be done successfully ***(Fox & Brown, 2016).***

As serendipity would have it, at the time that the technical feasibility of human LT was demonstrated, a critical discovery was made in the field of immunological therapeutics. *In 1969*, cyclosporine was isolated from the fungus Tolypocladiuminflatum in Norway. After almost a decade, it was put into clinical use and *in 1978 Sir Roy Calne* described the use of cyclosporine in renal transplantation. This was followed by his description of its use in other solid-organ transplants, including the liver ***(Calne et al., 1979).***

Liver Transplantation in Egypt

Legalizing deceased donation in Egypt was only made possible by the *2010* law, after a decades-long theological dispute on the definition of death was settled when Egypt's higher religious authorities, represented by the al-Azhar Islamic institution and the Coptic Church, officially approved it. According to most interpretations of the Islamic Sharia Law, the heart must stop beating before someone is legally declared dead. Thus, donation from brain-dead patients was not possible before 2010.The implementation of the law however, had been hindered by the political unrest in the country over the past few years ***(Ramadan, 2015).***

To this day, LDLT remains the only possible option for patients with ESLD in Egypt ***(Mehrez, 2017).***

LDLT was *first performed in Egypt in 1991* by the surgical team at the National Liver Institute (NLI), Menoufeya University, with the help of *Prof. Habib*. The longest recipient survival was 11 months. The breakthrough was made in Dar Al-Fouad Hospital by starting the program of LDLT *(August 2001), with Prof. Tanaka,* Kyoto University, Japan. This was followed by Wady El-Neel Hospital *(October 2001),* NLI, Menoufeya University