# Indocyanine Green Elimination Test in Orthotopic Liver Recipients

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***Objective.*** **To determine its predictive capability on graft quality and resultant clinical outcome, the indocyanine green (ICG) elimination test was performed by a spectrophotometric method and a noninvasive finger-piece method with 50 orthotopic liver transplantations.** ***Background.*** **Early detection of poor-functioning hepatic grafts is one of the most important issues in liver transplantation, but no reliable methods exist.** ***Methods.*** **The ICG test was performed after 50 orthotopic liver transplantations on postoperative days 1, 3, and 7. Indocyanine green elimination constants ($K_{ICG}$) were measured by both a standard spectrophotometric analysis ($K_{ICG}$-B) and by a finger-piece method ($K_{ICG}$-F). The patients were followed for a minimum of 3 months after transplantation. Results of ICG tests were correlated with various clinical determinations.** ***Results.*** **Twelve of the 50 grafts were lost within three months, of which 7 were related to graft failure. Multivariate analysis using the Cox proportional hazard model revealed that $K_{ICG}$ on postoperative day 1 was a better predictor of liver-related graft outcome than any of the conventional liver function tests. Furthermore, $K_{ICG}$ values showed significant correlation with the severity of preservation injury, longer intensive care unit (ICU) and hospital stay, prolonged liver dysfunction, and septic complications. Correlation of $K_{ICG}$ values by the spectrophotometric method with those by the finger-piece method was highly satisfactory in the grafts that had $K_{ICG}$-B $<0.15$ $min^{-1}$ ($y = 0.868x - 0.011$, $r = .955$).** ***Conclusion.*** **The ICG elimination test, conducted spectrophotometrically or optically on the day after liver transplantation, is a reliable indicator of graft quality and subsequent graft outcome early after liver transplantation. (HEPATOLOGY 1996;24:1165-1171.)**

Despite significant improvements in patient outcome after orthotopic liver transplantation, primary nonfunctioning and/or poor functioning grafts in the immediate postoperative period remain an important problem.[1,2] A reliable method to evaluate graft viability and to predict graft outcome in the perioperative period is needed; however, conventional liver function tests have limited reliability[3,4] and the results of various quantitative liver function tests have been conflicting.[5-10]

Recently, the indocyanine green (ICG) elimination test has been suggested as a predictor of graft viability and outcome, but its significance has not been fully clarified.[5-7,11,12] The primary goal of this study was to determine whether the ICG elimination test can predict graft viability and outcome in the early postoperative period. The secondary goal of this study was to evaluate the applicability of a new noninvasive optical finger-piece method[13] against the conventional spectrophotometric method for ICG determination.

## MATERIALS AND METHODS

### *Case Material*

From May 1, 1994 to October 31, 1994, 126 orthotopic liver transplantations were performed in 120 adult patients at Presbyterian University Hospital, Pittsburgh, PA. Of these, 50 liver transplantations in 47 patients were randomly chosen for this study. There were 26 male and 21 female patients with a median age of 53 years, ranging from 31 to 73 years. Of 43 patients who received a primary graft, 3 underwent liver retransplantation in the early posttransplantation period because of problems with the graft. The remaining 4 patients entered the study with replacement of a graft that had been transplanted previously.

### *Operative Procedure*

Cadaveric liver grafts were harvested by a flexible multiple organ procurement technique described elsewhere.[14] Median cold ischemia time of the liver was 12.1 hours, ranging from 7.6 to 25.0 hours. Recipient hepatectomy and liver replacement were performed by the standard technique in 30 cases and by the piggyback method in 20 cases.[15] Median warm ischemia time of the graft was 50 minutes, ranging from 28 to 68 minutes.

### *Postoperative Management*

Postoperative immunosuppression was with tacrolimus and steroids. The rationale for dose adjustment of these agents and supplementary administration of steroids, azathioprine, or OKT3 have been described elsewhere.[2]

Causes of graft malfunction were investigated by pathological, radiological, and microbiological studies.[1] Graft rejection was diagnosed from clinical findings followed by histopathology of needle liver biopsies. Vascular complications were examined by Doppler ultrasonography, followed by abdominal angiography when indicated. Percutaneous transhepatic cholangiography or T-tube cholangiography was performed in cases with possible biliary problems. Whenever infectious complications were suspected, the blood, sputum, urine, peritoneal fluid, and abdominal wound discharge were cultured to identify causative microorganisms.

### *ICG Study*

Indocyanine green elimination tests were simultaneously performed by the standard spectrophotometric method and with the optical finger-piece method. The study was performed with the approval of the Institutional Review Board. Consent forms were ob-

Abbreviations: ICG, indocyanine green; $K_{ICG}$-B, indocyanine green elimination constant measured by a standard spectrophotometric analysis; $K_{ICG}$-F, indocyanine green elimination constant measured by a finger-piece method; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PT, prothrombin time; ICU, intensive care unit; $K_{ICG}$, indocyanine green elimination constant; POD, postoperative day; MEGX, monoethylglycin-exylidide.

