Analysis of the Predictive Ability for Graft Loss and Mortality of Two Criteria for Early Allograft Dysfunction After Liver Transplantation

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ABSTRACT

Introduction. The current imbalance between available donors and potential recipients for orthotopic liver transplantation (OLT) has led to a liberalization of organ acceptance criteria, increasing the risk of post-transplant complications such as early allograft dysfunction (EAD). Consequently, we need accurate criteria to detect patients with early poor graft function to guide the strategies of management. We evaluated the usefulness of two frequently used criteria: the definition from Olthoff et al and the Model for Early Allograft Function (MEAF) scoring.

Patients and Methods. Unicentric cohort study of patients undergoing OLT between January 1, 2010, and November 20, 2016. We performed a univariate study to detect donor, recipient, and transplant factors favoring EAD, defined both by Olthoff criteria and a MEAF score higher than 7. Finally, we developed a comparative survival analysis for cases having or not EAD.

Results. In all, 201 transplants met inclusion criteria. According to the stated cutoff for MEAF score, the frequency of EAD was 9.3%, with a significant association to low recipient body mass index and prolonged total graft ischemia time, resulting in lower patient 3-month postoperative survival. According to Olthoff criteria, EAD incidence was 22.1% and was associated with younger donor and recipient ages and higher Model for End-stage Liver Disease and Child-Pugh recipient scores. Its development resulted in lower graft and recipient survival at 3 months after OLT.

Conclusion. MEAF score and Olthoff criteria are useful tools for detection of EAD. The latter could select more appropriately patients at risk, but its calculation cannot be done until the seventh day after OLT, unlike MEAF score, available on third day.

CURRENTLY, orthotopic liver transplantation (OLT) represents a cornerstone for management of acute liver failure and end-stage liver diseases. The imbalance between the numbers of donors and patients on the waiting list for OLT, the development of donation after cardiac death (DCD), and the progressively older age of donors has led transplant units to expand the criteria for donor liver allografts acceptance, increasing the risk of adverse outcomes. In addition, most of the allocation systems prioritize the waiting list for OLT using the Model for End-stage Liver Disease (MELD) score, allowing the access to the transplant to sicker patients [1].

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For these reasons, it is important to have accurate systems that allow an early evaluation of the graft function and detect patients with inappropriate liver performance. To achieve this, some definitions of early allograft dysfunction (EAD) have been created (for example, the criteria stated by Olthoff et al [2]). On the other hand, we can use functional tests (indocyanine green plasma disappearance rate [3]) or laboratory tests like platelet count, levels of transaminase, bilirubin factor V, lactate, insulin growth factor 1, and the international normalized ratio (INR) [4]. Finally we can check liver function with scores and scales: MELD, acute physiology and chronic health evaluation (APACHE) [5], chronic liver failure -sequential organ failure assessment (CLIF-SOFA) [6] and model of early allograft function (MEAF) [7].

Most used methods are Olthoff et al criteria [2] and MEAF score. Both were designed by logistic-regression multivariate data analysis. The first one, from 300 liver transplant recipients at 3 different transplant units in the United States, detected EAD when one or more of the following variables were present: (1) bilirubin greater than or equal to 10 mg/dL on postoperative day 7; (2) INR greater than or equal to 1.6 on postoperative day 7; (3) aminotransferase level (alanine aminotransferase or aspartate aminotransferase) greater than or equal to 2000 IU/mL within the first 7 postoperative days.

MEAF score has been developed from a study cohort of 829 liver recipients at the La Fe University Hospital in Valencia (Spain) and has been validated with an independent cohort of 200 OLT recipients at Cruces University Hospital in Bilbao (Spain). From the peak values of alanine aminotransferase, INR, and bilirubin during the first 3 postoperative days, a nonlinear regression model was used to get a 1 (best data) to 10 (worst value) scoring, highly predictive of mortality and graft loss within the 3 first postoperative months.

Our goals in this study were to evaluate the usefulness and applicability of MEAF score and Olthoff et al criteria [2] to identify EAD in our setting; detect recipient, donor, and transplant factors involved in its development; and evaluate its impact on the evolution and survival of the recipient.

PATIENTS AND METHODS

This was an observational unicentric study from a cohort of 204 patients who underwent OLT at Hospital Universitario Virgen de las Nieves between January 1, 2010, and November 20, 2016, with a minimum follow-up of 6 months. Eligibility criteria include (1) patients undergoing cadaveric donor OLT in our institution during the inclusion period; (2) availability in the clinical report of all relevant clinical and laboratory information; (3) a minimum survival of 3 days (for the MEAF score) and 7 days (for the Olthoff et al criteria); (4) a minimum 6 months of follow-up.

The analyzed variables included donor (age, gender, brain death or non–heart-beating donor), recipient (age, gender, body mass index [BMI], previous liver transplantation, pretransplant status, severity according to Child-Pugh and MELD scores), and transplantation data itself (presence of portal thrombosis, performance or not of temporary portocaval shunt, type of biliary reconstruction, severity of postreperfusion syndrome, number of transfused red blood cells packs, total ischemia and surgical time).

The analyzed postoperative variables included morbidity, intensive care unit (ICU) and overall stay, along with graft and recipient survival.

Defined dependent variables were the development of primary graft dysfunction according Olthoff et al criteria [2] and MEAF score, along with short (3 months) and long-term graft and patient survival. Quantitative variables were described by their median and interquartile range (IR).

A univariate study (with nonparametric tests for quantitative variables and χ^2 or Fisher exact tests for qualitative tests) was performed to detect donor, recipient, and transplant factors favoring the onset of EAD. The cutoff point in MEAF score for definition of EAD was stated in a value of 7. The performance of MEAF score to predict short-term patient and graft survival was tested by receiver operating characteristic curves and area under the curves. Survival analysis was performed according Kaplan-Meier method. Log-rank test (Mantel-Cox) was used to compare graft and patient survival (dividing the cohort into patients with and without development of EAD, according to Olthoff et al criteria [2] and MEAF score). Data were analyzed with SPSS 20.0 program (SPSS, Chicago, Ill, United States).

RESULTS

Recipient Characteristics

From 204 eligible OLTs performed in the study period, 3 patients were excluded of the study because they died before 3 days postsurgery; no one was excluded because of lack of information or incomplete follow-up. Because of this, the final cohort consists of 201 transplants.

There was predominance of male subjects (83.8%), with a median age of 55 years (IR 49–61). Median BMI was 27 kg/m^2 (IR 23.9–30.5). Only 12 recipients (5.8%) had undergone previous liver transplantation, and 18.1% of patient needed to be admitted before OLT. Median (IR) MELD and Child-Pugh scores were 16 (12–20) and 7 (5–11), respectively. Most frequent indications were alcoholic cirrhosis (57.8%), virus C cirrhosis (30.3%), and hepatocarcinoma (26.9%).

Donor Characteristics

In donors, men were also predominant (63.2%), with a median age (IR) of 64 (51–75). Although the vast majority (91.1%) of our grafts arises from donors in brain death, 8.9% came from DCDs. Only 2.4% of the grafts were derived from a hepatic bipartition.

Transplant Details

Median waiting list time (IR) was 203 days (100–303). A portal thromboses was intraoperatively detected in 21.1% of the cases. Temporary portocaval shunt was performed in almost half (47.5%) of the transplants. Median (IR) total ischemia time was 340 minutes (255–391), not exceeding 10 hours in any case. Only in 5.4% of transplants was hepaticojejunostomy performed as the biliary reconstruction technique. Postreperfusion syndrome was absent in 70.1% of cases, mild in 12.3%, medium in 12.3%, and severe in