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ABOUT COVER

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AIMS AND SCOPE

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    WJH mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

INDEXING/ABSTRACTING

The *WJH* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2021 edition of Journal Citation Reports® cites the 2020 Journal Citation Indicator (JCI) for *WJH* as 0.61. The *WJH*'s CiteScore for 2020 is 5.6 and Scopus CiteScore rank 2020: Hepatology is 24/62.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Risk factors and prediction of acute kidney injury after liver transplantation: Logistic regression and artificial neural network approaches

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Abstract

BACKGROUND

Acute kidney injury (AKI) has serious consequences on the prognosis of patients undergoing liver transplantation. Recently, artificial neural network (ANN) was reported to have better predictive ability than the classical logistic regression (LR) for this postoperative outcome.

AIM

To identify the risk factors of AKI after deceased-donor liver transplantation (DDLT) and compare the prediction performance of ANN with that of LR for this complication.

METHODS

Adult patients with no evidence of end-stage kidney dysfunction (KD) who underwent the first DDLT according to model for end-stage liver disease (MELD) score allocation system was evaluated. AKI was defined according to the International Club of Ascites criteria, and potential predictors of postoperative AKI were identified by LR. The prediction performance of both ANN and LR was tested.

RESULTS

The incidence of AKI was 60.6% (n = 88/145) and the following predictors were identified by LR: MELD score > 25 (odds ratio [OR] = 1.999), preoperative kidney dysfunction (OR = 1.279), extended criteria donors (OR = 1.191), intraoperative arterial hypotension (OR = 1.935), intraoperative massive blood transfusion (MBT) (OR = 1.830), and postoperative serum lactate (SL) (OR = 2.001). The area under the receiver-operating characteristic curve was best for ANN (0.81, 95% confidence interval [CI]: 0.75-0.83) than for LR (0.71, 95%CI: 0.67-0.76). The root-mean-square error and mean absolute error in the ANN model were 0.47 and 0.38, respectively.

CONCLUSION
The severity of liver disease, pre-existing kidney dysfunction, marginal grafts, hemodynamic instability, MBT, and SL are predictors of postoperative AKI, and ANN has better prediction performance than LR in this scenario.

Core Tip: This study aimed to identify the risk factors of acute kidney injury (AKI) after deceased-donor liver transplantation and compare the performance of artificial neural network (ANN) with that of logistic regression (LR) analysis to predict this complication. LR analysis revealed the following predictors of AKI: Previous kidney dysfunction, marginal grafts, intra-operative arterial hypotension, massive blood transfusion, and serum lactate. ANN prediction had better performance than LR in this scenario.

INTRODUCTION

Among the possible complications of complex abdominal and liver procedures, acute kidney injury (AKI) should be considered a major cause of postoperative morbidity and mortality[1-6]. Updated data report a 0.9%-17.9% incidence of AKI after liver resection[7-9], and 4%-94% after LT[10,11], either living-donor (LDLT) or deceased-donor LT (DDLT). Although there is a lack of a reported standard definition of postoperative AKI[12] after DDLT, it is of fundamental importance to identify patients at risk for AKI after LT, ideally by the set of preoperative clinical evaluation, as well as by the complementary information of the intraoperative period, thus enabling the adoption of preventive measures or early therapies for AKI in the postoperative period.

There are many studies available based on deep learning models for different clinical purposes in distinct fields of medicine, such as for complex imaging acquisition and processing[13-17], and artificial neural network (ANN) as a deep learning modality is commonly used to solve complex problems, where the behavior of variables is not rigorously known. In the specific field of AKI after LT, along with other machine learning techniques (gradient boosting machine, random forest, decision tree, support vector machine, naïve Bayes, and deep belief network), ANN has already been compared to multivariable logistic regression (LR) regarding their prediction performance[18]. We hypothesized that ANN would be a feasible alternative with higher performance than the classic LR model, reinforcing the wide applicability of ANN and its ability to learn from input data with or without supervision.

The multifactorial origin of AKI after LT makes it complex to predict which candidate for the procedure has an increased risk of this complication, and in the face of this complexity, along with the classical LR, ANN would be a very reliable prognostic tool for AKI risk assessment, where the relative risk term is parameterized by an ANN instead of regression, enabling the application of deep learning, whereas comparative studies evaluating such a promising tool for predicting AKI following LT are scarce[19-20].

In face of this serious postoperative complication, this retrospective study of patients who underwent only-first DDLT aimed to identify the risk factors for postoperative AKI and compare the prediction performance of ANN with that of LR for this complication.

MATERIALS AND METHODS

Study design

A retrospective study was conducted on patients of both sexes, aged > 18 yr, diagnosed with liver cirrhosis and portal hypertension (platelets < 100000/mm^3, splenomegaly and/or esophageal varices), eventually associated with hepatocellular carcinoma (HCC), and undergoing the first DDLT at a tertiary referral hospital between September 2017 and June 2021. The patients were allocated according to Model for End-Stage Liver Disease (MELD) score, with no evidence of end-stage kidney disease. The MELD score was dichotomized at 25 points for statistical purposes according to Romano *et al*[21], and the minimum hospital stay was 7 d according to Wong *et al*[22] and the International Club of Ascites (ICA) definitions for the onset of AKI[23].