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tained from all of the study participants. The results of the ICG tests were blinded to the attending physicians who manage liver recipients.

***Standard Method.*** On the mornings of postoperative days 1, 3, and 7, ICG (Cardio-green, Hynson, Westcott & Denning, Baltimore, MD) at a dose of 0.5 mg/kg was given as an intravenous bolus through a peripheral vein. Two milliliters of blood was collected via an arterial or central venous line 5, 7, 10, and 15 minutes after ICG injection. After two-fold dilution of the plasma with saline, ICG absorbance was measured using a UV/VIS spectrophotometer (Lambda 1, Perkin-Elmer, Norwalk, CT) at 805 nm and 900 nm. The correction for blank density of the plasma was performed by the method of Nielsen.[16] The ICG plasma elimination data were fitted to a monoexponential equation using a log-linear least square method. Indocyanine green elimination rate constant ($K_{ICG}$-B), which represented the slope of the exponential equation, was used as a representative parameter of ICG elimination.

***Optical Finger-Piece Method.*** An ICG clearance meter (RK-1000, Sumitomo Electric, Osaka, Japan) was used to optically measure ICG elimination. A finger-piece optical sensor was adopted onto the tip of the index finger of the arm not being used for ICG injection, and the lead wires were connected to a microcomputer. The optical sensor was composed of a pair of light-emitting diodes and a photo diode, by which faint changes in ICG concentration in the fingertip could be monitored as changes in sensor signal voltage per second. The ICG elimination rate constant ($K_{ICG}$-F) was calculated automatically using the 600 data obtained between 5 minutes and 15 minutes after ICG injection.[13]

### *Clinical Determinations*

The clinical course of all recipients was followed for a minimum of 3 months after transplantation. Information on the donor, operative procedure, postoperative graft function, and graft outcome were prospectively collected for each transplantation. Routine liver function tests, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), prothrombin time (PT), and total bilirubin, were serially followed. Information on intensive care unit (ICU) and hospital stay, cause of graft loss and patient death, histological severity of graft rejection and preservation injury, and the occurrence of sepsis were also recorded. Graft losses were classified into two groups: those resulting from graft failure with final total bilirubin greater than 10 mg/dL, and others caused by technical failure or extrahepatic reasons. Prolonged postoperative liver dysfunction was defined by total bilirubin greater than 5 mg/dL at postoperative day 14. The severity of graft rejection and preservation injury was evaluated by a single pathologist and subjectively graded as none, mild, moderate, and severe. Finally, sepsis was diagnosed according to the Critical Care Medicine Consensus Conference.[17]

### *Statistics*

Continuous data were presented as median and ranges, and comparisons between groups were performed using the Mann-Whitney U test or the Kruskal-Wallis test. Categorical data are presented as a percentage, and the difference was evaluated by the $\chi^2$ test. Correlation was tested by means of linear regression analysis. To determine independent variables that were significantly related to the elected end-points, univariate analysis was performed to enter the Cox proportional hazard model for stepwise logistic regression analysis, followed by forward stepwise multivariate analysis using the univariate significant variables. These statistical analyses were performed using the statistical software packages Statistica (StatSoft, Tulsa, OK) and SPSS (SPSS Inc., Chicago, IL).

## RESULTS

***Graft Outcome.*** After a 3-month follow-up, 38 (35 primary grafts and 3 of the retransplanted grafts) of 50 grafts were functioning (group I). Three-month graft survival was 76% (38/50), and patient survival was 81% (38/47). Twelve grafts were lost to retransplantation or patient death, of which seven were related to graft failure (group IIA), and 5 were caused by technical or extrahepatic reasons (group IIB). Table 1 summarizes the causes of the 12 graft losses. Of the parameters studied with the donor, recipient, and operative procedure, only old donor age was significantly related to poor graft outcome. The median age and range of the liver donors in group I was: 39 (11 to 63) years old; group IIA: 59 (31 to 69) years old; and group IIB: 32 (6 to 43) years old. Group IIA was significantly disadvantaged ($P = .0089$).

***Other Clinical Results.*** Median duration of ICU stay was 11 days. Twenty patients (40%) stayed in the ICU longer than 7 days, and 10 more patients (20%) died while in the ICU. Mean hospitalization was 44 days. Sixteen patients (32%) required hospitalization for more than 30 days, and 13 other patients (26%) could not be discharged from the hospital. Total bilirubin decreased to <5 mg/dL within 14 days in 35 grafts (70%), but 15 grafts (30%) showed prolonged graft dysfunction or graft failure. By histological study of liver biopsy specimens or removed grafts, 35 grafts (70%) had preservation injury, with moderate to severe grade in 20 (40%). Histological evidence of graft rejection was diagnosed in 22 grafts (44%), of which 6 were graded moderate to severe. Twelve grafts (24%) developed septic complications caused by bacteria (n = 9) or fungi (n = 3).

***ICG Elimination Test.*** A total of 146 ICG injections were performed in this study. None of the patients developed hypotension, dyspnea, headache, or rash, abrupt worsening of graft function, or any other side effects. When the 50 ICG-studied grafts were compared with 67 grafts that received no ICG tests during the study period, there were no statistical differences in graft and patient survival and postoperative changes in routine liver function tests.

