Determinants of splanchnic blood flow

J. TAKALA

The splanchnic region participates in the regulation of circulating blood volume and systemic blood pressure [60]. Major reduction of splanchnic blood volume and flow can be vital in defending the perfusion of the brain and the heart in acute hypovolaemia, but prolonged hypoperfusion of the splanchnic region will inevitably lead to hypoxic tissue injury [55]. The splanchnic region is also an important source and target of inflammatory mediators, which have a major impact on both systemic and regional blood flow and tissue functions [45]. The splanchnic circulation is in close interaction with the systemic haemodynamics under normal conditions. In the intensive care patient at risk of multiple organ failure, there is a complex and poorly understood interaction between the splanchnic blood flow, metabolic demands of the tissues and the mediators of inflammation and vasoregulation.

Inadequate splanchnic blood flow and tissue perfusion are likely to contribute to the development of organ failures and increased mortality in various categories of intensive care patients [8]. Monitoring of gastric intramucosal pH (pH_i) or intramucosal P_{CO_2} by gastrointestinal tonometry has provided an indicator of splanchnic tissue perfusion that is feasible for clinical use in intensive care [15, 18, 19, 27, 30, 32, 47, 48, 49]. Clinical studies using gastrointestinal tonometry have produced evidence to support the concept of a link between inadequate splanchnic tissue perfusion and multiple organ failure.

Gastric intramucosal acidosis, suggesting inadequate splanchnic tissue perfusion, is relatively common: up to 50 % of patients admitted to intensive care with signs of circulatory failure, 50 % of patients undergoing elective cardiac surgery and 18 % of patients undergoing abdominal aortic surgery have at least transient episodes of gastric intramucosal acidosis [15, 18, 19, 30, 32, 47, 48, 49]. Patients with gastric intramucosal acidosis on admission to intensive care have an increased occurrence of multiple organ failure and increased mortality [30, 32, 47, 48]. Prevention and treatment of gastric intramucosal acidosis by administration of fluids and vasoactive drugs improves the outcome of those patients with normal pH_i on admission [32, 49].

The mechanisms responsible for the increased morbidity and mortality related to the inadequate splanchnic perfusion are far from being solved. Evidently alterations in systemic haemodynamics can impair the splanchnic blood flow and tissue perfusion [33, 55]. Tissue hypoxia with consequent direct hypoxic tissue injury, although likely to contribute, is clearly a too simplistic explanation. Translocation of bacteria and toxic substances, as a result of hypoxic intestinal mucosal injury, may occur but is unlikely to be a major factor [14]. Inadequate mucosal perfusion increases the intestinal mucosal permeability [20]. All these mechanisms and ischaemia and reperfusion of splanchnic tissues may contribute to the activation of inflammatory mediator networks, and thereby further modify the circulatory and metabolic responses locally, within the splanchnic region and in extrasplanchnic organs [46].

This review discusses the physiology of splanchnic blood flow, obtained largely from experimental studies, and the relatively limited available human data on splanchnic blood flow in patients at risk of multiple organ failure.

Splanchnic blood flow in normal conditions

The arterial inflow to the splanchnic region is via the coeliac trunk and the superior and inferior mesenteric arteries [17] (table 1). The venous efflux via the portal vein represents the sum of all splanchnic arterial influx, except the hepatic arterial flow. The venous efflux via the hepatic veins (i.e. the blood flow through the liver) represents the total hepato-splanchnic bloodflow; inprinciple, the hepaticarterial flow could be estimated as the difference between portal venous flow and total hepatic venous efflux.

Hepatic arterial and portal venous blood flow interact closely. Owing to this "hydrodynamic" interaction, an alteration of flow to one of the circuits leads to an opposite change in the other circuit. The interaction tends to maintain total liver blood flow constant [57].

The blood flow of the small intestinal villus deserves special consideration. The artery and vein of the villus run in parallel but their blood flows are

JUKKA TAKALA, MD, PHD, Critical Care Research Program, Department of Intensive Care, Kuopio University Hospital, PO Box 1777, FIN-70211, Kuopio, Finland.