Renal dysfunction definitions

Kidney dysfunction (KD) subtypes were defined according to Wong *et al*[22] (Table 1) and the ICA definitions (Table 2)[23], and both the acute deterioration of renal function and the background CKD could be structural or functional in nature, including hepatorenal syndrome (HRS) types 1 and 2 (Table 3)[23]. Estimated glomerular filtration rate (eGFR) was calculated by the Modified Diet in Renal Disease 6 (MDRD6) formula: eGFR = 198 × [serum creatinine (mg/dL)$^{-0.858}$ × age$^{-0.167}$ × 0.822 if patient is female × 1.178 if patient is black] × [serum urea nitrogen concentration (mg/dL)]$^{-0.293}$ × [urine urea nitrogen excretion (g/d)]$^{0.249}$[3].

Graft definitions

Marginal liver grafts of extended criteria donor (ECD) were defined as grafts with three or more of the following donor features: > 60 yr, body mass index (BMI) > 27-30 kg/m^2, macrovesicular steatosis > 30%, intensive care unit (ICU) stay > 4 d, sustained arterial hypotension > 1 h, cold ischemia times (CIT) > 8 h, warm ischemia times (WIT) > 40-45 min, controlled sepsis, history of alcoholism, serum creatinine > 1.2 mg/dL, arterial hypotensive episodes < 60 mmHg for > 1 h, bilirubin > 2.0 mg/dL, alanine transaminase (ALT) > 170 U/L and aspartate transaminase (AST) > 140 U/L, the use of dopamine doses > 10 microg/kg per min, and peak serum sodium > 155 mEq/L[24-26].

Routine biopsy was performed on the donor allograft for all patients included in the study. Liver specimens were evaluated by hematoxylin and eosin staining using either frozen or permanent section. Macrovesicular steatosis was defined as a single vacuole larger than the nucleus, replacing most of the hepatocyte cytoplasm and displacing the nucleus to the cell membrane[27]. Macrosteatosis was categorized as no steatosis (< 5%), mild steatosis (10%-29%), moderate steatosis (30%-60%), and severe steatosis (> 60%)[28].

Hemodynamic status and monitoring

Fluid administration consisted of a baseline infusion of a balanced crystalloid (Plasmalyte, Baxter, Belgium) with or without 4% albumin (depending on patient conditions). Rapid infusers, perfusion heaters, and a Cell Saver (Haemonetics, Massachusetts, EUA) for blood recovery were ready for use prior to induction. In accordance to American Society of Anaesthesiologists (ASA) guidelines, Cell Saver has effectiveness in reducing the volume of allogeneic blood transfused[29].

A Flow Trac/EV1000 System (Edwards Lifesciences, Irvine, USA) was inserted and hemodynamic interventions were guided using continuous cardiac index (CCI), stroke volume index (SVI), mixed venous oxygen saturation (SvO$_2$), central venous pressure (CVP), and mean arterial pressure (MAP). Fluids were administered if SVI was < 30 mL/m^2 and/or CCI < 2 L/min/m^2 for compensation for blood loss *via* 250-500 mL fluid boluses of Plasmalyte, to strictly maintain MAP > 65 mmHg, avoiding hemodynamic instability as described elsewhere[30,31].

Blood loss monitoring consisted of visual assessment of the surgical field, including the extent of blood present, presence of microvascular bleeding, surgical sponges, clot size and shape, and volume in suction canister. In case of active hemorrhage, blood product administration was guided by using rotational thromboelastometry monitoring *via* ROTEM (Tem Innovations GmbH, Munich, Germany), hemoglobin/hematocrit monitoring, coagulation tests (international normalized ratio [INR]), activated partial thromboplastin time [aPTT], fibrinogen concentration [normal range: 200 to 400 mg/dL], and platelet count[29]. Whereas there is no clear evidence that ROTEM improved survival in LT patients, it was effective in reducing bleeding and fewer patients required both platelets and fresh frozen plasma (FFP) transfusion[32]. Monitoring for perfusion of vital organs included standard ASA monitoring, renal monitoring (urine output), and analysis of arterial blood gases and serum (SL) level (cutoff of 2.0 mmol/L)[29].