Figure 1 illustrates the correlation of indocyanine green elimination constant ($K_{ICG}$) values determined by the $K_{ICG}$-B method and the $K_{ICG}$-F method. Irrespective of postoperative days on which the ICG tests were performed, both measurements showed highly significant correlation ($y = 0.861x - 0.009$, $r = .886$, $n = 146$). If $K_{ICG}$-B was $>0.15$ $min^{-1}$ and $K_{ICG}$-F was $>0.12$ $min^{-1}$, the correlation between the two was rather scattered ($y = 0.533x + 0.055$, $r = .323$, $n = 68$), because $K_{ICG}$-F values fluctuated at this or higher levels. At lower levels, however, both $K_{ICG}$-B and $K_{ICG}$-F had an almost linear correlation ($y = 0.868x - 0.011$, $r = .955$, $n = 78$).

***$K_{ICG}$ and Clinical Outcome.*** Postoperative changes in $K_{ICG}$ of individual patients from the three groups are shown in Fig. 2, where $K_{ICG}$ levels are arbitrarily divided into three classes: class A ($K_{ICG}$-B $> 0.10$ $min^{-1}$); class B ($0.10$ $min^{-1} >$ $K_{ICG}$-B $> 0.06$ $min^{-1}$); and class C ($K_{ICG}$-B $< 0.06$ $min^{-1}$). Using the equation determined with lower $K_{ICG}$-B values, $K_{ICG}$-B at $0.10$ $min^{-1}$ and $0.06$ $min^{-1}$ corresponded to $K_{ICG}$-F at $0.075$ $min^{-1}$ and $0.04$ $min^{-1}$, respectively. On postoperative day (POD) 1, 32 of the 38 group I patients (84%) had $K_{ICG}$ in class A, whereas all of the group IIA patients were either class B (3/7) or class C (4/7). Graft failure occurred in 0% (0/36) of class A, 30% (3/10) of class B, and 100% (4/4) of class C when classified by $K_{ICG}$ on POD 1. After POD 1, $K_{ICG}$ of most group I patients remained high, but that of group IIA and group IIB showed further reductions. Of the 20 grafts that showed moderate to severe preservation injury on needle biopsy or removed graft, one patient died of primary nonfunction at POD 2, and 17 grafts had $K_{ICG}$ at class B or class C on POD 3. The incidence of moderate to severe preservation injury was 7.1% (2/28) of class A, 66.7% (8/12) of class B, and 100% (9/9) of class C by $K_{ICG}$ on POD 3 (Fig. 3A). Similarly, the incidence of sepsis was 3.6% (1/28) of class A, 80% (8/10) of class B, and 75% (3/4) of class C by $K_{ICG}$ on POD 7 (Fig. 3B).

***$K_{ICG}$ and Liver Function Tests.*** Correlation of $K_{ICG}$-B levels with those of AST, ALT, PT, and total bilirubin on POD 1 is shown in Fig. 4. Although both AST ($y = -7759x + 3238$, $r^2 = .02$, not significant) and ALT ($y = -675x + 975$, $r^2 = .00$,

**TABLE 1. Causes of Graft Loss and Mortality in 12 Group-II Patients**

| | Patient # | Graft Survival Days | $K_{ICG}$-B ($min^{-1}$) | | | $K_{ICG}$-F ($min^{-1}$) | | | Re-OLTX | Patient Outcome (d), Cause of Death |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | POD 1 | POD 3 | POD 7 | POD 1 | POD 3 | POD 7 | | |
| Group IIA | | | | | | | | | | |
| 1 | 3 | 2 | .047 | — | — | .026 | — | — | No | Died (2), PNF |
| 2 | 13 | 20 | .058 | .048 | .044 | .031 | .029 | .026 | No | Died (20), sepsis |
| 3 | 16 | 25 | .045 | .014 | .015 | .028 | .003 | .000 | No | Died (25), sepsis |
| 4 | 31 | 40 | .087 | .078 | .062 | .061 | .069 | .048 | No | Died (40), sepsis |
| 5 | 32 | 5 | .034 | .012 | — | .018 | .003 | — | Yes | Alive after Re-OLTX for PNF |
| 6 | 36 | 5 | .079 | .021 | — | .053 | .006 | — | Yes | Alive after Re-OLTX for PNF |
| 7 | 50 | 73 | .081 | .07 | .054 | .063 | .051 | .038 | No | Died (73), sepsis |
| Group IIB | | | | | | | | | | |
| 1 | 8 | 74 | .156 | .107 | .093 | .093 | .058 | .061 | No | Died (74), CNS, withdrawal of support |
| 2 | 25 | 39 | .178 | .141 | .069 | .178 | .115 | .050 | No | Died (39), TTP, withdrawal of support |
| 3 | 27 | 74 | .107 | .081 | .061 | .053 | .063 | .040 | Yes | Died (92), sepsis |
| 4 | 35 | 18 | .123 | .231 | .184 | .094 | .202 | .157 | Yes | Alive after Re-OLTX for HAT |
| 5 | 49 | 64 | .07 | .036 | .081 | .046 | .021 | .059 | No | Died (64), pulmonary bleeding |