Table 1 Arterial blood supply to the splanchnic region (general overview, anatomical variation is common)

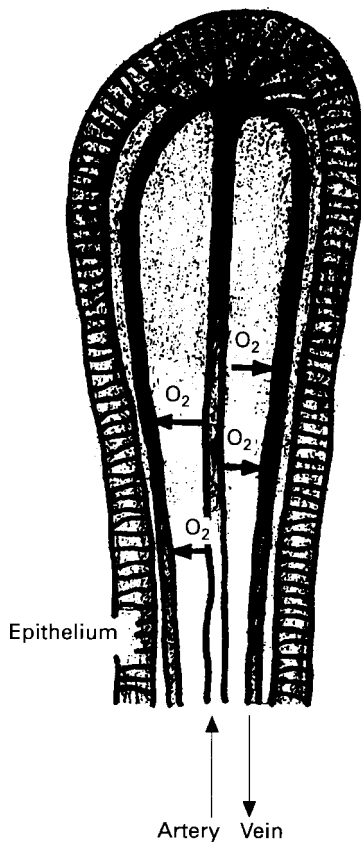| Main artery	Main tributary arteries	Main areas supplied
Coeliac trunk	Common hepatic (branches: right gastric and gastroduodenal)	Liver; parts of stomach, duodenum and pancreas
	Splenic	Spleen; parts of stomach and pancreas
	Left gastric	Parts of stomach and lower oesophagus
Superior mesenteric artery	Inferior pancreaticoduodenal, intestinal (12–15 branches), ileocolic, right colic, middle colic	Small intestine, caecum, ascending colon, most of transverse colon; parts of duodenum and pancreas
Inferior mesenteric artery	Left colic, sigmoid, superior rectal	Descending and sigmoid colon; parts of transverse colon and rectum

Figure 1 Schematic presentation of the intestinal villus countercurrent exchange of oxygen. Oxygen diffuses from the artery to the villous veins throughout their course to the tip of the villus. This results in a descending gradient of P_{O_2} from the base of the villus to the tip.

Table 2 Splanchnic and whole body blood flow and oxygen uptake at rest [6, 24, 57, 77]

	Splanchnic	Whole body	Splanchnic contribution to total (%)
Blood flow (litre min^{-1} m^{-2})	0.50–0.80	2.5–4.0	20–30
Oxygen consumption (ml min^{-1} m^2)	20–40	110–150	20–35
Oxygen extraction fraction	0.22–0.35	0.22–0.30	

MEASUREMENT OF SPLANCHNIC BLOOD FLOW

Human studies on splanchnic blood flow are relatively scarce owing to methodological difficulties of quantitative measurements. Direct measurement of splanchnic blood flow is practically impossible without surgery for anatomical reasons (table 1; multivessel influx and efflux, mixing of portal venous and hepatic arterial blood within the liver). The same is true for intravascular pressures within the splanchnic bed. Accordingly, much of the basic splanchnic circulatory physiology has been extrapolated from experimental studies and has not been confirmed in normal humans.

Total hepatosplanchnic blood flow can be estimated according to the Fick principle from the hepatic uptake of substances that are exclusive metabolized by the liver and distributed in the plasma [9, 36, 71]. Hepatic venous catheterization is necessary for the measurement. A detailed description of this technique and its evaluation both in normal subjects and in intensive care patients has been published [71].

SPLANCHNIC BLOOD FLOW AND OXYGEN UPTAKE

The splanchnic blood flow should be considered in relation to the splanchnic metabolic activity and the oxygen extraction capabilities of the splanchnic tissues. Normally, the total hepatosplanchnic blood flow is approximately 20–30 % of cardiac output. Roughly 80 % of the total hepatic blood flow reaches the liver via the portal vein and 20 % via the hepatic artery (a tributary of the coeliac trunk). The splanchnic oxygen consumption at rest is approximately 20–35 % of whole body oxygen consumption.

in opposite directions (fig. 1). The artery forms a dense capillary network close to the top of the villus. This anatomical arrangement allows countercurrent exchange of oxygen from the artery to the vein along their course within the villus [42]. This results in a descending gradient of tissue P_{O_2} from the base of the villus to its tip. This gradient is inversely related to the blood flow. An alternative explanation for the tissue P_{O_2} gradient in the villus may be a higher metabolic activity of the absorptive cells at the tip [42]. Regardless of the mechanism, the lower P_{O_2} at the tip may make the villus susceptible to tissue hypoxia, if vasoconstriction occurs for any reason.

