





# Impact of hepatopulmonary syndrome in liver transplantation candidates and the role of angiogenesis

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The presence of hepatopulmonary syndrome with even mild oxygenation abnormalities was associated with shorter survival in candidates evaluated for liver transplantation and was characterised by higher levels of pro-angiogenic biomarkers <https://bit.ly/3Eaihtf>

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## Abstract

**Background** Hepatopulmonary syndrome affects 10–30% of patients with cirrhosis and portal hypertension. We evaluated the serum angiogenic profile of hepatopulmonary syndrome and assessed the clinical impact of hepatopulmonary syndrome in patients evaluated for liver transplantation.

**Methods** The Pulmonary Vascular Complications of Liver Disease 2 study was a multicentre, prospective cohort study of adults undergoing their first liver transplantation evaluation. Hepatopulmonary syndrome was defined as an alveolar–arterial oxygen gradient  $\geq 15$  mmHg ( $\geq 20$  mmHg if age  $>64$  years), positive contrast-enhanced transthoracic echocardiography and absence of lung disease.

**Results** We included 85 patients with hepatopulmonary syndrome and 146 patients without hepatopulmonary syndrome. Patients with hepatopulmonary syndrome had more complications of portal hypertension and slightly higher Model for End-Stage Liver Disease–Na score compared to those without hepatopulmonary syndrome (median (interquartile range) 15 (12–19) *versus* 14 (10–17),  $p=0.006$ ). Hepatopulmonary syndrome patients had significantly lower 6-min walk distance and worse functional class. Hepatopulmonary syndrome patients had higher circulating angiopoietin 2, Tie2, tenascin C, tyrosine protein kinase Kit (c-Kit), vascular cell adhesion molecule 1 and von Willebrand factor levels, and lower E-selectin levels. Patients with hepatopulmonary syndrome had an increased risk of death (hazard ratio 1.80, 95% CI 1.03–3.16,  $p=0.04$ ), which persisted despite adjustment for covariates (hazard ratio 1.79, 95% CI 1.02–3.15,  $p=0.04$ ). This association did not vary based on levels of oxygenation, reflecting the severity of hepatopulmonary syndrome.

**Conclusion** Hepatopulmonary syndrome was associated with a profile of abnormal systemic angiogenesis, worse exercise and functional capacity, and an overall increased risk of death.