Journal of Clinical Anesthesia 44 (2018) 35–40

Contents lists available at ScienceDirect

Journal of Clinical Anesthesia

Original Contribution

Factors associated with mortality within 24 h of liver transplantation: An updated analysis of 65,308 adult liver transplant recipients between 2002 and 2013

Kyota Fukazawa, MD, PhD [a,*], Ernesto A. Pretto Jr., MD, MPH [b], Seigo Nishida, MD, PhD [c], Jorge D. Reyes, MD [d], Edward Gologorsky, MD, FASE [e]

[a] Department of Anesthesiology and Pain Medicine, University of Washington School of Medicine,1959 NE Pacific Street, Seattle, WA 98195, USA
[b] Department of Anesthesiology, Perioperative Medicine and Pain Management, University of Miami Miller School of Medicine, 1611 NW 12th Avenue, D318, Miami, FL 33136, USA
[c] Department of Surgery, Division of Liver and Gastrointestinal Transplant, Westchester Medical Center, New York Medical College, Taylor Pavilion, Room D214, 100 Woods Road, Valhalla, NY 10595, USA
[d] Department of Surgery, University of Washington School of Medicine, 1959 NE Pacific Street, Seattle, WA 98195, USA
[e] Drexel University College of Medicine, Allegheny Health Network, Allegheny General Hospital, Department of Anesthesiology, 320 East North Avenue, Pittsburgh, PA 15212, USA

ARTICLE INFO

Article history:
Received 15 August 2017
Received in revised form 19 October 2017
Accepted 20 October 2017

Keywords:
Liver transplant
Pulmonary embolism
Mortality
Futile
Risk
Transesophageal echocardiography

ABSTRACT

Study objectives: Intracardiac and pulmonary thromboembolism (ICPTE), its risk factors and contribution to 24-hour mortality after adult liver transplantation for end-stage liver disease.
Design: Retrospective analysis of Standard Transplant Analysis and Research electronic database files.
Setting: Perioperative.
Patients: Electronic files of 65,308 adult liver transplant recipients between 2002 and 2013 obtained from Organ Procurement and Transplantation Network.
Interventions: Mortality cause analysis and design of a multivariable logistic regression model for predicting the risk of 24-hour mortality due to devastating ICPTE.
Measurements: Perioperative mortality, donor and recipient demographics, donor cause of death, graft ischemic times, etiologies of recipient end-stage liver disease, functional status, comorbidities, and laboratory values.
Main results: 41,324 patients were included. 38,293 (92.6%) survived 30 days after transplantation. Postoperative 24-hour mortality was 547 (1.3%) and 2484 (6.0%) within subsequent 30 days. Uncontrolled hemorrhage (57 patients, 0.14%), devastating ICPTE (54 patients, 0.13%) and primary graft failure (49 patients, 0.12%) contributed the most and equally to the 24-hour mortality. For the ICPTE, recipients' prior history of pulmonary embolism, portal vein thrombosis, functional status (Karnofsky score) <20, preoperative ventilator support, diabetes mellitus and Asian ethnicity emerged as significant independent hazard factors on multivariable regression analysis. These risk factors were expressed as an index to calculate the overall hazard of a devastating ICPTE; c-statistics 0.70 ($p < 0.001$).
Conclusions: Devastating ICPTE contributes significantly to the 24-hour mortality after adult cadaveric liver transplantation. Its most significant risk factors could be expressed as an index with a good predictive accuracy. Further studies of perioperative factors with potential impact on ICPTE and related mortality and morbidity are needed.

1. Introduction

Reports from the European Society for the Study of the Liver and from the American Association for the Study of Liver Diseases indicate a steady improvement in outcomes in liver transplantation over the last 25 years. In 2014, survival rates reached 96% one-year postoperatively, and 70% at ten years [1,2]. These statistics, however, may reflect gradually changing UNOS organ allocation policies derived from a wait list patient population with relatively high (close to 50%) proportion of Model for End-Stage Liver Disease (MELD) scores of <29, as well as liberal application of MELD point exceptions for hepatocellular carcinoma in 25%. The current organ-allocation scheme prioritizes recipients with 1A status and with higher MELD scores (Share 35), and limits the exception score points for hepatocellular carcinoma (HCC) [3–5]. That

* Corresponding author at: Division of Transplantation, Department of Anesthesiology and Pain Medicine, University of Washington School of Medicine, 1959 NE Pacific Street, Seattle, WA 98195, USA.
E-mail addresses: fukazawa@uw.edu (K. Fukazawa), epretto@med.miami.edu (E.A. Pretto), reyesjd@uw.edu (J.D. Reyes), egologor@wpahs.org (E. Gologorsky).

https://doi.org/10.1016/j.jclinane.2017.10.017
0952-8180/

policy resulted in a higher proportion of older, critically ill patients with severe and complex comorbidities presenting for liver transplant. American Society of Transplant Surgeons (ASTS) reported that these patients are more likely to be hospitalized, require intensive care and life-support devices more often (>35%) and have MELD scores >30 (40%) [2]. Not surprisingly, concurrent with the higher acuity and MELD scores, perioperative morbidity, mortality and resource utilization increased as well [6–8]. These challenges call for the determination of the factors that may be associated with specific risks, worse perioperative outcomes and futility [2].