Massive blood transfusion (MBT) protocol for avoidance of dilutional coagulopathy was activated when hemorrhage was expected to be massive (anticipated need to replace 50% or more of blood volume within 2 h), or bleeding continued after the transfusion of 4 units of packed red blood cells (PRBC) within a short period of time (1-2 h), or systolic blood pressure (SBP) was below 90 mmHg and heart rate was above 120 beats per minute in the presence of uncontrolled bleeding[33]. According to the Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) study group recommendations,

Table 1 Diagnostic criteria for kidney dysfunction in cirrhosis (Wong *et al*[22], 2011)

Diagnosis	Definition
AKI	Rise in serum creatinine of > 50% from baseline or rise of sCr by > 26.4 mmol/L (> 0.3 mg/dL) in < 48 h; HRS type 1 is a specific form of AKI
CKD	eGFR of < 60 mL/min for > 3 mo calculated using MDRD6 formula; HRS type 2 is a specific form of CKD
ACKD	Rise in serum creatinine of > 50% from baseline or rise of sCr by > 26.4 mmol/L (> 0.3 mg/dL) in < 48 h in a patient with cirrhosis whose eGFR is < 60 ml/min for > 3 mo calculated using MDRD6 formula

AKI: Acute kidney injury; sCr: Serum creatinine; HRS: Hepatorenal syndrome; CKD: Chronic kidney disease; eGFR: Estimated glomerular filtration rate; ACKD: Acute on chronic kidney disease; MDRD6: Modification of Diet in Renal Disease 6.

Table 2 Definition and classification of acute kidney injury for patients with liver cirrhosis according to the International Club of Ascites (Angeli *et al*[23], 2015)

Baseline sCr	A sCr value obtained in 3 mo prior to hospital admission, with preference to the value dated the closest to hospital admission. In patients without a previous sCr value, the value on admission should be used
AKI definition	Increase in sCr ≥ 0.3 mg/dL (≥ 26.5 μmol/L) within 48 h; or the percentage increase in sCr ≥ 50%, which occurred in the last 7 d
Stage 1 AKI	Increase in sCr ≥ 0.3 mg/dL (26.5 μmol/L) or an increase of 1.5 to 2 times the baseline value
Stage 2 AKI	Increase of sCr 2 to 3 times the baseline value
Stage 3 AKI	Increase in sCr > 3 times the baseline or sCr ≥ 4.0 mg/dL (353.6 μmol/L), with acute increase in sCr ≥ 0.3 mg/dL (26.5 μmol/L) or onset of RRT

AKI: Acute kidney injury; ICA: International Club of Ascites. sCr: Serum creatinine; RRT: Renal replacement therapy.

Table 3 Diagnostic criteria and hepatorenal syndrome subtypes (Angeli *et al*[23], 2015)

Diagnostic criteria for HRS	HRS subtype
1) Presence of cirrhosis or ascites; 2) sCr > 1.5 mg/dL or 133 μmoles/L; 3) No improvement in sCr (below 1.5 mg/dL) after at least 48 h of diuretic withdrawal and volume expansion with albumin; 4) Absence of shock; 5) Has not undergone recent treatment with nephrotoxic drugs; 6) Absence of parenchymal kidney disease as indicated by proteinuria less than 500 mg/d, microhematuria (less than 50 erythrocytes/high-magnification field), and/or abnormal renal ultrasound findings	HRS type 1-Rapidly progressive renal failure defined as the doubling of initial serum creatinine to a level greater than 2.5 mg/dL or 220 μmoles/L in less than 3 wk, and associated with a very poor prognosis; HRS type 2-Moderate renal failure (sCr > 1.5 mg/dL or 133 μmoles/L), following a stable or slowly progressive course, often associated with refractory ascites

HRS: Hepatorenal syndrome; sCr: Serum creatinine.

blood transfusion of RBC, fresh frozen plasma (FFP), and platelets were at a 1:1:1 ratio[34].

Postreperfusion (PRS) was defined as a decrease in MAP > 30% below the baseline value, for at least 1 min, occurring during the first 5 min after reperfusion of the liver graft, asystole, or hemodynamically significant arrhythmias, or the need to start the infusion of vasopressors during the postreperfusion period[35]. Intraoperative arterial hypotension (IOAH) was defined as MAP less than 65-60 mmHg for at least 5 min, or any exposure to MAP less than 55-50 mmHg[31], irrespective of the cause: Prolonged surgery time, massive bleeding, PRS, and/or hemodynamic instability because of end-stage liver disease.

Statistical analysis

The baseline characteristics of the patients are expressed in absolute values, the mean ± SD, and percentages, when appropriate. The comparison between groups was performed for continuous variables using the Kruskal-Wallis test and the Mann-Whitney test. The assumptions were made to perform or not the parametric tests, and the categorical variables were compared using the chi-square test. Independent variables with significance in the univariate model was selected for the bootstrap classical LR model to assess the effect of bivariate independent variables (graft quality, patients characteristics, and intraoperative events) on the incidence of postoperative AKI. The results of the model are expressed by odds ratio (OR), together with the corresponding 95% confidence intervals [CIs], Nagelkerke R^2 statistic, and Hosmer and Lemeshow goodness of fit test. P values < 0.05 were considered significant. A relationship map between the significant variables in the LR model was also

Table 4 Acute kidney injury stages according to International Club of Ascites criteria (*n* = 145)

Overall incidence (*n* = 88)	Stage 1 (*n* = 22)	Stage 2 (*n* = 36)	Stage 3/RRT (*n* = 30/12)
60.6%	15.1%	24.8%	20.6/8.7%

RRT: Renal replacement therapy.

constructed.

