Title
A rapid, reproducible, noninvasive predictor of liver graft survival

Journal
Journal of Surgical Research, 197(1)

ISSN
0022-4804

Authors
Zarrinpar, A
Lee, C
Noguchi, E
et al.

Publication Date
2015-07-01

DOI
10.1016/j.jss.2015.03.093

Peer reviewed

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

A rapid, reproducible, noninvasive predictor of liver graft survival

Ali Zarrinpar, MD, PhD, Coney Lee, MS, Emily Noguchi, MS, Hasan Yersiz, MD, Vatche G. Agopian, MD, Fady M. Kaldas, MD, Douglas G. Farmer, MD, and Ronald W. Busuttil, MD, PhD*

Dumont-UCLA Transplant Center, Division of Liver and Pancreas Transplantation, Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, California

ARTICLE INFO

Article history:
Received 19 January 2015
Received in revised form
3 March 2015
Accepted 27 March 2015
Available online 7 April 2015

Keywords:
Deceased donor
Organ procurement
Liver graft assessment
Liver graft utilization
Indocyanine green

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

* *Corresponding author*. Dumont-UCLA Transplant Center, Division of Liver and Pancreas Transplantation, Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA 90095. Tel.: 310-267-9610; fax: 310-267-3590.
E-mail address: azarrinpar@mednet.ucla.edu (A. Zarrinpar).
0022-4804/$ – see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2015.03.093

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.

2. Materials and methods

2.1. Patient population and design

Consecutive adult brain-dead donors in a large urban donation service area whose livers were offered to recipients at our center were enrolled in the study with signed informed consent, provided donor research consent was also available. We excluded split liver and donation after cardiac death grafts to minimize variability not strictly due to liver function. All available donor data were collected before procurement. These data included age, gender, race and/or ethnicity, cause of death, length of hospitalization, height, weight, number of vasopressors, history of diabetes, hypertension, substance abuse, hepatitis B and C serology, downtime, vital signs, and laboratory values at presentation, peak, and procurement (Table 1). At the donor hospital, immediately before organ procurement, ICG-PDR was measured using the noninvasive liver function monitoring system, LiMON (PULSION Medical Systems, Munich, Germany). LiMON measures ICG clearance by noninvasive pulse-densitometry. Injected ICG is detected from fractional pulsatile changes in optical absorption. This allows for continuous and repeated measurements of ICG-PDR. Two liver transplant perfusionists trained in using the device carried the device and ICG with them to the site of organ procurement. An ICG finger clip placed on the donor was connected to a liver function monitor. A dose of 0.25 mg/kg ICG was given through a central or peripheral vein as a bolus and immediately flushed with 10 mL of normal saline [15]. ICG-PDR measurements were automatically performed by the monitor. Both donor and recipient surgeons were blinded to ICG-PDR measurements.

The transplant team made an independent decision of whether to transplant the graft. After transplantation, the function of the allograft was evaluated using standard laboratory criteria of the recipient. For patients transplanted at the primary center, values of international normalized ratio (INR), serum bilirubin, lactate dehydrogenase, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were recorded up to postoperative day 30; patient and graft survival were also recorded for 1 y. For patients transplanted at backup centers, only 7- and 30-d graft survivals were available. This study was reviewed and approved by the University of California, Los Angeles, Institutional Review Board and the local OPO OneLegacy Research Review Board.

2.2. Statistical analysis

Descriptive statistics were used to describe study samples. The chi-square test was used to assess association between categorical variable. Box plot, scatter plot, and histogram were displayed to graphically show the distribution of ICG-PDR. Univariate logistic regression analysis was used to examine the association between covariates and the outcome variable (status of graft). This was further used to generate an receiver operating characteristic (ROC) curve. The covariates that had a P value <0.2 in the univariate analysis were included in the multivariate logistic regression analysis, and forward selection and backward elimination method was used in finding the best

Table 2 – Donor characteristics.