While graft loss due to acute rejection continues to decline, infections and perioperative surgical complications account for almost 60% of deaths or graft losses in the first operative year [1,2]. The focus of this investigations was the 24-hour mortality in adult patients with end-stage liver disease (ESLD) presenting for cadaveric orthotopic liver transplantation (OLT), and specifically, recipient risk factors associated with patient deaths due to devastating intracardiac and pulmonary thromboembolism (ICPTE).

2. Methods

2.1. Study population

After University of Washington Institutional Review Board (IRB) approval and exemption by the Human Subject Division (IRB#STUDY00002306), the Standard Transplant Analysis and Research (STAR) electronic database of all patients who underwent orthotopic liver transplantation (OLT) in the United States between 2002 and 2013 (as of May 1, 2014) was obtained from the Organ Procurement and Transplantation Network (OPTN). The recipient and donor variables in this analysis consisted of the demographic information of recipient and donor, relevant serum laboratory values at the time of transplantation, and outcomes. Only adults who underwent OLT in the United States for ESLD were included in the analysis. Exclusion criteria included recipient characteristics (age <18 years old, hepatocellular carcinoma, acute/fulminant hepatic failure, and category 1A), donor (live-donor liver transplantations) and intraoperative data (split or partial liver transplant and simultaneous other organs' transplantation, such as multivisceral, liver-kidney, liver-heart and liver-intestine) (Table 1).

2.2. Study definitions

This study followed United Network for Organ Sharing (UNOS) diagnostic codes for the cause of death after transplantation. UNOS MELD score at transplant was calculated as [serum total bilirubin (mg/dL)] + 11.2 × Ln [prothrombin-INR] + 9.57 × [serum creatinine (mg/dL)]. UNOS assessed functional status of recipients using Karnofsky performance status scale, which assigns, in increments of 10, a score ranging from 10 (moribund, does not get out of bed) to 100 (no impairment due to disease, fully active) [9,10].

Table 1
Inclusion and exclusion criteria.

Inclusion criteria
1. Orthotopic liver transplantation performed in the United States between 2002 and 2013
2. Adult (recipient age ≥ 18)
Exclusion criteria
1. Recipient age <18 years old
2. Hepatocellular carcinoma
3. Acute/fulminant hepatic failure
4. Category 1A
5. Live-donor liver transplantations
6. Split or partial liver transplantations
7. Simultaneous other organ transplantations

2.3. Functional status score (Karnofsky score)

10%: no play; does not get out of bed
20%: often sleeping; play entirely limited to very passive activities
30%: in bed; needs assistance even for quiet play
40%: mostly in bed; participates in quiet activities
50%: can dress but lies around much of day; no active play
60%: up and around, but minimal active play
70%: both greater restriction of and less time spent in play activity
80%: active, but tires more quickly
90%: minor restrictions in physically strenuous activity
100%: fully active, normal

2.4. Outcomes

STAR electronic data files were searched for outcomes after OLT. The control group included all recipients who survived at least 30 days after transplantation. Postoperative mortality included all causes of recipient deaths within 24 h postoperatively. Within this category, available donor and recipient characteristics of the patients who were reported as having suffered devastating ICPTE (the group of interest) were compared to those who survived >30 days after OLT (control group).

Descriptors included donor and recipient demographics such as age and ethnicity, donor cause of death, graft ischemic times, causes of recipient end-stage liver failure and its complications, comorbidities, functional status and laboratory values.

2.5. Statistical analysis

Descriptors associated with immediate 24-hour postoperative mortality due to ICPTE were analyzed using univariate logistic regression model to determine the magnitude of contribution of each variable and to calculate its odds ratio. Wald statistics was used to calculate p value with 95% confidence interval; $p < 0.05$ was considered to indicate statistical significance. Only significant variables with $p < 0.01$ in the univariable analysis were further fitted into multivariable logistic regression model and adjusted odds ratios were calculated. Mathematical formula predicting the risk of devastating ICPTE was proposed based on the relative contributions of various significant risk factors, and its Receiver Operating Characteristic curve plotted. MELD scores were not used to calculate adjusted odds ratio to avoid multicollinearity with laboratory variables used to calculate MELD scores. SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for statistical analysis. All reported p values were two-sided.

3. Results

3.1. Characteristics of study cohort

Our study cohort consisted of 65,308 adult OLT cases. Split or reduced size liver transplantation (3137 cases), recipient with status 1A at transplantation (3112 cases), living related liver transplantation (2407 cases), and simultaneous other organ transplantation (4701 cases), malignancy as an indication for liver transplantation (13,937 cases) were excluded from our study, which left 41,324 patients included in the analysis. Of these, 38,293 (92.6%) survived at least 30 days after transplantation (control group); postoperative mortality included 547 within 24 h (1.3%) and additional 2484 (6.0%) within subsequent 30 days. The causes of death within 24 h after transplant are summarized in Table 2 and Fig. 1. The three most common causes of recipient death within 24 h after transplant were hemorrhage (0.14%), ICPTE (0.13%), and primary graft failure (0.12%), followed by right heart failure due to pulmonary hypertension (17 patients, 0.04%), respiratory failure (17 patients, 0.04%), myocardial infarction (15 patients, 0.04%), cardiac