This results in a slightly increased oxygen extraction fraction, compared with the systemic oxygen extraction at rest [6, 24, 57, 77] (table 2).

When the metabolic demands of the splanchnic region increase, for example, as the result of feeding, blood flow to the relevant organs increases in proportion to the increase in regional oxygen consumption. Accordingly, the splanchnic oxygen extraction ratio is well maintained. If the oxygen extraction is very low, increased extraction may precede increases in blood flow. The appropriate increase in splanchnic perfusion can be obtained by either increased cardiac output or its redistribution, or by the combination of the two mechanisms [5, 23, 57, 67].

Probably because of its important role in the regulation of blood volume and redistribution of blood flow, the splanchnic region has a large capacity to adapt to reduced blood flow by increasing the oxygen extraction. During exercise, blood flow is redistributed from the splanchnic region to the working muscle [58, 59]. Splanchnic oxygen extraction increases consequently. At least in the short term, the normal metabolic processes are maintained at high levels of oxygen extraction. In extreme conditions, when hypoxia due to reduced inspired oxygen fraction is superimposed on exercise, splanchnic oxygen extraction may increase to close to 90 %. During this acute experiment, hepatic extraction of indocyanine green decreased, suggesting that the liver function was deteriorating [58].

The available data in humans suggest that the liver is well protected against hypoxia in normal subjects, at least when the exposure is short. On the other hand, the gut may be more susceptible to develop local or regional hypoxia. Experimental studies suggest that the gut may become hypoxic already, when its oxygen extraction approaches 70 % [50, 78].

CONTROL OF SPLANCHNIC BLOOD FLOW

Gut blood flow

Gut blood flow is regulated by intrinsic and extrinsic mechanisms. The intrinsic factors include local metabolic control and myogenic control, local reflexes and locally produced vasoactive substances. The extrinsic factors include sympathetic innervation, circulating vasoactive substances and systemic haemodynamic changes [23]. The total blood flow to the gut wall is unevenly distributed in the four main layers—the mucosa, the submucosa, the muscularis and the serosa. The mucosa and the submucosa receive most of the flow, up to 90 %. Changes in the total gut blood flow may influence the flow to the different layers to varying extent.

The local metabolic control responds by local vasodilatation, if blood flow is insufficient for the local metabolic needs [23, 25]. The actual signal for the vasodilatation is not known. Both tissue P_{O_2} and products of cell metabolism have been proposed. The myogenic control responds to an increase in vascular transmural pressure by arteriolar vasoconstriction [23, 35]. These two control mechanisms interact to maintain blood flow adequate for metabolic needs, and to minimize changes in the intestinal
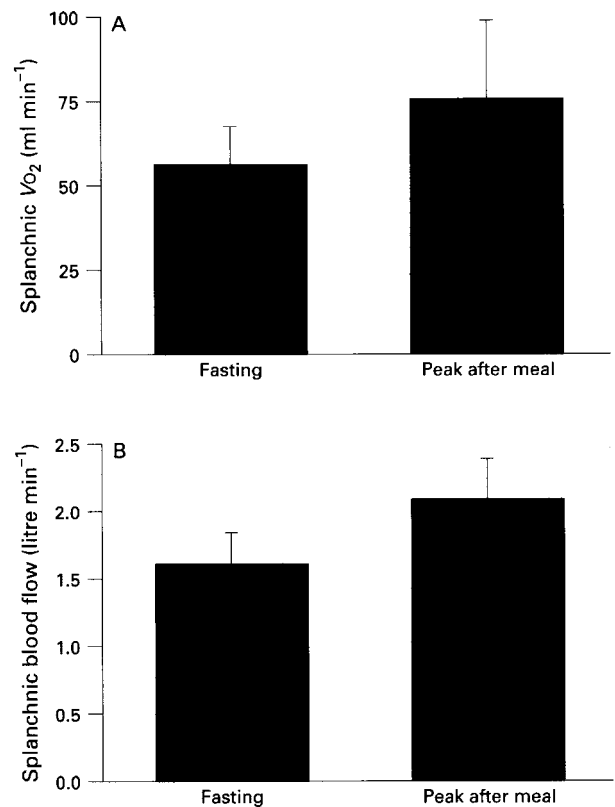

Figure 2 Effect of feeding on splanchnic blood flow and oxygen consumption in healthy subjects [data adapted from ref. 34]. A: Peak splanchnic oxygen consumption following a standard meal (mean (SD)). B: Peak splanchnic blood flow following a standard meal (mean (SD)).

capillary pressure and transcapillary fluid flux. Nitric oxide participates the vasoregulation of the hepato-splanchnic bed; its role is discussed separately later.