The explanatory variables selected in the LR model were used for the ANN machine learning. Before developing prediction models, our collected data were divided into 70% of training dataset cases and 30% of test dataset cases. The cases in the training dataset were used for developing machine learning models. The ANN method had its own hyperparameters (number of layers in multilayer perceptron ANN), with a 10-fold cross-validation. This cross-validation process was used for developing the model, and performance was evaluated. The activation function of the hidden layer was made by hyperbolic tangent activation function, and Softmax for the output layer. All possible combinations of hyperparameters were investigated, and the hyperparameters with the highest average validation AUROC (area under the receiver-operating characteristic curve) were considered as optimal hyperparameters, and after that, the final model was tested for performance by root-mean-square error (RMSE) and mean absolute error (MAE) calculation. The importance of variables for the model was calculated. ANN structural model was constructed according to Haykin[36].

Our primary analysis attempted to analyze the prediction ability of machine learning and LR model in terms of AUROC. Accuracy was defined as the sum of the number of cases with true positive and true negative results divided by the total number of test sets. Statistical calculations were performed using the SPSS 28.0 software for Windows.

RESULTS

During the period from September 2017 to June 2021, 145 DDLT cases were included in the present study. Of the total patients included, 88 (60.6%) presented any further stage of postoperative AKI during the 7-d follow-up, 22 (15.1%) developed stage 1 AKI, 36 (24.8%) developed stage 2, and 30 (20.6%) developed stage 3 AKI (Table 4); renal replacement therapy (RRT) was required in 12 patients (8.7%). All patients' preoperative baseline information, donors, and grafts characteristics according to the occurrence of AKI are shown in Tables 5 and 6. The intraoperative data related to IOAH, blood derivatives transfusion, and piggy-back clamping, and laboratorial tests until the seventh postoperative (PO) day are shown in Table 7.

In the LR analysis, Nagelkerke R2 statistic was 0.147. Hosmer and Lemeshow goodness of fit test was not significant at 5% (P = 0.247). The six following factors were confirmed as predictors (Table 8): Biological (not adjusted) MELD score ≥ 25 (OR = 1.999, 95%CI = 1.586-2.503, P < 0.001), pre-existing KD (OR = 1.279, 95%CI = 0.916-1.686, P < 0.001), ECD (OR = 1.191, 95%CI = 0.711-1.787, P = 0.002), IOAH (OR = 1.935, 95%CI = 1.505-2.344, P < 0.001), MBT (OR = 1.830, 95%CI = 1.428-2.241, P < 0.001), serum lactate at the end of LT (OR = 2.001, 95%CI = 1.616-2.421, P < 0.001). The relationships between the significant variables were explored by a relationship map detailed in Figure 1.

Data of the two models with regard to AUROC for predicting AKI of all stages are detailed in Figure 2. ANN had the largest test AUROC (0.81, 95%CI: 0.75-0.83) and highest accuracy (0.68) than LR analysis [AUROC (0.71, 95%CI: 0.67 to 0.76), accuracy = 0.68].

Importance plot for ANN is shown in Figure 3 (KD and MELD score ranked first and second, respectively). Multilayer perceptron ANN presented one hidden layer by hyperbolic tangent activation function with four nodes in the layer, as presented in the ANN structural model diagram (Figure 4), and the prediction RMSE was 0.47 and the prediction MAE was 0.38.

DISCUSSION

As described elsewhere[36], the findings in the present study demonstrated a high incidence of postoperative AKI, and the predictive ability of ANN and LR models for this complication. An important point in this research is that AKI prediction was focused on the identification of significant risk factors at the end of the procedure, thus enabling the adoption of preventive measures or early therapies for AKI in the postoperative period.

In the present study, the severity of chronic liver disease, pre-existing KD, marginal grafts, hemodynamic instability, MBT, and consequent inadequate tissue perfusion during LT were predictors of AKI after DDLT, and the relationship map illustrated through a visual pattern, the relationship

Table 5 Patients' preoperative baseline information according to the occurrence of acute kidney injury after deceased-donor liver transplantation (*n* = 145)