Abbreviations: Re-OLTX, retransplantation of the liver; PNF, primary nonfunction (graft loss within 2 weeks after transplantation); CNS, central nervous system dysfunction; TTP, thrombotic thrombocytopenic purpura; HAT, hepatic artery thrombosis.

not significant) were not correlated, PT ($y = -27.3x + 21.1$, $r^2 = .18$, $P < .005$) and total bilirubin ($y = -66.1x + 18.1$, $r^2 = .36$, $P < .001$) values had an inverse relationship with $K_{ICG}$-B. However, in contrast to $K_{ICG}$-B, higher PT and total bilirubin on POD 1 did not always reflect poor outcome of transplanted grafts.

***Correlation of $K_{ICG}$ and Liver Function Tests With Clinical Outcome.*** Correlation of various clinical outcomes with the results of the ICG elimination test and routine liver function tests was examined (Table 2). Using a univariate analysis, $K_{ICG}$ values determined both spectrophotometrically and optically showed significant correlation with all determinants except for nonliver-related graft loss and rejection. Of the routine liver function tests, total bilirubin level and highest PT within 7 postoperative days reflected the incidence of overall and liver-related graft loss. The highest levels of ALT, AST, PT, and total bilirubin correlated with preservation injury. When multivariate analysis was applied, $K_{ICG}$-B at POD 1 was the best indicator for overall and liver-related graft loss, and $K_{ICG}$-F at POD 7 reflected prolonged hospitalization. The incidence of liver-unrelated graft loss and graft rejection was unpredictable using any of these parameters.

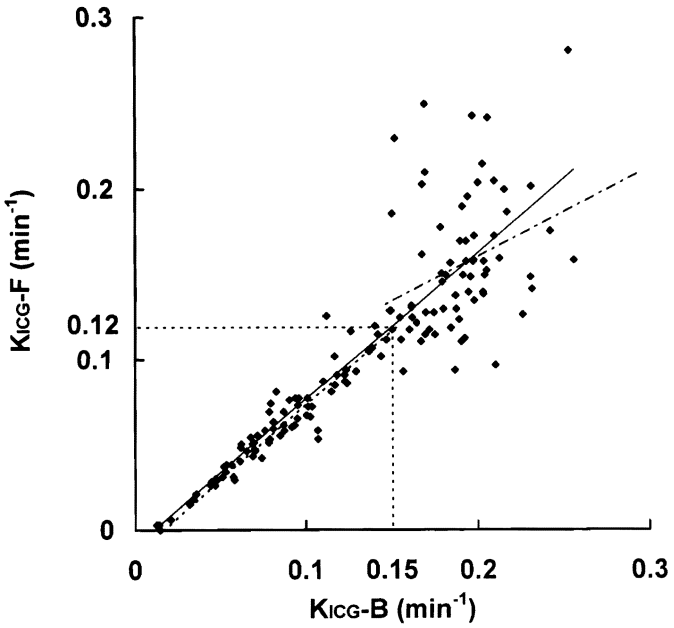


FIG. 1. Relationship between $K_{ICG}$-B and $K_{ICG}$-F. Data represent all 146 ICG elimination tests. See text for linear regression.

## DISCUSSION

Causes of primary nonfunction and dysfunction in hepatic allografts after orthotopic transplantation are multifactorial. The risk factors include age, gender, and medical condition of the donor, cause and severity of the recipient's liver disease, cold ischemia time and warm ischemia time of the graft, difficulty and amount of blood transfused during surgery, and blood type and immunological compatibility between the donor and the recipient. Whatever the causes, 5% of the grafts require urgent retransplantation, and 15% of the grafts need prolonged management for survival, because of poor initial graft function.[1-4] A reliable method enabling early determination of such grafts is crucial.

Clinically, malfunction of hepatic allografts is predicted if the recipients remain unconscious, hypotensive, and oliguric or anuric after transplantation. The grafts make small amounts of pale bile. Laboratory findings, including acidosis, hypoglycemia, PT prolongation, elevated liver enzymes, and high bilirubin level, are supportive of the diagnosis of irreversible graft damage, but are not always conclusive. With

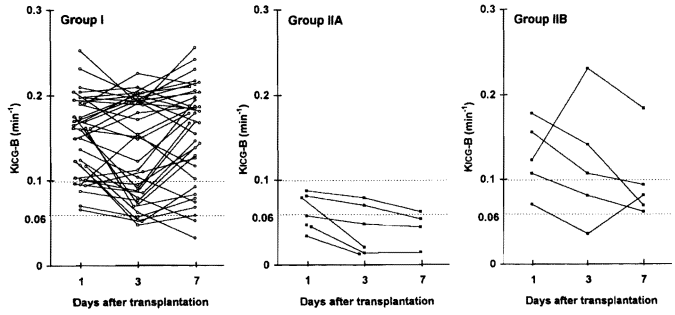


FIG. 2. Changes in $K_{ICG}$-B levels of liver recipients with a functioning graft (group I) or graft loss from either graft failure (group IIA) or liver-unrelated reasons (group IIB).