Intestinal blood pressure–flow autoregulation is much weaker than the autoregulation of, for example, renal blood flow [23]. When arterial pressure decreases, blood flow decreases despite a vasodilatory response. The autoregulation is enhanced by feeding: the blood flow is better maintained in response to a decrease in perfusion pressure in the fed state (i.e. with intraluminal food present) than in the starved condition.

The response of the intestinal vasculature to an increase in venous outflow pressure depends on the adequacy of perfusion [23, 68]. If perfusion is sufficient for metabolic needs, an increase in the venous pressure results in arteriolar vasoconstriction (myogenic control). If perfusion is poor and venous pressure increases, the vascular resistance decreases and the capillary density increases (metabolic control).

The gut blood flow has a distinct response to feeding [23]. Digestion results in pronounced postprandial hyperaemia (fig. 2). Several mechanisms are probably involved: a local reflex to the presence of luminal contents, the release of vasoactive gastrointestinal hormones (e.g. gastrin, secretin, cholecystokinin) and the increase in gut metabolism (metabolic control) [23, 34].

The extrinsic neural control of gut blood flow is limited primarily to the sympathetic nervous system.

Sympathetic nervous activity reduces gut blood flow by increasing the vascular resistance of the arteries and arterioles; the veins have more limited sympathetic innervation. During persisting stimulation, the blood flow starts to recover after initial reduction ("autoregulatory escape") [23, 65]. After the stimulation, blood flow increases transiently to a higher level than before the stimulation [23].

Catecholamines are the most important circulating endogenous vasoactive substances that influence the gut blood flow. Alpha-adrenoceptor stimulation results in vasoconstriction and beta-adrenoceptor stimulation in vasodilatation. Accordingly, noradrenaline with predominantly alpha-adrenoceptor activity can be expected to increase the intestinal vascular resistance, whereas the effects of adrenaline are dose-dependent: vasodilatation at low doses and vasoconstriction at increasing doses when alpha-stimulation predominates. The net effects of circulating catecholamines on gut blood flow depend on the concomitant effects on cardiac output [3, 23]. Vasopressin and angiotensin are both potent intestinal vasoconstrictors. Their physiological role in the control of gut blood flow is not certain. They may both be involved in the intestinal vasoconstriction in acute hypovolaemia, and also modulate the response to sympathetic nerve stimulation and noradrenaline [16, 23].

Hepatic blood flow

There are three principal determinants of hepatic blood flow. The vascular resistance across the intestine determines the mesenteric influx and thereby the portal venous flow. The hepatic arterial resistance determines the hepatic arterial flow. The intrahepatic portal venous resistance is less important, since the portal venous flow is mainly determined by the outflow from the intestine, that is the resistance across the intestine. Finally, the hydrodynamic interaction between the hepatic arterial and portal venous flow, as described before, tends to compensate for any change in one of the inflows to the liver by a reciprocal change in the other [6, 57]. The hydrodynamic interaction, also called the hepatic arterial buffer response, is regulated by adenosine [39].

Autoregulation has little importance in the regulation of hepatic arterial pressure-volume relationship; the relationship between the arterial pressure and the flow is approximately linear. The hepatic portal venous bed clearly lacks autoregulation and has a linear pressure–flow relationship [6, 57].

Sympathetic nervous activity is the principal neural mechanism that influences hepatic blood flow. Sympathetic nerve stimulation evokes an increase in the hepatic arterial and portal resistance. The arterial vasoconstriction is transient and has similar autoregulatory escape as the intestinal vasoconstriction. In contrast, the portal response has a slower onset, but the increase in resistance is sustained, once established [26, 57]. In addition to the changes in vascular resistances, sympathetic nerve stimulation also reduces the hepatic volume, probably via contraction of the hepatic capacitance vessels. The volume reduction has a slow onset, persists throughout the stimulation and recovers more slowly than it develops [7, 57].