Characteristic	Value
Age (y)	
Median	47.5
Interquartile range	26–57
Gender, *n* (%)	
Male	39 (73.6)
Female	14 (26.4)
Race/ethnicity, *n* (%)	
Hispanic/Latino	24 (45.3)
White	19 (35.8)
Black	5 (9.4)
Other	5 (9.4)
BMI (kg/m^2)	
Median	26.8
Interquartile range	24.2–30.6
Cause of death, *n* (%)	
Intracranial bleed	29 (54.7)
Blunt trauma	11 (20.8)
Penetrating trauma	7 (13.2)
Anoxia	6 (11.3)
Pressors at procurement, *n* (%)	
0	2 (3.8)
1	15 (28.3)
>1	36 (67.9)
Medical/social history, *n* (%)	
Hypertension	17 (32.1)
Alcohol abuse	8 (15.7)
Diabetes	5 (9.4)
Hepatitis C	2 (3.8)

BMI = body mass index.

Table 3 – Recipient characteristics.

Characteristic	Value
Age (y)	
Median	56
Interquartile range	46–63
Gender, *n* (%)	
Male	38 (74.5)
Female	13 (25.5)
Race/ethnicity, *n* (%)	
White	21 (41.2)
Hispanic/Latino	19 (37.3)
Black	4 (7.8)
Other	7 (13.7)
Physiological MELD	
Median	30
Interquartile range	10.5–38.5
Preoperative hemodialysis, *n* (%)	18 (35.3)
Preoperative ventilator, *n* (%)	10 (19.6)
Redo liver transplant, *n* (%)	6 (11.8)
Simultaneous liver/kidney transplant, *n* (%)	5 (9.8)
Pressors, *n* (%)	
0	44 (86.3)
1	5 (9.8)
>1	2 (3.9)
BMI (kg/m^2)	
Median	27.7
Interquartile range	23.7–30.5

BMI = body mass index; MELD = Model for End-Stage Liver Disease score.

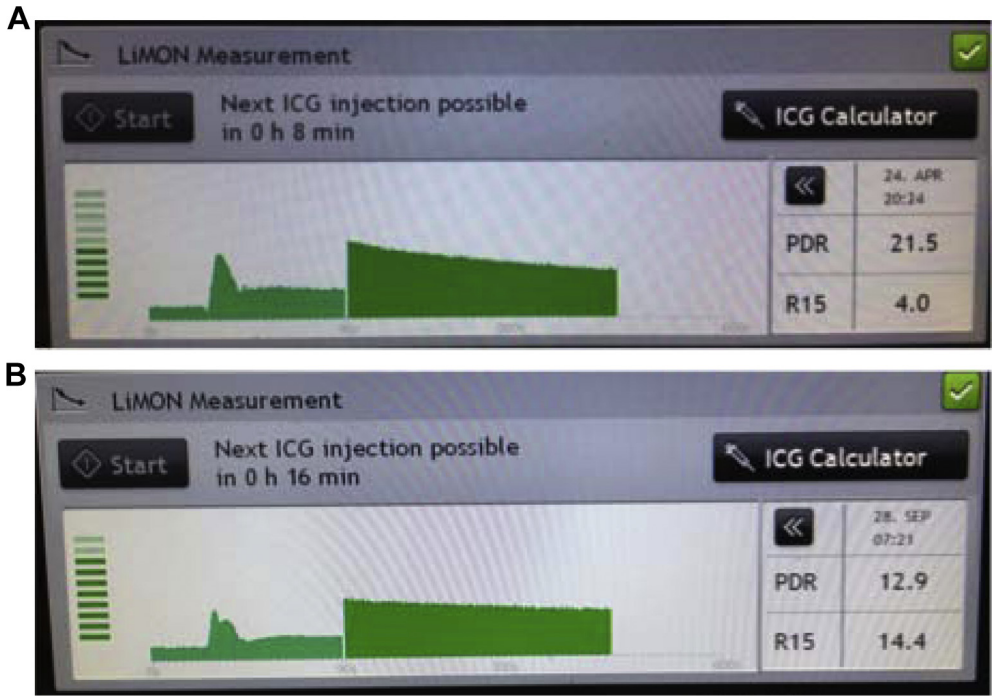

Fig. 1 – Sample PULSION-LiMON ICG trace of an accepted (A) and a rejected (B) graft. (Color version of figure is available online.)

