Commentary

Hyperdynamic circulation in liver cirrhosis: not peripheral vasodilatation but ‘splanchnic steal’

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Introduction

It is generally accepted that liver cirrhosis is associated with a hyperdynamic circulation and peripheral vasodilatation. The Oxford Textbook of Medicine describes the clinical features of ‘flushed extremities, bounding pulses and capillary pulsations’ in cirrhosis, and a resting tachycardia and systemic hypotension, with experimental evidence of elevated cardiac output and reduced total systemic vascular resistance, confirm the existence of a hyperdynamic circulation. In 1988, Schrier and colleagues proposed the ‘peripheral arterial vasodilatation hypothesis’ to account for this hyperdynamic circulation as well as the initiation of sodium and water retention in cirrhosis. Many subsequent theories have been expounded to explain the underlying mechanism of this peripheral arterial vasodilatation. Most suggest the production of, or failure to metabolize, a circulating vasodilator substance that causes decreased vascular tone, recruitment of arteriovenous anastomoses and systemic hypotension. Various candidate vasodilators have been proposed, including nitric oxide, eicosanoids, bile salts, adenosine and tachykinins, such as substance P, and calcitonin-gene-related peptide. This unidentified vasodilator substance has been held responsible for the sodium and water retention associated with ascites, due to the consequent activation of the sympathetic nervous, renin-angiotensin-aldosterone and vasopressin systems. Nitric oxide has gained the most attention, although it is interesting to note that there is little evidence of elevated basal nitric oxide release in the peripheral circulation of patients with early or advanced cirrhosis.

Although there is a marked reduction in total systemic vascular resistance, we contest the belief that liver cirrhosis is associated with peripheral vasodilatation, and that this is due to the effects of a systemic circulating vasodilator substance. This is not consistent with clinical observations or experimental evidence, which have shown little evidence of peripheral vasodilatation. In our experience, patients with advanced cirrhosis rarely have ‘flushed peripheries and capillary pulsations’. Although arteriolar vasodilatation in the form of spider naevi and palmar erythema may be present, their occurrence is unpredictable and does not correlate with disease severity. Thermography demonstrates that patients with advanced liver cirrhosis have cool peripheries, with skin pallor and poor capillary perfusion. Indeed, in clinical questionnaires, patients with cirrhosis are more likely to complain of cold hands. Haemodynamic measurements show that, while splanchnic blood flow is markedly increased, blood flow is significantly reduced in the upper and lower limbs as well as the extra-splanchnic viscera including the brain.

How then do we account for the findings of peripheral vasoconstriction in the face of a hyperdynamic circulation? We propose that the high cardiac output and systemic hypotension relate to...
Figure 1. Schematic representation of the splanchnic steal phenomenon.
the marked and dysregulated splanchnic vasodilatation consequent on the development of liver cirrhosis, and as a result of portal hypertension. Hepatic fibrosis causes a marked impairment of portal blood flow into the liver, and maladaptive splanchnic vasodilatation attempts to rectify the associated reduction in hepatic perfusion by increasing blood flow and pressure in the portal venous system. However, rather than increasing perfusion of the liver, this hyperaemia and hypertension results in incremental shunting of portal blood into the systemic circulation via portal systemic collateral anastomoses. Progressive collateral shunting exacerbates the reduction in portal blood flow to the liver, creating a true ‘steal’ phenomenon (Figure 1). Both arterial and venous steals take place in this model: arterial steal occurs from the systemic circulation into the splanchnic arterial system, while venous steal occurs from the portal vein inflow of the liver into the porto-systemic collaterals. This latter steal becomes extreme in advanced liver disease, where blood flow in the portal vein may even become reversed. This is supported by the correlation of worsening liver function with increases in cardiac output and ayzygous (collateral) blood flow,15 and decreases in hepatic perfusion.16

The fundamental cardiovascular consequences of liver cirrhosis would, therefore, appear to be due to a ‘splanchnic steal’ where progressive and inexorable vasodilatation of the splanchnic bed occurs. Homeostatic mechanisms, including activation of neurohumoral reflexes, attempt to correct these derangements and lead not to peripheral vasodilatation, but peripheral vasoconstriction with reduced tissue perfusion. Plasma concentrations of vasconstrictor mediators such as catecholamines, angiotensin II, and endothelin are elevated, and lead to increases in peripheral vascular tone.7,12 Indeed, systemic blockade of the sympathetic nervous or renin-angiotensin systems causes profound hypotension in patients with cirrhosis.17,18 This again indicates that the peripheral circulation is under increased vasoconstrictor tone, despite systemic hypotension and a reduction in total systemic vascular resistance: homeostatic mechanisms attempting to sustain blood pressure despite resistant and persistent splanchnic vasodilatation. This also explains the impaired pressor responses to exogenously administered vasoconstrictor agents, such as noradrenaline and angiotensin II,19,20 since the basal vascular tone of the extra-splanchnic circulations is already increased, and additional stimulation will be unable to produce the same incremental response as that observed in normal healthy volunteers.

This ‘splanchnic steal’ is consistent with, and assists in the explanation of, the observed haemodynamic responses to two therapeutic manoeuvres used in patients with cirrhosis. A transjugular intrahepatic portosystemic shunt (TIPSS) is inserted to reduce the risk of variceal bleeding by alleviating portal hypertension through increased collateral shunting. This exacerbates the haemodynamic derangements of cirrhosis,21 leading to increases in cardiac output, reductions in hepatic sinusoidal perfusion and progressive peripheral vasoconstriction. In contrast, terlipressin, a long-acting analogue of vasopressin, causes selective splanchnic vasoconstriction and is used in the treatment of hepatorenal syndrome.22 Administration of terlipressin improves blood pressure and renal function by reducing the steal into the splanchnic circulation, and diverting blood to the systemic and renal circulations.

We would, therefore, suggest that, although liver cirrhosis is associated with a hyperdynamic circulation and low total systemic vascular resistance, marked peripheral arterial vasoconstriction is the dominant clinical picture. We hypothesize that these apparently contradictory phenomena reflect a ‘splanchnic steal’ effect where dysregulated splanchnic vasodilatation and porto-systemic shunting induce a high cardiac output state associated with peripheral extra-splanchnic vasoconstriction. 

References