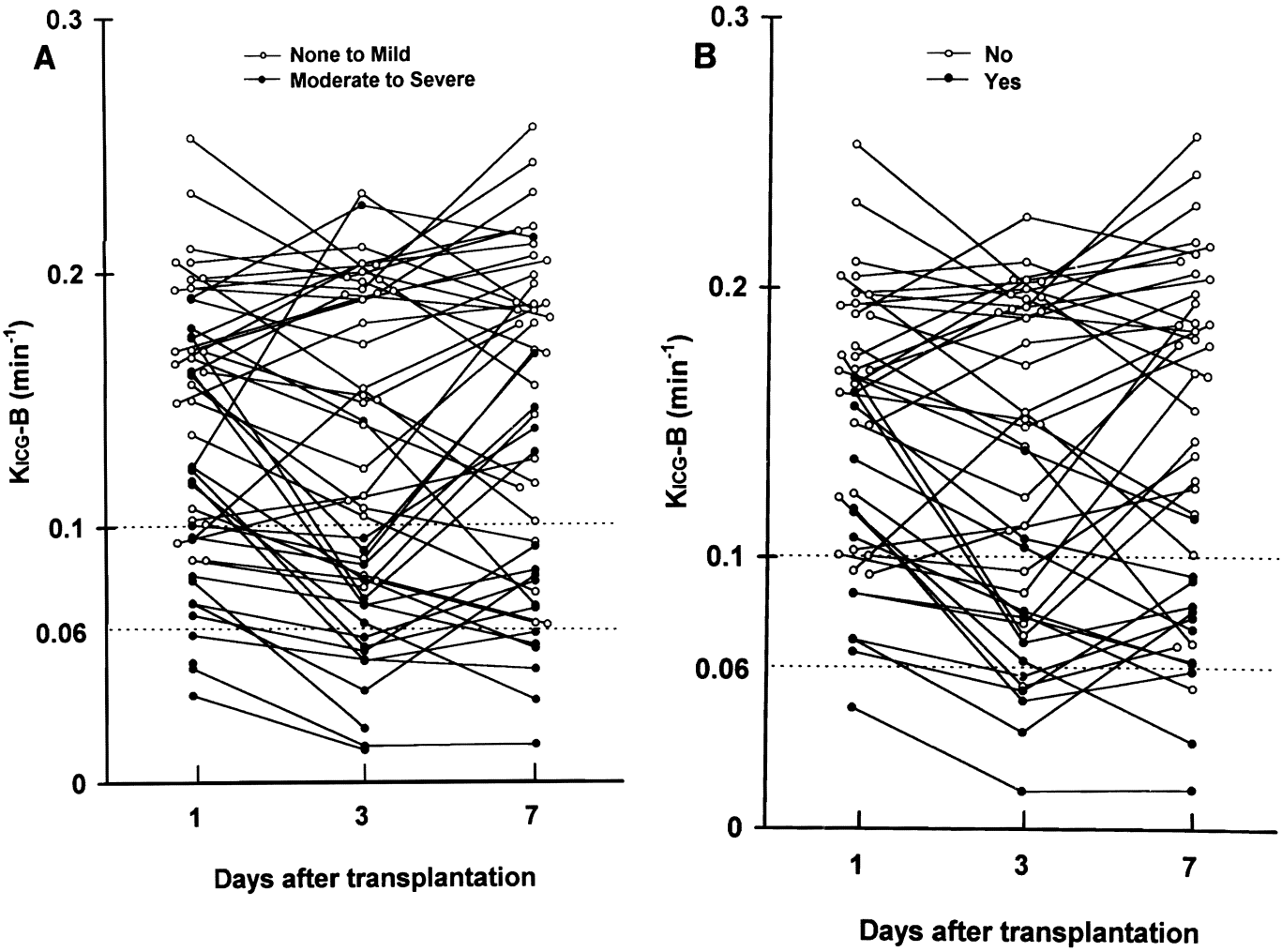


FIG. 3. Correlation of $K_{ICG}$-B with (A) histological preservation injury and (B) the occurrence of septic complications.

the aid of clinical chemical, histological and radiological studies, the decision to regraft is made mostly from the experience of the liver transplantation surgeons.[1]