parsimonious final model. We examined the relationship between the donor variables and 7- and 30-d graft survival or postoperative markers of early graft dysfunction [16], specifically bilirubin ≥10 mg/dL or INR ≥ 1.6 on post-operative day 7, or ALT or AST ≥ 2000 within the first 7 d. A *P* value of <0.05 was considered statistically significant. Subjects for whom the ICG-PDR values were unobtainable were excluded from the statistical analysis. All statistical analyses were conducted using JMP, version 9 (SAS Institute Inc, Cary, NC).

3. Results

3.1. *ICG clearance*

ICG-PDR measurements were performed on 53 consecutive donors for 51 potential recipients. The recorded donor and recipient variables are listed in Table 1. Some demographic data of donors and recipients are listed in Tables 2 and 3. Measurement of ICG-PDR took an average of 14 min to perform (range, 9–24 min) from the time the patient was placed on the operating table to the time the ICG-PDR value was obtained (Fig. 1). Values were not obtained (i.e., the device did not give a reading) for three cases, two in organs that were transplanted and one in an organ that was not transplanted. This was likely due to severe vasoconstriction from vasopressors in one donor, false nails in another donor, and for undetermined reasons in the remaining donor. The ICG-PDR values in the study population, 22.5 ± 6.8% per min, match well with what is reported in the literature for normal individuals [17] (Fig. 2A). Linear fit of the variables shows that ICG-PDR decreases with the age of the donor (Fig. 2B). No other donor variables, including medical history, mechanism of death, and laboratory values at admission, peak, or procurement, were significantly associated with ICG-PDR. For example, there was no association with gender, height,

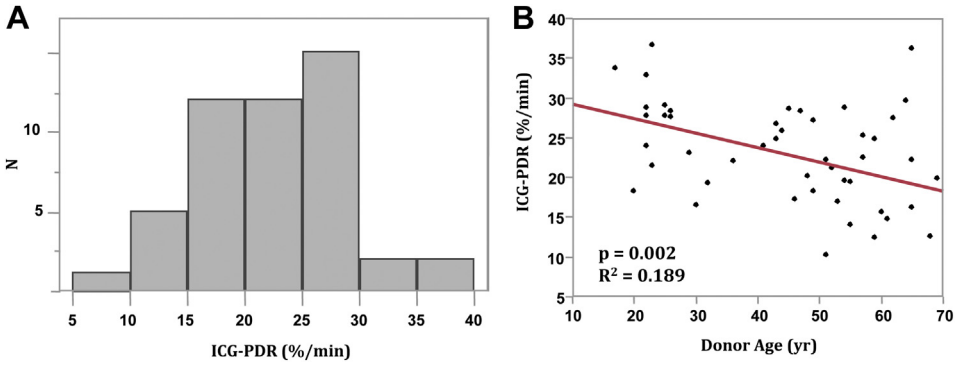

Fig. 2 – (A) Histogram of ICG-PDR values in donors. (B) Scatter plot of ICG-PDR *versus* donor age. Linear fit of the variables shows a correlation of ICG-PDR with donor age. (Color version of figure is available online.)

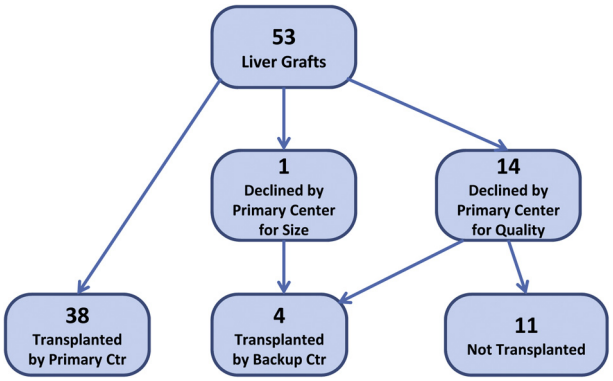

Fig. 3 – Flowsheet describing the utilization for all evaluated grafts. (Color version of figure is available online.)

weight, body mass index, ALT, AST, bilirubin, INR, number of vasopressors, or blood gas chemistry. Furthermore, there was no association with either total or macrovesicular steatosis on biopsy.

