Georg SEMMLER

Hypercoagulable state, hepatic microenvironment, and liver fibrogenesis inadvanced chronic liver disease

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Background: Patients with cirrhosis are considered to have a rebalanced, but instable haemostatic system tilting easier towards bleeding or thrombosis. As disease progresses, this system turns into a hypercoagulable state which is believed to contribute to parenchymal extinction and liver fibrogenesis. On the other hand, (systemic) inflammation - aggravated by an impaired intestinal barrier (i.e., the 'gut-liver axis') and endothelial dysfunction – triggers profibrogenic pathways within the liver and thus promotes disease progression. While these mechanisms have been investigated mostly in experimental studies focusing on a specific aspect, holistic clinical studies that combine these pieces are lacking.

Objectives: The primary aim of the proposed research project is to study the link between the haemostatic balance and liver fibrogenesis as well as matrix turnover in patients with advanced chronic liver disease. Secondary aims include the prognostic impact of the procoagulant state and its relationship with systemic inflammation/bacterial translocation and endothelial dysfunction.

Methods: The study cohorts will include 240 thoroughly characterized patients with advanced chronic liver disease (ACLD) undergoing HVPG-measurements as part of the prospective VIenna CIrrhosis Study (VICIS). An extensive profile of haemostasis, fibrogenesis and matrix remodeling, bacterial translocation and systemic inflammation as well as endothelial dysfunction will be put in context to each other and disease progression.