A few quantitative functional tests have been proposed for determining posttransplant graft quality. However, each has limitations *per se* in terms of sensitivity, specificity, and practicality. For instance, biochemical recovery of hepatocyte energy metabolism[18] and serum amino acids profile[19] after liver transplantation correlates with the quality of the graft, but the determination is too complex and takes too long to apply clinically. Some investigators[5,8] have reported that measurement of monoethylglycin-exylidide (MEGX) formation after intravenous lidocaine administration is a good predictor of graft function. However, because lidocaine is metabolized by the drug-metabolizing enzyme P-450,[20] the rate of formation could be influenced by the medications routinely used after liver transplantation such as immunosuppressants, steroids, antibiotics, and calcium ion channel blockers. The rate of MEGX formation can also be affected by extrahepatic lidocaine metabolism.[21] In this study, MEGX was determined by a high-pressure liquid chromatography method simultaneously with the ICG elimination test (Fig. 5). Although the correlation between $K_{ICG}$-B and MEGX was highly significant ($y = 276x + 13$, $r^2 = .28$, $P < .001$), a low MEGX value did not predict poor graft outcome when compared with low $K_{ICG}$-B. Arterial ketone body ratio, which reflects the redox state of hepatocytes, has limitations for routine clinical use because of the need for glucose loading before measurements, and of the exclusion of diabetic patients.[10] A recent report has indicated that AKBR may be influenced by extrahepatic metabolism of the ketone bodies.[22]

The present investigation was conducted to study whether the ICG elimination test can safely be used as a predictor of graft quality after liver transplantation in patients. The results suggest that low $K_{ICG}$ levels ($<0.06$ $min^{-1}$ using $K_{ICG}$-B and $<0.04$ $min^{-1}$ using $K_{ICG}$-F), especially on POD 1 after transplantation, is a good indicator of graft failure and subsequent graft loss. In addition, continued suppression of $K_{ICG}$ ($<0.10$ $min^{-1}$ by $K_{ICG}$-B and $<0.075$ $min^{-1}$ by $K_{ICG}$-F) during the early postoperative period of 7 days was found to be closely associated with the severity of preservation injury, prolonged liver dysfunction, or septic complication, and resulting longer ICU and hospital stay. Irrespective of postoperative days and graft quality, administration of ICG to recipients, at a dose of 0.5 mg/kg, had no detrimental effect on graft survival and function of hepatic allografts.

Because of its safety and negligible extrahepatic elimination, the ICG test has been used, by either bolus injection or continuous infusion, to medically determine the functional capacity of diseased livers.[23,24] In the field of general surgery, it has also been used to predict the outcome of patients with liver abnormalities before and/or after major hepatic resections.[25,26] Recently, the application of ICG testing has gradually expanded to liver transplantation.[5-7,11,12] While the abil-