3.2. *Graft survival*

The 51 recipients in this study constituted a representative subset of our general recipient patient population. Their characteristics are listed in Table 3. Of the 53 donors we examined for them, 14 liver grafts were declined by our center owing to quality and one was declined for size. Of those turned down for quality, six were deemed fibrotic (four by biopsy and two by palpation), four were felt to be too stiff on palpation after cold perfusion (one with 30% steatosis by biopsy), two were too steatotic (50% and 70% macrosteatosis), and two had poor quality arteries. Because all the donors were within our Donor Service Area, cold ischemia time likely did not figure significantly into the decision to use the graft. Of these organs, four were used by a backup center (one that was turned down for size and three that were turned down for quality; Fig. 3). Grafts that were not transplanted due to quality were counted as nonsurviving grafts. Thus, the primary surgeon's assessment of the graft at the time of procurement was highly correlated with 7-d survival ($P < 0.001$). Nevertheless, ICG-PDR was the only donor factor associated with 7-d survival of a liver graft (Table 4). The mean ICG-PDR for grafts surviving 7 d was 24.2% per min and for nonsurviving grafts was 18.7% per min. Using logistic regression, we calculated an ROC curve. Setting the cutoff value of ICG-PDR at 19.3% per min as a predictor of 7-d graft survival maximized specificity and sensitivity with an area under the curve (AUC) of 0.747 (Fig. 4). Donor Risk Index, donor age, and transaminase levels at peak or procurement were not significantly associated with 7-d graft survival (Table 4), neither were any recorded recipient factors nor the training level of the procuring surgeon. On multivariate analysis, only ICG-PDR stayed significant with an odds ratio of 1.08 (1.04–1.12; $P < 0.0001$).

3.3. *Comparison of ICG-PDR values with graft outcomes*

There were four grafts with ICG-PDR values above 19.3% per min that did not survive 7 d (Table 5). Two of these grafts (ICG-PDR values of 28.3 and 24.9% per min) were deemed good grafts by the procuring surgeon and were used by the primary center. One graft failure was in a patient who underwent a redo liver transplant operation requiring massive transfusions; he died of cardiac failure on postoperative day 2. The second graft failure was in a patient who died of cardiac arrest shortly after reperfusion. These deaths were likely not graft quality related. The remaining two grafts were discarded because the procuring surgeon deemed them too stiff and fibrotic on cold perfusion on inspection in the donor operating room. One had fibrosis on frozen section analysis at the procurement hospital. Likely because of those assessments, the grafts were declined by all backup centers. It is unknowable whether these grafts would have survived had they been used.

There were six organs that did survive beyond 7 d despite having an ICG-PDR value <19.3% per min (Table 5). Four of these grafts were used in recipients with physiological Model for End-Stage Liver Disease (MELD) scores of ≤16, one was used in a status 1a patient, and one (declined by the procuring surgeon) was used in a patient not at the primary center with undisclosed MELD and disease etiology. Of the 14 organs turned down for quality by the procuring surgeon, three were used by a backup center. All those grafts survived >30 d. Two of the grafts had ICG-PDR >19.3% per min.

4. Discussion

Liver allograft quality varies widely. The ultimate goal of being able to reliably predict risk of graft failure has not yet been achieved. The liver DRI has met with very limited use because of concerns that it does not accurately predict post-transplant survival, excludes relevant donor factors, and that it is too complicated for ease of use [18]. Currently, physician expertise and experience is the dominant determinant of liver graft utilization, something that does not allow for standardization and critical evaluation of how to improve the system. This also limits liver graft portability and sharing among Donor Service Areas and regions. Furthermore, the lack of a reliable means of assessing liver function places much pressure on the OPO to expend a great deal of energy evaluating possibly unusable liver grafts or not evaluating perfectly good grafts.