	No AKI (*n* = 57)	AKI (*n* = 88)	*P* value
Male gender, *n* (%)	29 (50.8)	49 (55.6)	0.441
Age (yr), mean (± SD)	53.2 (± 13.56)	56.2 (± 13.26)	0.352
BMI, mean (± SD)	18.2(± 4.54)	22.7 (± 4.92)	0.065
Biological MELD score, mean (± SD)	21.67 (± 2.15)	26.05 (± 3.05)	< 0.001
Previous ascites, *n* (%)	24 (42.1)	52 (59.0)	0.013
Previous encephalopathy, *n* (%)	18 (31.5)	39 (44.3)	0.025
Previous upper digestive bleeding, *n* (%)	21 (36.8)	45 (51.1)	0.018
Preexisting KD, *n* (%)	15 (26.3)	60 (68.1)	< 0.001
HCC, *n* (%)	20 (35.0)	37 (42.0)	0.069
Systemic arterial hypertension, *n* (%)	28 (49.1)	46 (52.2)	0.083
Diabetes mellitus, *n* (%)	23 (40.3)	43 (48.8)	0.254

AKI: Acute kidney injury; LT: Liver transplantation; SD: Standard deviation; KD; Kidney dysfunction; BMI: Body mass index; MELD: Model for End-stage Liver Disease; HCC: Hepatocellular carcinoma.

Table 6 Donor and graft characteristics according to the occurrence of acute kidney injury after deceased-donor liver transplantation (*n* = 145)

	No AKI (*n* = 57)	AKI (*n* = 88)	*P* value
Donor > 60 yr, *n* (%)	16 (28.0)	31 (35.2)	0.346
Donor BMI > 27-30 kg/m^2, *n* (%)	14(24.5)	28 (31.8)	0.039
Graft macrosteatosis > 30%, *n* (%)	11 (19.2)	32 (36.3)	0.024
GCIT > 8 h, *n* (%)	0	0	-
GWIT > 40-45 min	38 (66.6)	54 (61.3)	0.349
Donor ICU stay > 4 d, *n* (%)	11 (19.2)	22 (25.0)	0.088
Donor controlled sepsis, *n* (%)	05 (8.7)	11 (12.5)	0.061
History of alcoholism of donor, *n* (%)	08 (14.0)	15 (17.0)	0.255
Donor sCr > 1.2 mg/dL, *n* (%)	16 (28.0)	31 (35.2)	0.024
Donor hypotensive episodes (< 60 mmHg) > 1 h, *n* (%)	10 (17.5)	18 (20.4)	0.127
Donor serum bilirubin > 2.0 mg/dL, *n* (%)	25 (43.8)	48 (54.5)	0.087
Donor serum ALT > 170 U/L, *n* (%)	11 (19.2)	22 (25.0)	0.073
Donor serum AST > 140 U/L, *n* (%)	05 (8.7)	13 (14.7)	0.023
Use of dopamine doses > 10 microg/kg per min, *n* (%)	10 (17.5)	13 (14.7)	0.176
Donor peak serum sodium > 155 mEq/L, *n* (%)	02 (3.5)	5 (5.6)	0.219
ECD (3 or more factors above), *n* (%)	07 (12.2)	31 (35.2)	< 0.001

AKI: Acute kidney injury; LT: Liver transplantation; BMI: Body mass index; GCIT: Graft cold ischemia times; GWIT: Graft warm ischemia times; ICU: Intensive care unit: sCr: Serum creatinine; ALT: Alanine transaminase; AST: Aspartate transaminase; ECD: Extended criteria donor.

between the variables, although it is important to understand that a visual relationship does not always mean statistical causation. As demonstrated in our study, in the case of machine learning-based techniques, the importance of each variable in the dataset can be indicated by the characteristic importance measure, which can improve the transparency of the algorithm according to He *et al*[20].

Table 7 Intraoperative events in 145 deceased-donor liver transplantations according to the occurrence of postoperative acute kidney injury

	Without AKI (*n* = 57)	With AKI (*n* = 88)	*P* value
IOAH (bleeding/PRS), *n* (%)	14 (24.5)	54 (61.3)	< 0.001
MBT, *n* (%)	5 (8.7)	15 (17.0)	< 0.001
Vasoactive drugs, *n* (%)	38(66.6)	48 (54.5)	0.197
Cryoprecipitate transfusion, *n* (%)	10 (17.5)	18 (20.4)	0.169
Piggy-back clamping, *n* (%)	30 (52.6)	48 (54.5)	0.072
SL (mmol/L) at the end of LT, mean (± SD)	1.4 (± 0.3)	2.8 (± 0.7)	< 0.001
Lower serum fibrinogen (mg/dL), mean (± SD)	242 (± 34)	214 (± 24)	0.090

AKI: Acute kidney injury; IOAH: Intraoperative arterial hypotension; MBT: Massive blood transfusion; SL: Serum lactate; SD: Standard deviation.

