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Proteins in Preservation Fluid as Predictors of Delayed Graft Function in Kidneys from Donors after Circulatory Death

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Abstract

Background and objectives Kidney transplantation is the preferred treatment for ESRD, and donor kidney shortage urges proper donor–recipient matching. Zero-hour biopsies provide predictive values for short- and long-term transplantation outcomes, but are invasive and may not reflect the entire organ. Alternative, more representative methods to predict transplantation outcome are required. We hypothesized that proteins accumulating in preservation fluid during cold ischemic storage can serve as biomarkers to predict post-transplantation graft function.

Design, setting, participants, & measurements Levels of 158 proteins were measured in preservation fluids from kidneys donated after circulatory death (Maastricht category III) collected in two Dutch centers (University Medical Center Utrecht and Erasmus Medical Center Rotterdam) between 2013 and 2015. Five candidate biomarkers identified in a discovery set of eight kidneys with immediate function (IF) versus eight with delayed graft function (DGF) were subsequently analyzed in a verification set of 40 additional preservation fluids to establish a prediction model.

Results Variables tested for their contribution to a prediction model included five proteins (leptin, periostin, GM-CSF, plasminogen activator inhibitor-1, and osteopontin) and two clinical parameters (recipient body mass index [BMI] and dialysis duration) that distinguished between IF and DGF in the discovery set. Stepwise multivariable logistic regression provided a prediction model on the basis of leptin and GM-CSF. Receiver operating characteristic analysis showed an area under the curve (AUC) of 0.87, and addition of recipient BMI generated a model with an AUC of 0.89, outperforming the Kidney Donor Risk Index and the DGF risk calculator, showing AUCs of 0.55 and 0.59, respectively.

Conclusions We demonstrate that donor kidney preservation fluid harbors biomarkers that, together with information on recipient BMI, predict short-term post-transplantation kidney function. Our approach is safe, easy, and performs better than current prediction algorithms, which are only on the basis of clinical parameters.

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