Although transplant surgeons depend greatly on the gross appearance of liver grafts and routine liver function tests obtained during the donor's hospitalization, many studies have shown that these factors are often unreliable and irreproducible [8,19]. Furthermore, a large amount of money and resources are involved merely to arrange for the operative evaluation of liver grafts.

Our study, too, shows that the donor liver function tests and history do not correlate with ICG clearance, graft utilization, graft survival, and post-transplant graft function. Although several assays to measure the synthetic or clearance capabilities of the liver have been reported in the literature, including lidocaine metabolite clearance [20], all these assays

Table 4 – Univariate predictors of 7-d graft survival.

Median (interquartile range)			
Donor variable	Nonsurvival ($n = 13$)	Survival ($n = 40$)	P value
ICG-PDR (%/min)	17.1 (13.2–24.2)	23.9 (19.8–28.5)	0.006
AST at peak (U/L)	109 (48.5–322)	59.5 (41.8–134.5)	0.06
Length of hospitalization (d)	5 (4–15.5)	4.5 (4–6.8)	0.07
ALT at peak (U/L)	100 (36–203)	43.5 (30–104)	0.11
pH at procurement	7.39 (7.35–7.44)	7.42 (7.36–7.46)	0.19
Vasopressors (*n*)	2 (1.5–2)	2 (1–2)	0.21
ALT at procurement (U/L)	53 (29.5–104.5)	34 (21–56.8)	0.22
AST at procurement (U/L)	49 (3.25–150)	28 (22–47)	0.26
Age (y)	49 (34.5–57)	47 (24–57)	0.47
DRI	1.584 (1.210–1.867)	1.422 (1.208–1.822)	0.85

experience being either difficult or time intensive to perform. Previous studies to measure ICG-PDR in liver grafts have been performed, although none have been performed to predict graft survival [13,14]. All these studies have been limited technically by the inability to perform this assay quickly in the donor hospital. Increasingly, frozen section histologic examination of grafts before implantation is being used, looking for microscopic features of steatosis, fibrosis, necrosis, and inflammation [21].

A simple reproducible quantitation of the risk of liver graft failure would immensely help OPOs triage possible donors and aid transplant physicians in deciding whether to use an organ and also in discussing with their patients the suitability of offered organs. Here, we report the successful use of a portable quantitative means of assessing liver function and its association with graft survival. This test can be performed easily and routinely, at the bedside by nurses and perfusionists from the procurement team and also by OPO personnel before organ offers are made.

Although it is possible that this study was not adequately powered strictly to address this question, our findings further validate the widely held notion that no single commonly used donor history, laboratory value, or index (DRI, age, liver function tests, and so forth) correlates with graft survival or utilization. There are likely multiple interrelated donor factors, not to mention recipient factors, that make predicting graft utilization and donor–recipient matching difficult. A quantitative measure of graft function validated by a larger study with a wider variety of donors and recipients is necessary to better address that question and would facilitate graft–recipient matching.

The fact that the procuring surgeon was superior to ICG-PDR measurement in predicting graft survival is at least partially due to the inherent bias of the study, as they are the established gold standard and that in this blinded study, the ICG-PDR measurement did not affect whether a graft was discarded or used. It is also likely that surgeon assessment is quite good at minimizing poor outcomes. However, we cannot standardize surgeon assessments and we cannot even obtain such an assessment without taking the donor to the operating room and doing the procurement operation. It is unknown whether we can increase utilization by providing a quantitative means of measuring liver function. It is possible that a validated preprocurement assessment of donor liver graft function would alter the number or improve the selection of potential liver donors, leading to greater efficiency. It is also possible that ICG-PDR cutoff values may be derived to match graft quality to recipient severity of illness.