Role of nitric oxide in splanchnic blood flow regulation

Recent experimental studies have demonstrated that nitric oxide is important in the maintenance of basal vasodilatation in the mesenteric vasculature and the hepatic artery [2, 44]. In an anaesthetized pig model, inhibition of nitric oxide synthesis (non-selective inhibition of both constitutive and inducible nitric oxide synthase) increased hepatic arterial resistance but had no effect on the portal vascular resistance, while the hepatic arterial autoregulation was enhanced. The hydrodynamic interaction between the hepatic arterial and portal vein blood flow (hepatic arterial buffer response) was present after nitric oxide inhibition. After administration of endotoxin, both the hepatic arterial buffer response and autoregulation were abolished, independent of nitric oxide. Inhibition of nitric oxide synthesis after endotoxin increased the resistance of both hepatic artery and portal vein [2]. This suggests that during experimental endotoxin shock, nitric oxide is important in preserving the blood flow across the splanchnic bed. While these observations cannot be directly extrapolated to human septic shock, they do suggest that non-selective nitric oxide inhibition in septic shock may improve blood pressure at the expense of splanchnic perfusion.

Splanchnic blood flow in patients at risk of multiple organ failure

Only very few studies with quantitative measurements of splanchnic blood flow in intensive care patients have been published [1, 10, 11, 22, 28, 29, 52–54, 62, 63, 69, 71–73, 76]. The results have clearly demonstrated that data obtained from experimental studies or more stable patients should be extrapolated to the intensive care patient with great caution. The determinants, clinical relevance and the time course of splanchnic blood flow abnormalities in patients at risk of multiple organ failure have not been well established.

All quantitative splanchnic blood flow studies in intensive care patients at risk of multiple organ failure deal with the total hepatosplanchnic blood flow as measured by the Fick principle [1, 10, 11, 22, 28, 29, 52–54, 62, 63, 69, 71–73, 76]. Gastrointestinal tonometry cannot be used as a surrogate measure of hepatosplanchnic blood flow, since there is no consistent relationship between splanchnic blood flow and measurements obtained by gastric tonometry [53, 54, 72, 73]. Hence, pH_i will be only discussed briefly in the context of response to therapy aimed at improving splanchnic perfusion.

The pathophysiology of splanchnic blood flow and inadequate splanchnic tissue perfusion in intensive care patients is multifactorial. Two substantially different patterns of changes in splanchnic blood flow and metabolic demand are common in intensive care patients: one observed in low flow states [38, 53,
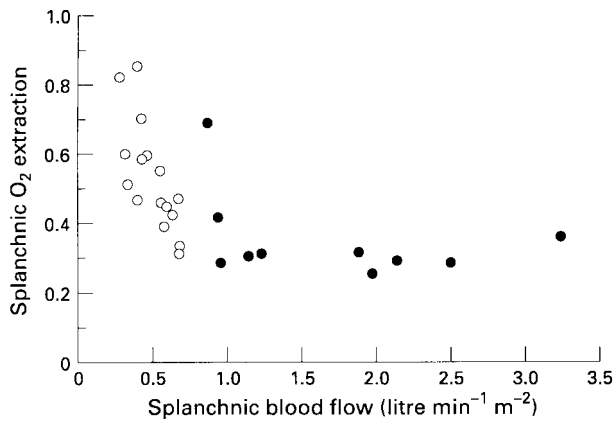
Figure 3 Splanchnic blood flow and oxygen extraction after cardiac surgery and in patients with septic shock and vasopressor therapy [data adapted from refs 62 and 63]. (O) After cardiac surgery; (●) septic shock + vasopressors.

54, 63, 64, 72, 73] and another in severe inflammatory conditions, infections and septic shock [1, 10, 11, 22, 28, 29, 62, 69, 76].

SPLANCHNIC BLOOD FLOW IN LOW FLOW STATES

In low flow states (e.g. cardiogenic shock) and hypovolaemia (without major injury or sepsis), splanchnic blood flow decreases without major changes in splanchnic metabolic demand [53, 54, 63, 72, 73]. In these conditions, perfusion of the heart and the central nervous system is maintained at the expense of the peripheral tissues and the splanchnic region. Once splanchnic vasoconstriction develops in response to hypovolaemia, the recovery of the blood flow will be prolonged: the increased splanchnic vascular resistance and reduced blood flow persists after the circulating blood volume has been restored and systemic haemodynamics have been stabilized [16]. This may increase the risk of inadequate splanchnic perfusion both after resuscitation of hypovolaemia and in intensive care patients susceptible to acute blood volume changes (e.g. as a result of capillary leak) [70].

