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Predictors for Post Transplant Survival in Patients with Acute-on-Chronic Liver Failure

Martina Sterneck[1], Peter Huebener[1], Katrin Bangert[2], Andreas Drolz[2], Stefan Kluge[2], Ansgar Lohse[1], Lutz Fischer[3], Valentin Fuhrmann[2]
[1]Department of Internal Medicine, University Medical Center Hamburg, Hamburg, Germany; [2]Department of Intensive Care Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [3]Department of Hepatobiliary Surgery and Transplantation, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

Background: Acute-on-chronic liver failure (ACLF) is a severe complication of liver cirrhosis associated with excess short-term mortality rates. Orthotopic liver transplantation (OLT) is a potentially life-saving therapeutic modality for ACLF patients, but selection of transplant candidates with an acceptable post-OLT outcome is difficult. Objective: The aim of this study was to assess the risk of OLT in patients with ACLF, and to determine parameters that predict post-OLT survival in this patient cohort.
Methods: We retrospectively analyzed all patients with liver cirrhosis who underwent their first liver transplantation at the University Hospital Hamburg Eppendorf between 2009 and 2014 and assessed risk factors for post-transplant outcomes. Results: Of 250 cirrhotic liver transplant recipients, 98 patients fulfilled the diagnostic criteria for ACLF in the 3-month pre-transplant period. Compared to non-ACLF patients, ACLF was associated with significantly higher short-term morbidity and mortality after OLT (90-day patient survival: non-ACLF 96.1% versus ACLF patients 72.4%, p<0.0001). Clinical improvement in the pre-transplant period, as defined by recovery of at least one previously failed organ system, was observed in 37 of 98 (40%) ACLF patients, mostly within several days after diagnosis. In the multivariate analysis clinical improvement prior to OLT was the strongest predictor for post-transplant survival. In patients improving prior to transplantation post-transplant outcome was similar to non-ACLF OLT recipients. Following the 90-day post-transplant period, patient survival and long-term graft functions were comparable between ACLF and non-ACLF OLT recipients for up to five years.
Conclusion: Given the dismal prognosis of ACLF, our results indicate that ACLF patients can be transplanted with comparably good outcomes, in particular patients who improve under conservative therapeutic measures..

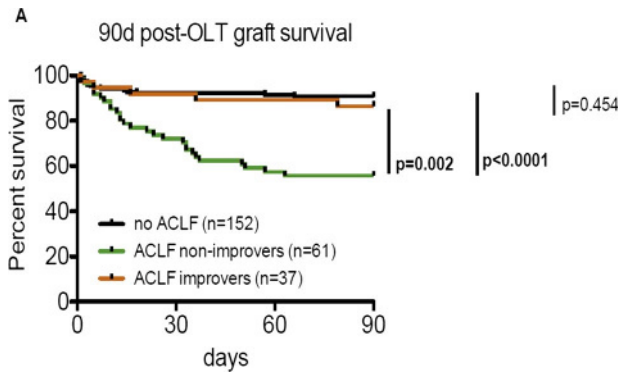

FIGURE 1.

618.7

Severe Injury of Common Bile Ducts in Donation after Circulatory Death Liver Transplantation: Histological and immunohistochemical Evaluation

Francesca Tinti[1,2], Ilaria Umbro[1,2], Stefan Hübscher[4], John Isaac[3], Paolo Onori[2], Antonio Franchitto[2], Eugenio Gaudio[2], Paolo Muiesan[3], Anna Paola Mitterhofer[1]
[1]Department of Clinical Medicine, Nephrology Unit, Sapienza University of Rome, Rome, Italy; [2]Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences, Sapienza University of Rome, Rome, Italy; [3]Liver Unit, Queen Elizabeth Hospital, Birmingham, United Kingdom; [4]Department of Cellular Pathology, Queen Elizabeth Hospital, Birmingham, United Kingdom.

Introduction: Within the model of donation after circulatory death (DCD), a more severe degree of ischaemia-reperfusion injury (IRI) is occurring, that seems to play a role on the pathogenesis of biliary complications.

Aim of the study was to assess the bile duct injury occurring in two different models of ischaemia, DCD and donation after brain death (DBD), in liver transplanted grafts.
Methods: Bile duct injury was evaluated on histological samples of common bile duct retrieved after liver graft reperfusion, before biliary anastomosis.

Severity of donor bile duct injury was assessed and scored on the basis of Biliary epithelial cell loss, Mural stroma necrosis, Inflammation, Peribiliary vascular plexus damage, Arteriolonecrosis, Thrombosis, Periluminal and deep peribiliary glands damage.

Cholangiocyte apoptosis in periluminal and peribiliary glands was evaluated by quantitative terminal deoxy-nucleotidyl transferase dUTP-mediated nick-end labeling (TUNEL) analysis on bile duct sections. Cholangiocyte proliferation was studied in bile duct sections by PCNA immunohistochemical expression.
Results: Sixty-two patients had the bile duct sample available for histological evaluation (2014-2015). A significantly higher number of DCD patients presented necrosis >50% of the bile duct wall [DCD 14/28 (50%), DBD 9/34 (26.5%) p=0.056], peribiliary vascular plexus damage [DCD 8/28 (29%), DBD 3/34 (9%); p=0.053] and periluminal peribiliary gland damage [DCD 20/28 (71%), DBD 14/34 (41%); p=0.016], defining the occurrence of severe histological injury, that was significantly more frequent in DCD liver transplant patients [15/28 (53.6%)] compared to DBD [7/34 (20.6%)] (p=0.007). A significant increased apoptosis and decreased proliferation was evidenced in both periluminal (Tunel assay p=0.029; PCNA expression p=0.029) and deep PBGs (Tunel assay p=0.002; PCNA expression p=0.006) from bile duct sample with severe histological injury.
Discussion: This study shows an early picture of microscopic damage at the level of the bile duct soon after reperfusion of liver graft during transplantation. Bile duct samples retrieved from DCD grafts expressed more severe injury at the histological level, defining the new feature of severe histological injury. Bile ducts with severe histological injury showed increased apoptosis and reduced proliferation as evaluated by Tunel assay and PCNA expression, both on periluminal and deep PBG. This study raises the hypothesis of a correlation between the occurrence of microscopic damage and the development of ischaemic biliary complications.

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