These data warrant further exploration in a larger trial in a variety of settings to evaluate acceptable values for donated livers. At a time of increasing regional sharing and calls for national organ sharing, this method would assist in the

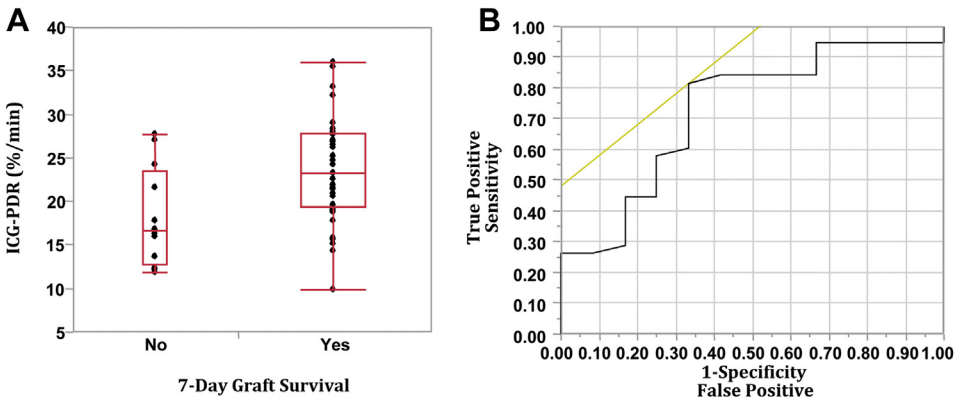

Fig. 4 – (A) Box plot of ICG-PDR *versus* 7-d graft survival. Quartiles are designated. (B) ROC curve for predicting graft utilization based on ICG-PDR. AUC = 0.747. AUC = area under the curve; ROC = receiver operating characteristic. (Color version of figure is available online.)

Table 5 – Donor and recipient characteristics of select grafts.

Donor							Recipient			
Age and gender	ICG-PDR (%/min)	Cause of death	BMI (kg/m^2)	LOH (d)	Pressors (*n*)	ALT peak (U/L)	Age and gender	Redo OLT	Physiological MELD	Notes
Grafts with ICG-PDR <19.3%/min with >7-d survival										
20F	18.3	Blunt trauma	24.5	2	1	227	52M	No	13	HCC exception points
48M	16.3	ICH	21.5	4	2	49	Information unavailable. Transplant performed at backup center.			
65M	16.2	ICH	24.7	6	2	47	52M	No	16	HCC exception points
60M	15.6	ICH	27.3	5	2	73	65M	No	8	HCC exception points
61M	14.8	ICH	26.6	3	1	28	62F	No	9	HCC exception points
51F	10.3	ICH	30.8	4	1	24	26M	No	Status 1A	Acetaminophen overdose
Grafts with ICG-PDR >19.3%/min with <7-d survival										
26M	28.3	ICH	25.5	4	2	34	61M	Yes	42	Massive transfusion redo OLT. Recipient death from cardiac failure. CIT 6 h.
25F	27.7	ICH	30	17	2	126	Liver was pale and stiff at procurement. Graft declined by all centers. No biopsy performed.			
43M	24.9	Anoxia	27.6	14	1	531	60M	No	42	Intraoperative cardiac arrest. CIT 10 h.
65M	22.2	ICH	25.4	7	2	209	Liver had fibrosis on frozen section at procurement. Graft declined by all centers.			

BMI = body mass index; CIT = cold ischemia time; HCC = hepatocellular carcinoma; ICH = intracranial hemorrhage; LOH = length of hospitalization; OLT = orthotopic liver transplantation.

standardization of graft evaluation. It could also lead to increasing liver graft utilization while decreasing travel risk and expense.

Acknowledgment

The authors acknowledge the help and cooperation of One-Legacy in facilitating this project, PULSION for providing us with the LiMON device for use during the study, and to the Clinical and Translational Science Institute statistical consultation service for advice on data analysis and presentation. The research described was supported by the Dumont-UCLA Transplant Center and the National Institutes of Health/National Center for Advancing Translational Science Clinical and Translational Science Institute grant number UL1TR000124.