In low flow states, vasoregulation is usually well preserved and an increased oxyg enextraction compensates for the reduction of blood flow (fig. 3). Fully developed physiological compensation may preserve adequate splanchnic tissue oxygenation even during markedly reduced hepatosplanchnic blood flow. The limits of compensation and the time of tolerance for splanchnic hypoperfusion have not been well defined. Perioperative hepatic vein oxygen saturation below 30 % during liver resection was associated with postoperative liver dysfunction [37], whereas brief exposure to lower hepatic venous saturation (or increased splanchnic oxygen extraction) have been reported during and after cardiac surgery without any major consequences [38, 53, 63, 64]. The splanchnic blood is defended at the expense of peripheral blood flow in low cardiac output syndrome after cardiac surgery [53, 63].

Nevertheless, prolonged hypovolaemia or low cardiac output will inevitably lead to splanchnic tissue hypoxia and increase the risk of multiple organ
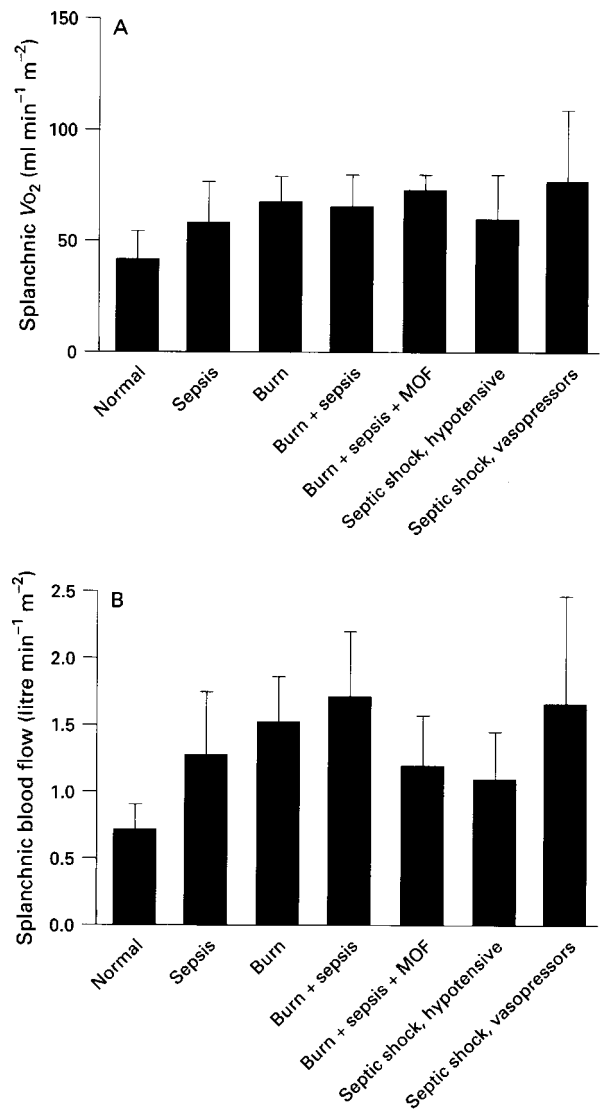

Figure 4 Increased splanchnic oxygen demand and blood flow in sepsis. A: Splanchnic hypermetabolism tends to increase with increasing severity of sepsis [data adapted from refs 11, 62 and 76]. B: Splanchnic blood flow and the severity of sepsis [data adapted from refs 11, 62 and 76].

failure. It is reasonable to assume that a slowly developing low splanchnic blood flow is better tolerated than an acute reduction.