Table 8 Logistic regression analysis of risk factors for acute kidney injury after deceased-donor liver transplantation (*n* = 145)

Logistic regression	Beta coeficient	OR	95%CI		*P* value
Biological MELD score ≥ 25	0.194	1.999	1.586	2.503	< 0.001
Pre-existing KD, *n* (%)	0.115	1.279	0.916	1.686	< 0.001
ECD (3 or more factors above)	0.911	1.191	0.711	1.787	0.002
IOAH (bleeding/PRS), *n* (%)	0.169	1.935	1.505	2.344	< 0.001
MBT, n (%)	0.125	1.830	1.428	2.241	< 0.001
SL (mmol/L) ≥ 2.0 at the end of LT	0.110	2.001	1.616	2.421	< 0.001

Hosmer and Lemeshow goodness of fit test not significant at 5% (P = 0.701); Nagelkerke R2 statistic = 0.163). LR: Logistic regression; AKI: Acute kidney injury; MELD: Model for End-stage Liver Disease; OR: Odds ratio; CI: Confidence interval; KD: Kidney dysfunction; ECD: Extended criteria donor; IOAH: Intra-operative arterial hypotension; MBT: Massive blood transfusion; SL: Serum lactate.

According to our results, ANN had larger AUROC and higher accuracy to predict AKI after DDLT than LR, which is consistent with the previous study with different machine learning tools, whereas the performance of the ANN was inferior to that of all other machine learning techniques in prediction of AKI after LT[19]. Multilayer perceptron has already been associated to a good performance in predicting in-hospital mortality, reinforcing the good performance of ANN to predict clinical outcomes, although there have been some reports that the performance of the machine learning techniques is not superior to that of LR model in predicting mortality[18].

Regarding the risk factors identified in the present research, several other authors have already described that higher MELD scores[37] were associated with AKI after LT[20,38]. Xu *et al*[21] showed that MELD score > 25 was a predictor of AKI, and in patients with MELD scores > 30, the most required RRT [11,39]. Moreover, in the cirrhosis scenario, the functional renal disorders can be added as risk factors for AKI, such as recipient HRS[11,23,40]. Donor marginal liver grafts of ECD were identified elsewhere as a strong predictor of PGD[24-26] and post-LT AKI[20]. Patients undergoing LT can experience IOAH and consequent AKI because of multiple factors, including the duration of surgery, massive bleeding[16, 40-42], the severity of the PRS[36,43,44], and the severity of the end-stage liver disease[21,45-49]. In addition, MBT may be an additional risk factor for postoperative AKI[34,49,50].

The present retrospective study has important limitations, regarding sample size and moreover, the lack of evaluation of clinical outcomes of patients according to the occurrence of post-LT AKI, either for short or long-term evolution of patients. Despite these limitations, the high incidence of AKI reported highlights the importance of this issue, and the predictors identified may provide a focus for further research. ANN methods may provide feasible tools for forecasting AKI after LT, and perhaps provide a high-performance predictive model that may ultimately improve perioperative management of these patients at risk for this serious complication.
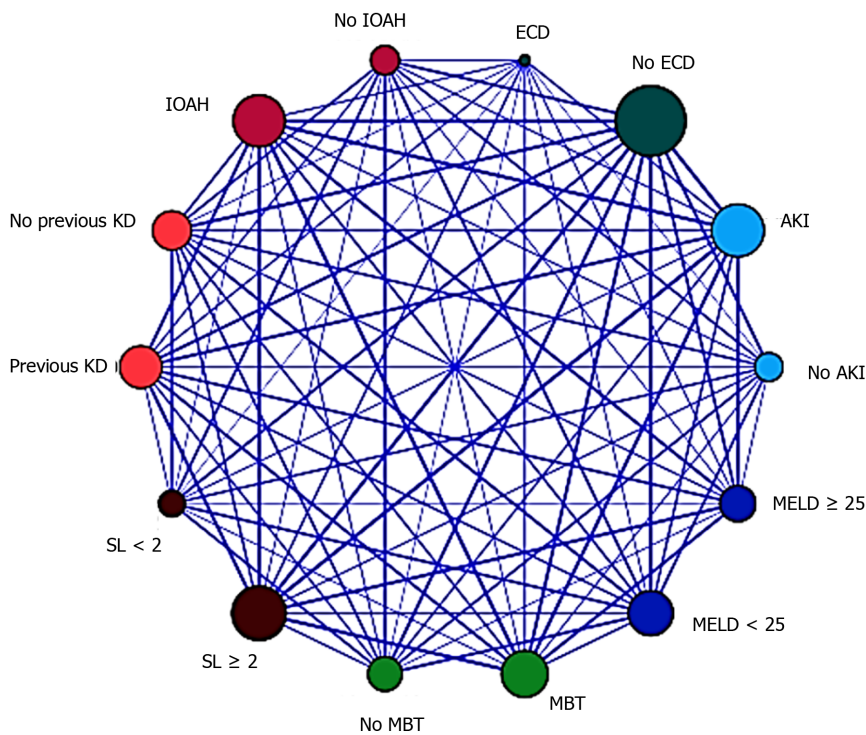
Figure 1 Relationship map between the selected variables in the logistic regression for acute kidney injury after deceased-donor liver transplantation (*n* = 145). MELD: Model for End-stage Liver Disease; KD: Kidney dysfunction; ECD: Extended criteria donor; IOAH: Intra-operative arterial hypotension; MBT: Massive blood transfusion; SL: Serum lactate. LR: Logistic regression; AKI: Acute kidney injury.