Authors' contributions: A.Z. was involved in the study conception and design, acquisition of data, analysis and interpretation of data, and writing the article, and C.L., E.N., H.Y., V.G.A., F.M.K., D.G.F., and R.W.B. were involved in the study design, acquisition of data, and review of the article.

Disclosure

The authors of this article have no conflicts of interest to disclose as described by the *Journal of Surgical Research*.

REFERENCES

[1] Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2013 annual data report: liver. Am J Transplant 2015;15(Suppl 2):1.
[2] Cameron AM, Ghobrial RM, Yersiz H, et al. Optimal utilization of donor grafts with extended criteria: a single-center experience in over 1000 liver transplants. Ann Surg 2006;243:748. discussion 53–5.
[3] Cardillo M, De Fazio N, Pedotti P, et al. Split and whole liver transplantation outcomes: a comparative cohort study. Liver Transplant 2006;12:402.
[4] Rodriguez-Davalos MI, Arvelakis A, Umman V, et al. Segmental grafts in adult and pediatric liver transplantation: improving outcomes by minimizing vascular complications. JAMA Surg 2014;149:63.
[5] Yersiz H, Cameron AM, Carmody I, et al. Split liver transplantation. Transplant Proc 2006;38:602.
[6] Rao PS, Schaubel DE, Guidinger MK, et al. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. Transplantation 2009;88:231.
[7] Feng S, Goodrich NP, Bragg-Gresham JL, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. Am J Transplant 2006;6:783.
[8] Yersiz H, Lee C, Kaldas FM, et al. Assessment of hepatic steatosis by transplant surgeon and expert pathologist: a prospective, double-blind evaluation of 201 donor livers. Liver Transplant 2013;19:437.
[9] Busuttil RW, Tanaka K. The utility of marginal donors in liver transplantation. Liver Transplant 2003;9:651.
[10] Christie JH, Chaudhuri TK. Measurement of hepatic blood flow. Semin Nucl Med 1972;2:97.
[11] Wheeler HO, Cranston WI, Meltzer JI. Hepatic uptake and biliary excretion of indocyanine green in the dog. Proc Soc Exp Biol Med 1958;99:11.

[12] Hoekstra LT, de Graaf W, Nibourg GA, et al. Physiological and biochemical basis of clinical liver function tests: a review. Ann Surg 2013;257:27.
[13] Wesslau C, Kruger R, May G. Clinical investigations using indocyanine green clearance for evaluation of liver function in organ donors. Transplantology 1994;5:1.
[14] Koneru B, Leevy CB, Klein KM, Zweil P. Clearance of indocyanine green in the evaluation of liver donors. Transplantation 1994;58:729.
[15] Levesque E, Hoti E, Azoulay D, et al. Non-invasive ICG-clearance: a useful tool for the management of hepatic artery thrombosis following liver transplantation. Clin Transplant 2011;25:297.
[16] Olthoff KM, Kulik L, Samstein B, et al. Validation of a current definition of early allograft dysfunction in liver transplant recipients and analysis of risk factors. Liver Transplant 2010; 16:943.
[17] Leevy CM, Smith F, Longueville J, Paumgartner G, Howard MM. Indocyanine green clearance as a test for hepatic function. Evaluation by dichromatic ear densitometry. JAMA 1967;200:236.
[18] Mataya L, Aronsohn A, Thistlethwaite JR Jr, Friedman Ross L. Decision making in liver transplantation—limited application of the liver donor risk index. Liver Transplant 2014;20:831.
[19] Makowka L, Gordon RD, Todo S, et al. Analysis of donor criteria for the prediction of outcome in clinical liver transplantation. Transplant Proc 1987;19(1 Pt 3):2378.
[20] Oellerich M, Burdelski M, Lautz HU, Schulz M, Schmidt FW, Herrmann H. Lidocaine metabolite formation as a measure of liver function in patients with cirrhosis. Ther Drug Monit 1990;12:219.
[21] Brunt EM. Surgical assessment of significant steatosis in donor livers: the beginning of the end for frozen-section analysis? Liver Transplant 2013;19:360.