Plasma from liver transplant patients with persistent ascites increases endothelial permeability and has decreased vessel integrity proteins

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Abstract

Introduction: Persistent ascites (PA) is a common and serious complication following liver transplant (LT) with unclear mechanisms. In other diseases, ascites is associated with increased endothelial permeability induced by pro-inflammatory mediators. Our findings suggest a connection between a pro-inflammatory post-transplant milieu, loss of endothelial integrity, and PA. We hypothesized that plasma of LT recipients with PA will result in impaired endothelial barrier function.

Methods: Plasma from 32 LT patients was collected pre-operatively, on post-operative day (POD) 1 and POD5. PA was defined as drain output >1L on POD7. Electric cell-substrate impedance sensing (ECIS) was used to measure endothelial permeability. Human umbilical vein endothelial cells (HUVECs) were plated, grown to confluence, and incubated with patient plasma. Additionally, proteomic analysis by mass spectrometry was conducted on anhepatic, reperfusion, and POD1 plasma.

Results: The median age was 52, 27% were female, the median MELD-Na was 24, and 12 (38%) patients developed PA. At baseline, there was no difference in permeabilities between PA and control groups. On POD1, PA plasma significantly increased permeability compared to controls ($p=0.0034$), and to baseline plasma with PA ($p=0.0003$) and without ($p<0.0001$). Proteomics analysis on 10 patients identified increased degranulation and oxidative stress, and decreased complement, coagulation, and vessel integrity proteins at both anhepatic and POD1 stages.

Conclusions: POD1 PA plasma increased endothelial permeability *in vitro.* Our proteomics findings suggest there are circulating mediators immediately surrounding transplant impacting endothelial integrity. These findings are an important step toward uncovering a mechanism for PA in LT recipients.