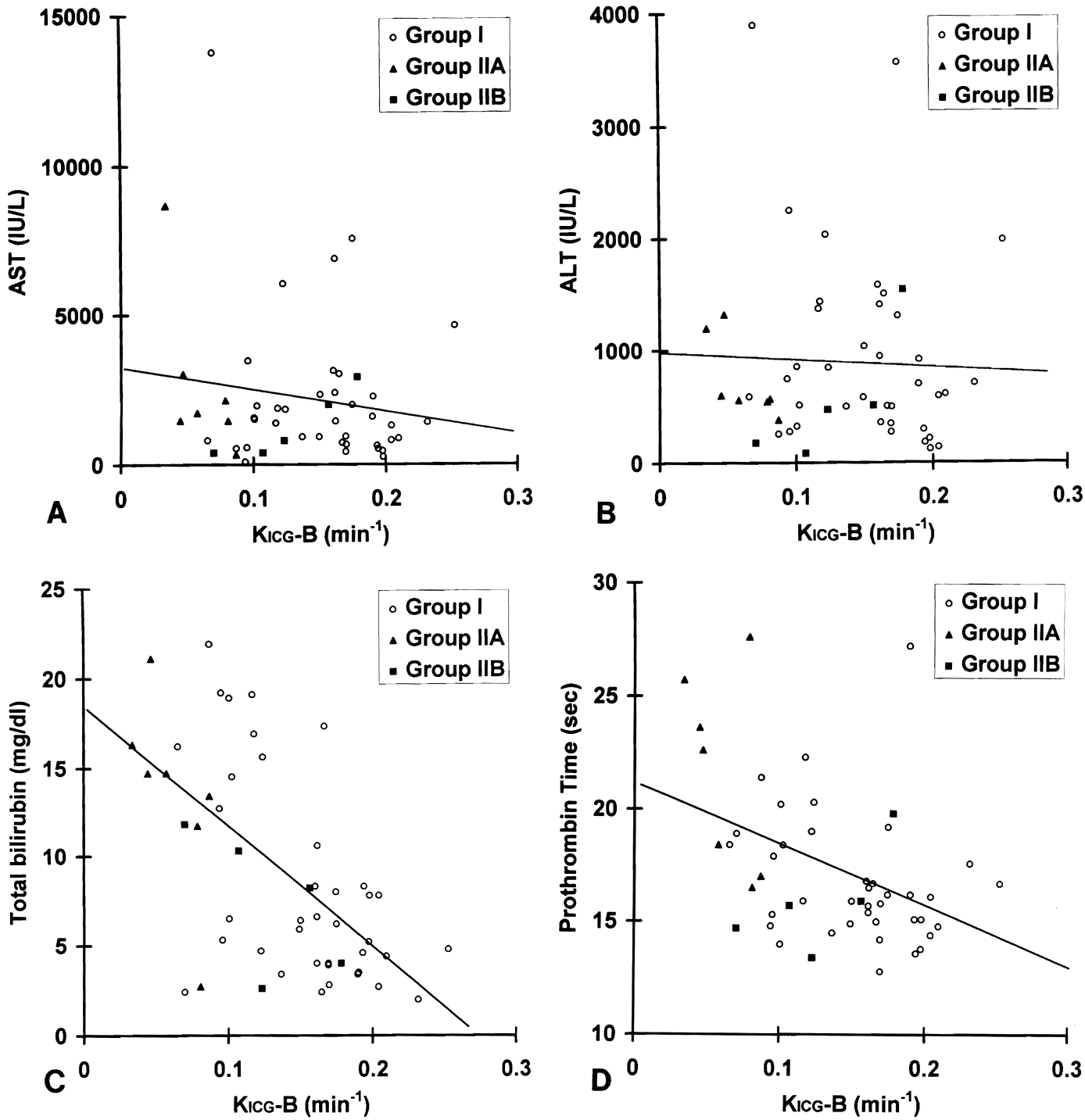


FIG. 4. Correlation of $K_{ICG}$-B levels with (A) AST, (B) ALT, (C) total bilirubin, and (D) prothrombin time on POD 1. Group I: patients with a functioning graft; group IIA: patients with graft loss caused by graft failure; and group IIB: liver-unrelated graft loss. See text for linear regression.

ity of ICG test results to predict short-term graft outcome is controversial when applied to donors before procurement,[11,12] this test has been reported to have some prognostic power when used in smaller numbers of patients after liver transplantation.[5,6] This finding has been confirmed by our study. As a primary cutoff value for predicting graft failure, Lamesch et al.[5] used an ICG half-life of 12 minutes, and Jalan et al.[6] selected an ICG clearance of 200 mL/min. These figures correspond well to our cutoff of $K_{ICG}$-B at 0.06 $min^{-1}$ and $K_{ICG}$-F at 0.04 $min^{-1}$, assuming an average plasma volume of 50 mL/kg and body weight of 70 kg. In addition, most of the failed grafts in the Lamesch series had an ICG half-life greater than 7 minutes which is equivalent to our secondary cutoff levels of $K_{ICG}$-B at 0.10 $min^{-1}$ and $K_{ICG}$-F of 0.075 $min^{-1}$.

$K_{ICG}$ is a function of hepatic blood flow, hepatic dye clearance, and plasma volume; however, hepatic blood flow is the major determinant of $K_{ICG}$ in normal livers.[27] During the immediate postoperative period, plasma volume appears to have little influence on $K_{ICG}$ levels, because plasma volume is expanded as a result of fluid and blood supplementation during and after surgery. Although hepatic blood flow in functioning liver grafts after transplantation was reported to in-

crease by persistent hyperdynamic circulation and hepatic denervation,[28-30] $K_{ICG}$ levels on POD 1 of group I grafts, most of which had no to mild preservation injury ($K_{ICG}$-B: 0.169 [0.087 – 0.253], n = 26) were slightly lower than those of normal healthy volunteers ($K_{ICG}$-B: 0.187 [0.160-0.247], n = 20). The difference may reflect the presence of hepatocyte dysfunction even in well-functioning grafts caused during procurement, preservation, and transplantation. Although not investigated in this study, lower $K_{ICG}$ levels with group IIA grafts appeared to reflect decreased hepatic blood flow rather than hepatocyte damage because there was no correlation between values of $K_{ICG}$ and released liver enzymes. Recent experimental studies have shown that hypothermic preservation of the liver causes greater damage to the microvasculature than to the hepatocytes.[31] Using a microfil perfusion technique, we have previously shown that microcirculatory damage is augmented after graft reperfusion causing stagnation, pooling, and a filling-defect in the sinusoids, as well as a reduction in hepatic blood flow, particularly in arterial flow.[32] Studies aimed at expanding the microvasculature during liver preservation[33] or modulation of vasoactive substances[34] were shown to improve hepatic blood flow, ICG elimination, and graft function after reperfusion. Further study on the role of hepatic blood flow in the determination of $K_{ICG}$ levels and posttransplant graft function is needed.

Lower $K_{ICG}$ levels were not only related to poor outcome and preservation injury, but were also associated with septic complications, delayed graft function, and longer ICU and hospital stays. However, neither $K_{ICG}$ levels nor liver function tests correlated with the incidence of graft rejection. This is in contrast to the observation by Howard et al.[35] who reported that the incidence of rejection was higher in patients with "severe preservation injury" estimated by higher AST level after transplantation. The potent tacrolimus-based immunosuppression used with our patients may have concealed the effect of preservation injury on graft rejection.