SPLANCHNIC BLOOD FLOW IN INFLAMMATION AND INFECTION

In severe inflammation (e.g. systemic inflammatory response syndrome or SIRS, septic infections, septic shock), the metabolic demand for oxygen in the splanchnic region is increased [1, 10, 11, 22, 28, 29, 62, 69, 76]. In patients with normal or hyperdynamic haemodynamics, the total splanchnic blood flow is also higher than normal, but the increase in oxygen consumption is disproportionate to the increase in blood flow, and necessitates high oxygen extraction (figs 3 and 4). This appears to be the case regardless of whether stable haemodynamics have been obtained by fluids alone or with the aid of vasoactive
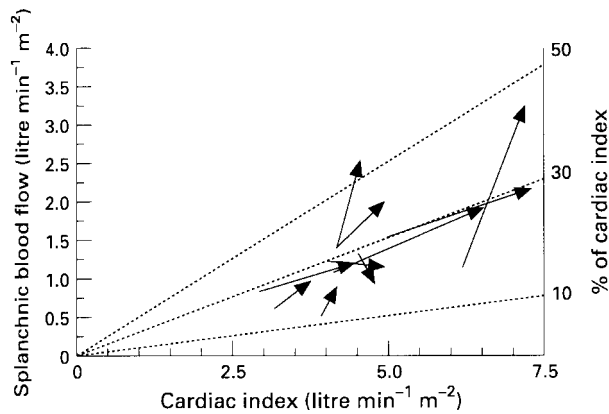
Figure 5 Changes in splanchnic blood flow in septic shock in response to treatment of hypotension with vasopressors [data adapted from ref. 62]. Wide interindividual variability is characteristic of the response.

Figure 6 Changes in splanchnic blood flow in response to dobutamine after cardiac surgery [data adapted from ref. 53]. Splanchnic blood flow changes parallel the changes in cardiac output.

drugs [1, 10, 11, 22, 28, 29, 62, 69, 76]. In hyperdynamic septic shock during hypotension, splanchnic blood flow and splanchnic oxygen consumption are higher than normal and the splanchnic oxygen extraction is high [62]. Correction of hypotension by vasopressor drugs tends to increase the splanchnic blood flow further in hyperdynamic septic shock, although individual responses may vary (fig. 5) [62].

Endothelial injury is common in sepsis and contributes to abnormal vascular tone, blood flow maldistribution and development of hypovolaemia [8, 14, 46]. In addition, severe sepsis is almost invariably accompanied by acute respiratory failure, which limits the systemic oxygen delivery. Myocardial depression is also common in sepsis and many limit the response of systemic blood flow to the increased oxygen demand [51]. Under these circumstances, the splanchnic hypermetabolism increases the risk of splanchnic oxygen delivery/demand mismatch, and even subtle changes in blood volume, cardiac output, arterial oxygenation or oxygen demand in other tissues may lead to an imbalance between splanchnic oxygen delivery and demand.

THERAPEUTIC INTERVENTIONS AND SPLANCHNIC BLOOD FLOW

Volume resuscitation

The blood volume can be expected to have a major impact on splanchnic blood flow [13, 16, 55]. Indeed, reduction of splanchnic blood flow has been demonstrated in normal subjects after controlled small-volume haemorrhage [12, 56], and after simulated hypovolaemia following the application of lower body negative pressure [16]. Restoration of blood volume after simulated hypovolaemia was associated with a protracted reduction of splanchnic blood flow. Effects of blood volume on splanchnic blood flow in intensive care patients have not been published. Indirect data from studies using volume resuscitation to improve gastric pH_i suggests that restoration of blood volume is of primary importance in assuring adequate splanchnic perfusion in intensive care patients [32, 47–49].
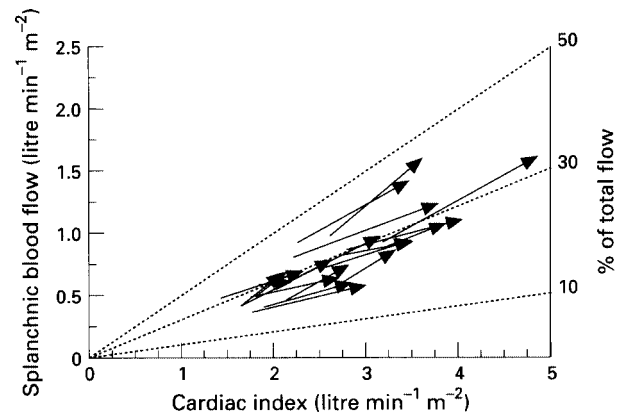
Adrenergic agents