LR – AUROC (95%) : 0.71 (0.67 – 0.76) / accuracy : 0.68
ANN – AUROC (95%) : 0.81 (0.75 – 0.83) / accuracy : 0.70
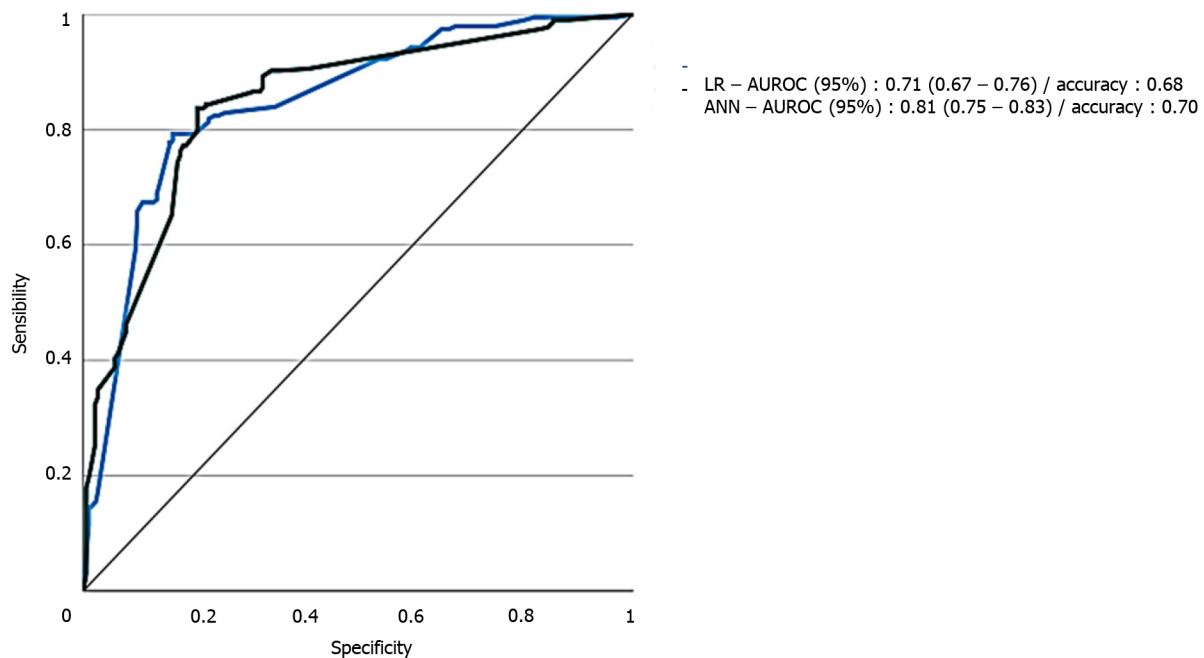
Figure 2 Area under the receiver-operating characteristic curve of the two different models for predicting acute kidney injury (*n* = 145). LR: Logistic regression; AUROC: Area under the receiver-operating characteristic curve; ANN: Artificial neural network; AKI: Acute kidney injury.