**TABLE 2. Correlation of $K_{ICG}$ and Liver Function Tests With Clinical Outcome After 50 Orthotopic Liver Transplantations**

| Outcome | (N) | Univariate Analysis: Variables (POD)* | Multivariate Analysis: Variables (POD) | *P* |
|---|---|---|---|---|
| Overall graft loss | (12) | $K_{ICG}$-B (1, 3, 7)<br>$K_{ICG}$-F (1, 3, 7)<br>T. Bil (3, 7)<br>Highest PT | $K_{ICG}$-B (1)<br>Highest PT | <br>.0899<br><br>.0063 |
| Hepatic graft loss | (7) | $K_{ICG}$-B (1, 3, 7)<br>$K_{ICG}$-F (1, 3, 7)<br>T. Bil (3, 7)<br>Highest PT | $K_{ICG}$-B (1)<br>Highest PT | .0003<br>.0815 |
| Nonhepatic graft loss | (5) | — | — | — |
| ICU stay > 7 days | (30) | $K_{ICG}$-B (3, 7)<br>$K_{ICG}$-F (3, 7) | $K_{ICG}$-F (7) | .004 |
| Hospital stay > 30 days | (29) | $K_{ICG}$-B (1, 3, 7)<br>$K_{ICG}$-F (1, 3, 7) | $K_{ICG}$-F (7) | <.0001 |
| Prolonged graft dysfunction | (15) | $K_{ICG}$-B (7)<br>$K_{ICG}$-F (7)<br>T. Bil (3, 7) | T. Bil (7) | .0001 |
| Preservation injury | (20) | $K_{ICG}$-B (1, 3, 7)<br>$K_{ICG}$-F (1, 3, 7)<br>T. Bil (3, 7)<br>Highest AST<br>Highest ALT<br>Highest PT | $K_{ICG}$-F (3)<br>Highest ALT | <.0001<br>.0004 |
| Sepsis | (12) | $K_{ICG}$-B (1, 3, 7)<br>$K_{ICG}$-F (1, 3, 7)<br>T. Bil (3, 7) | $K_{ICG}$-B (7) | .0001 |
| Rejection | (22) | — | — | — |

Abbreviations: T. Bil, total bilirubin; $K_{ICG}$-B, measurement by spectrophotometric method; $K_{ICG}$-F, measurement by finger-piece method.

* Parameters that have a *P* value < .01.

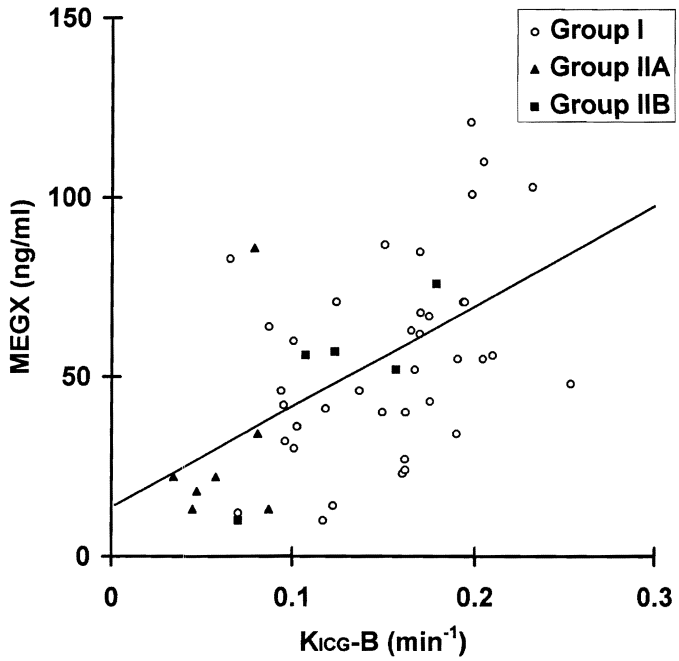


FIG. 5. Correlation of $K_{ICG}$-B levels with MEGX on POD 1. MEGX value was calculated by subtracting the 0-minute value from the 30-minute value. Group I: patients with a functioning graft; group IIA: patients with graft loss caused by graft failure; and group IIB: liver-unrelated graft loss.

Along with the standard spectrophotometric analysis, a new optical finger-piece method was used in this study to evaluate whether the latter can simplify the ICG elimination test and yet provide reliable results. Although $K_{ICG}$-F values were more widely dispersed at higher levels and were consistently lower at lower levels than those of $K_{ICG}$-B, both measurements showed strong correlation. The differing behavior of $K_{ICG}$-F in the higher and lower range may reflect changes in systemic or peripheral hemodynamics that invariably occur after liver transplantation and accompany the use of vasoactive agents and/or immunosuppressants. Whatever the reason, the fluctuation in $K_{ICG}$-F appears to be insignificant clinically, because lower $K_{ICG}$-F values always indicated lesser quality of hepatic allografts in our study. More importantly, this novel method has advantages in simplicity, noninvasiveness, real-time presentation of test results, and cost-effectiveness.[13] The optical finger-piece method also eliminates the need for serial blood samplings, their preparations, and actual measurements that are required for the standard spectrophotometric assay. In addition, the finger-piece method may be superior to the classic ear densitometry[36] in terms of short idling or calibration time, better baseline stability, and better fitness. The results of this study warrant a large scale investigation into the suitability of ICG for predicting outcome not only of the grafts after operation, but also of the patients awaiting liver transplantation.

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