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A rapid, reproducible, noninvasive predictor of liver graft survival

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ABSTRACT

Background: Clinical and laboratory criteria are not reliable predictors of deceased donor liver graft quality. Intraoperative assessment of experienced surgeons is the gold standard. Standardizing and quantifying this assessment is especially needed now that regional sharing is the rule. We prospectively evaluated a novel, simple, rapid, noninvasive, quantitative measure of liver function performed before graft procurement.

Materials and methods: Using a portable, finger-probe–based device, indocyanine green plasma disappearance rates (ICG-PDR) were measured in adult brain-dead donors in the local donor service area before organ procurement. Results were compared with graft function and outcomes. Both donor and recipient teams were blinded to ICG-PDR measurements.

Results: Measurements were performed on 53 consecutive donors. Eleven liver grafts were declined by all centers because of quality; the other 42 grafts were transplanted. Logistic regression analysis showed ICG-PDR to be the only donor variable to be significantly associated with 7-d graft survival. Donor risk index, donor age, and transaminase levels at peak or procurement were not significantly associated with 7-d graft survival.

Conclusions: We report the successful use of a portable quantitative means of measuring liver function and its association with graft survival. These data warrant further exploration in a variety of settings to evaluate acceptable values for donated liver grafts.

1. Introduction

Liver transplantation is the standard treatment for end-stage liver disease. Although the number of transplant candidates continues to grow, organ availability has plateaued resulting in increasing waitlist mortality [1]. The donor pool has been modestly expanded through increasingly aggressive organ utilization: the use of living donors, deceased donor split livers, and "extended criteria donors." Each opportunity for transplantation of every organ of all donors is thoroughly evaluated by each and every organ procurement organization (OPO) and transplant center. Used judiciously, these grafts provide an opportunity to address the shortage but not without costs. The use of extended criteria grafts predispose recipients to poor initial graft function and increased long-term risk [2]; the use of living and deceased donor split

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livers is associated with increased biliary and arterial complications [3–5].

Optimizing the use of these grafts while minimizing recipient risk requires accurate and reproducible assessment of graft quality. Quantitative descriptions of organ quality have yielded specific and accurate relative risks of graft failure for kidney donors [6]. This information has facilitated discussions among donor organizations, transplant surgeons, and even recipients. Similar methodology for liver grafts, namely the donor risk index (DRI), has been less accepted and infrequently used [7]. Standard clinical and laboratory criteria are not reliable predictors. Routine biopsy of donor livers is plagued by risk of injury to the graft, lack of uniformity and availability of microscopic interpretation, and increased cost and delay. Therefore, the gold standard remains physical assessment by transplant surgeons [8]. This, however, leads to inefficient use of resources, by having surgeons evaluate either too many livers only some of which are suitable for transplantation or too few livers, thus forgoing useable grafts. Furthermore, as regional sharing is becoming standard, centers will face increasing difficulties in having their own procurement teams assess all offered grafts. This means relying on surgeons from other centers to make graft suitability determinations, a prospect that makes many ill at ease.

Factors that have previously been shown to affect graft utilization and function include advanced donor age, hypernatremia, prolonged warm ischemia time, vasopressor requirement, and donation after cardiac death [9]. What is needed is a low cost, portable, rapid, noninvasive, standardized, quantitative measure of liver function performed before graft procurement. This study evaluates just such a technique that takes advantage of indocyanine green clearance by hepatocytes.

Indocyanine green clearance is a well-established quantitative test of liver function, used primarily before planning a liver resection [10–12]. A few previous studies have examined the role of indocyanine green clearance in the setting of liver transplantation. Wesslau *et al.* [13] assessed indocyanine green plasma disappearance rates (ICG-PDR) in donors and its association with graft utilization and function. Koneru *et al.* similarly tested ICG-PDR to predict graft function after transplant [14]. Both groups were handicapped by the fact that to measure ICG-PDR, they either had to use an invasive device or draw serial plasma samples and measure the level of ICG at each time point, a time- and resource-intensive process. We now have the distinct advantage of having access to a simple portable device that can easily perform a noninvasive rapid measurement of ICG clearance with minimal set up and training.

Table 1 – Recorded variables.

Donor	Recipient
Age	Age
Gender	Gender
Race/ethnicity	Race/ethnicity
Blood type	Blood type
Weight	Weight
Height	Height
Body mass index	Body mass index
Cause of death	Physiological MELD
Intracranial bleed, blunt trauma, penetrating trauma, and anoxia	List MELD
Presence of liver trauma	Status 1
Length of hospitalization	Ventilator status
Liver trauma	Dialysis
Vasopressors	Vasopressors
Medical history	Liver disease etiology
Diabetes, hypertension, hepatitis B, hepatitis C, other	Simultaneous liver/kidney recipient
Hemoglobin A1c	Laboratory values (at time of offer)
Substance abuse history	INR, Cr, bilirubin, platelets, albumin, and prealbumin
Alcohol, cocaine, methamphetamines, cannabis, other	Redo liver transplant status
Cardiac arrest	
Respiratory arrest	Operative
Total downtime	
CPR duration	Procuring surgeon training level (fellow, attending)
MAP range	Cold ischemia time
MAP at procurement	Warm ischemia time
Laboratory values (at presentation, peak, and procurement)	Transfusions
Na, Cr, bilirubin, AST, ALT, INR, pH, PCO_2, pO_2, HCO_3	Intraoperative temperature
Imaging studies	Base excess
	Venovenous bypass
Other	Intraoperative hemodialysis
	Hepatectomy duration
DRI	Total case duration
ICG-PDR	

Cr = creatinine; CPR = Cardiopulmunary Resuscitation; INR = International Normalized Ratio; MAP = Mean Arterial Pressure; MELD = Model for End-Stage Liver Disease score.