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The development of portosystemic shunts depends on liver dysfunction rather than on PIGF-driven neoangiogenesis

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Background and aims: Portosystemic shunts (PSS) are common in patients with advanced chronic liver disease (ACLD). However, the relative impact of liver dysfunction, portal pressure and splanchnic neoangiogenesis in the pathophysiological development of PSS remains unclear. The pro-angiogenic placental growth factor (PIGF) has been associated with the development of liver fibrosis and portal hypertension in experimental studies. We assessed the association between the extent of PSS and hepatic dysfunction, portal pressure and PIGF levels in ACLD patients.

Method: 107 patients with ACLD were prospectively enrolled. Portal hypertension was evaluated by hepatic venous pressure gradient (HVPG), severity of hepatic dysfunction was evaluated by ALBI score, FIB-4 score, MELD score and Child-Pugh score (CPS). PSS were semiquantitatively categorised as mild, moderate and severe on contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) scans by two experienced radiologists.

Results: N = 51 (47, 7%) showed mild PSS, while n = 38 (35, 5%) showed moderate and n = 18 (16, 8%) severe PSS. The extent of PSS (mild vs. moderate vs. severe) correlated with a higher prevalence of portal vein thrombosis (PVT: 3.9% vs. 26.3% vs. 44.0%; $p < 0.001$), higher ALBI score (-2.41 vs. -1.96 vs. -1.90; $p = 0.002$) and FIB-4 score (3.9 vs. 5.2 vs. 8.8; $p < 0.001$). There was a significant association of PSS severity with HVPG (12 vs. 19 vs. 15 mmHg; $p = 0.0095$) and MELD score (10 vs. 13 vs. 14; $p = 0.0022$). However, there was no significant association between PSS and CPS ($p = 0.1024$). Also, PIGF levels were not significantly different between patients with mild vs. moderate vs. severe PSS.

Conclusion: The development and extent of portosystemic shunts seems to be determined by severity of portal pressure and hepatic dysfunction. Importantly, the presence of PVT, i.e. prehepatic portal hypertension may be a major trigger for PSS development. Surprisingly, PIGF levels did not correlate with the extent of PSS.

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Optimal timing of endoscopy is associated with lower 42-day mortality in variceal bleeding

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Background and aims: The optimal timing of endoscopy in patients with variceal bleeding from the upper gastrointestinal tract is unknown. Current guidelines recommend performance of endoscopy within 12–24 hours from hospital admission, but the evidence is limited. Our aim was to describe the association between timing of endoscopy and 42-day mortality in variceal bleeding.

Method: Analyses were performed on prospective collected data on patients admitted with variceal bleeding at 34 centres in Europe and Canada during in the period October 2011 to May 2015. Patients transferred with bleeding from other hospitals and patients bleeding from post-banding ulcers, or non-specified sources, were excluded. Logistic regression analyses were used to investigate the association between timing of endoscopy and 42-day mortality following adjustment for confounding factors including age, sex, comorbidities, liver function, previous decompensation, laboratory values, haemodynamic parameters, and treatment with vasopressors. We evaluated the association in: 1. All patients with variceal bleeding; 2. Patients with Child-Pugh A or B-cirrhosis; and 3. Patients with systolic blood pressure (SBP) < 90mmHg.

Results: A total of 2, 138 patients were considered for inclusion. Following exclusion of transferred patients (n = 607) and patients with other sources of bleeding (n = 163), 1, 373 patients were included with mean age 59 years, and mean Child-Pugh score 8.2. 69%, 18%, 8% and 5% underwent endoscopy in the periods < 6, 6–12, 12–24, and > 24 hours, respectively. Mortality at 42 days was 26.2%. Following adjustment for confounding factors, performance of endoscopy within 24 hours from time of hospital admission was associated with lower mortality in patients with Child-Pugh A or B cirrhosis (Odds ratio (OR) 95% confidence interval (CI): 0.38 [0.16–0.86]; p = 0.020) and patients with SBP < 90 mmHg (OR [95% CI]: 0.053; [0.006–0.51]; p = 0.011). Performance of endoscopy within 6 or 12 hours was not associated with further reduction in mortality compared with endoscopy within 24 hours. We did not find a significant association between timing of endoscopy and mortality in the overall group of patients (OR [95% CI]: 0.51 [0.24–1.09]; p = 0.082).

Conclusion: Our data suggest that in patients presenting with variceal bleeding, performance of endoscopy within 24 hours is associated with reduced 42-day mortality in patients with Child-Pugh A or B cirrhosis and in those with SBP < 90mmHg.

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Factors predicting survival in patients with high-risk acute variceal bleeding treated with pre-emptive (Early)-TIPS

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