CONCLUSION

According to our results, the severity of chronic liver disease, pre-existing KD, marginal grafts, hemodynamic instability, MBT, and inadequate tissue perfusion during LT are predictors of AKI after
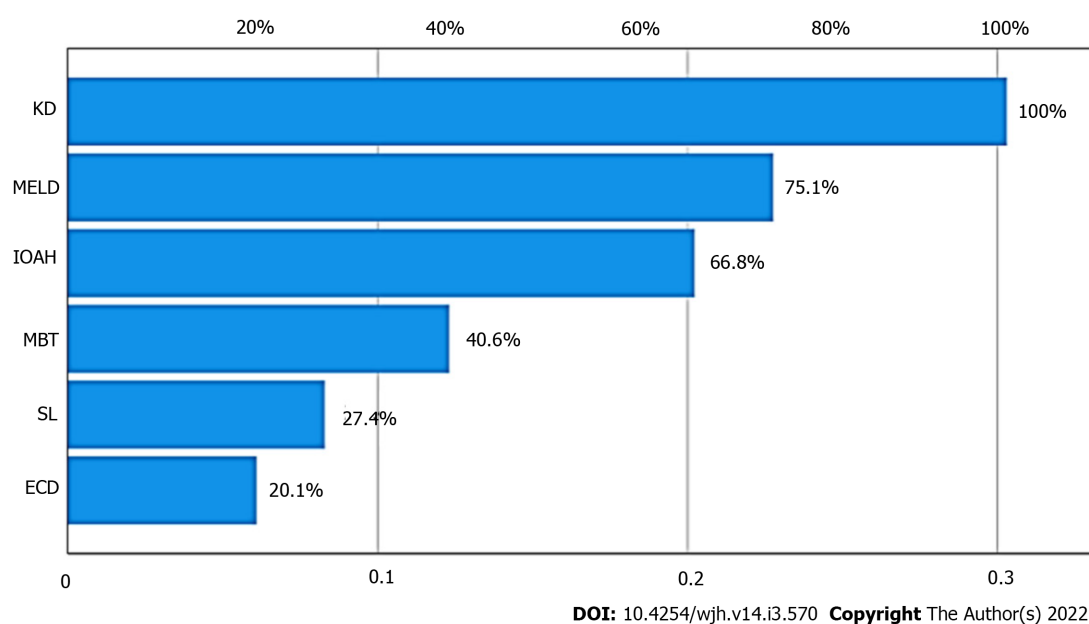
Figure 3 Variance importance plot of predictors of acute kidney injury for artificial neural network. KD: Kidney dysfunction; MELD: Model for End-stage Liver Disease; IOAH: Intra-operative arterial hypotension; MBT: Massive blood transfusion; ECD: Extended criteria donor; AKI: Acute kidney injury; ANN: Artificial neural network.
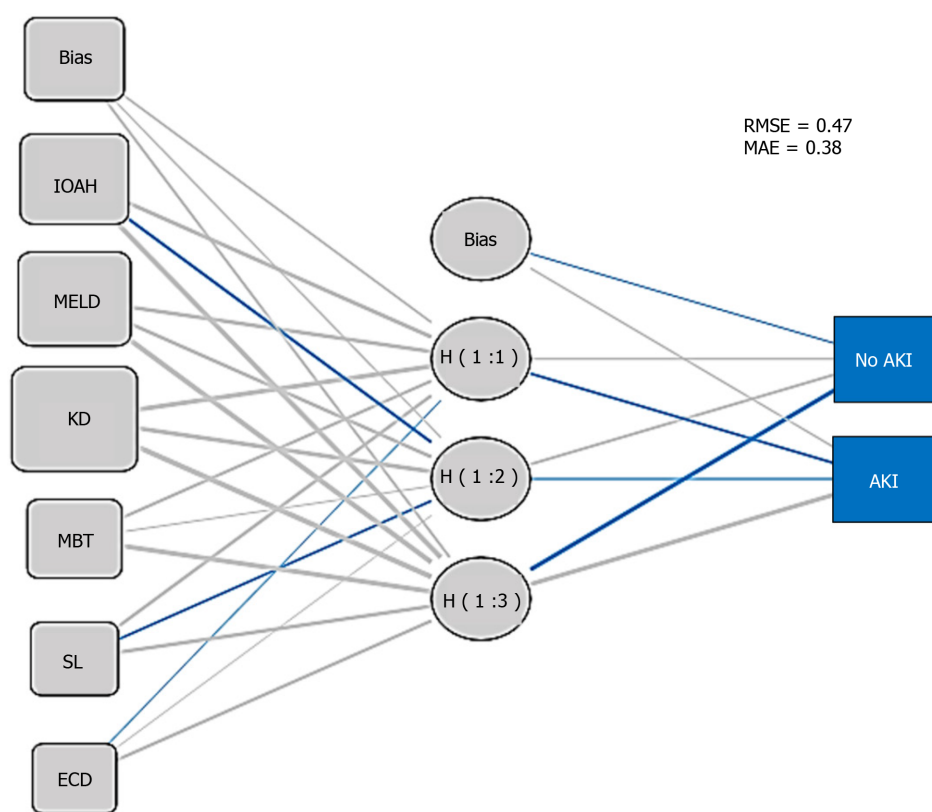
Figure 4 Artificial neural network structural model diagram for acute kidney injury after deceased-donor liver transplantation. IOAH: Intra-operative arterial hypotension; MELD: Model for End-stage Liver Disease; KD: Kidney dysfunction; MBT: Massive blood transfusion; ECD: Extended criteria donor; AKI: Acute kidney injury; ANN: Artificial neural network; RMSE: Root-mean-square error; MAE: Mean absolute error.

DDLT, and ANN has better prediction performance than LR in this scenario.

ARTICLE HIGHLIGHTS

Research background

Acute kidney injury (AKI) post-liver transplantation (LT) is a serious complication, and its prediction with validated tools is crucial.

Research motivation

To improve the perioperative management of patient candidates for LT.

Research objectives

To identify the risk factors for AKI after deceased-donor liver transplantation (DDLT) and validate a prediction tool for this complication.

Research methods

Logistic regression (LR) analysis for predictor identification, and comparative analysis of artificial neural network (ANN) and LR prediction performance were performed.

Research results

The severity of liver disease, preexisting kidney dysfunction, marginal grafts, hemodynamic instability, massive blood transfusion, and SL were predictors of postoperative AKI, and ANN had better prediction performance than LR.

Research conclusions

ANN has better performance than the classical LR for AKI prediction after DDLT.

Research perspectives

A risk score of AKI after DDLT can be developed according to these identified predictors.

FOOTNOTES

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