Vasoactive drugs, especially sympathomimetic amines are used frequently to support tissue perfusion in circulatory failure. The effects of sympathomimetic drugs on splanchnic blood flow in intensive care patients can not be predicted from their pharmacological characteristics alone or extrapolated from experimental models. Traditionally, the potential effects of adrenergic agents on regional perfusion have been interpreted in terms of their relative adrenergic receptor activity. In critically ill patients, the effects may be modified, for example as the result of receptor downregulation. In experimental studies, alpha-adrenergic stimulation by dopamine, noradrenaline and adrenaline increase renal and visceral vascular resistance and reduce renal and visceral blood flow [61]. The effects of dobutamine depend on the balance between its alpha-mediated vasoconstriction and beta-mediated vasodilation [74]. Dopexamine with $beta_2$- and dopaminergic properties and without alpha-stimulation may have beneficial effects on splanchnic blood flow [41].

In 10 patients with septic shock, correction of hypotension by administration of vasopressor doses of dopamine increased splanchnic blood flow, whereas the effects of noradrenaline were more variable [62]. On the other hand, dopamine worsened gastric mucosal acidosis in septic shock, while noradrenaline resulted increased gastric mucosal pH despite identical effects on systemic haemodynamics [43].

In patients with chronic congestive heart failure, dopexamine increased the splanchnic blood flow whereas neither dopamine nor dobutamine had an effect [40]. In contrast, both dobutamine and dopexamine consistently increased splanchnic blood flow immediately after cardiac surgery (figs 6 and 7) [53, 63, 72]. Despite the major increases in total splanchnic blood flow, both dobutamine and dopexamine lowered the gastric pH_i or failed to correct the gastric mucosal acidosis [53, 72]. These effects were even more prominent in patients with low cardiac output [53]. On the other hand, dobutamine corrected gastric mucosal acidosis in patients with
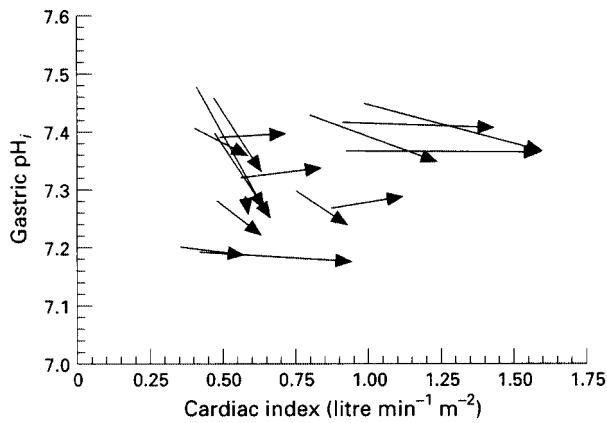
Figure 7 Changes in splanchnic blood flow and gastric pH$_i$ in response to dobutamine after cardiac surgery [data adapted from ref. 53]. Gastric mucosal acidosis worsens especially in patients with low cardiac output despite the increased splanchnic blood flow.

sepsis [31]. Evidently, the underlying disease can modify the splanchnic blood flow responses to vasoactive drugs.

The cause for the decrease in gastric pH$_i$ despite increased blood flow is not clear. The effects of a vasoactive drug may not be uniform throughout the splanchnic region: vasopressor therapy with dopamine or noradrenaline in experimental endotoxin shock increases regional vascular resistance of the colon, while the perfusion in the other parts of splanchnic region is well maintained [4]. The effects of vasoactive drugs on microcirculation may differ despite similar effects on blood flow distribution in major vessels [21]. Observations in experimental peritonitis support this concept: treatment with dobutamine produced more hepatocellular damage compared with dopexamine [75]. The catecholamines may also markedly modify the activity of various metabolic pathways in the liver [3] and simultaneously alter the splanchnic blood flow and its distribution. Accordingly, catecholamines may induce regional perfusion abnormalities and alter the balance between regional oxygen delivery and tissue metabolic demands.

Non-adrenergic vasodilators

The effects of vasodilators on splanchnic blood flow are controversial. Experimental studies suggest that vasodilators (adenosine and isoprenaline) may induce a vascular steal phenomenon within the intestinal circulation by redistributing the blood flow despite an overall increase [66].

In patients with chronic congestive heart failure, nitrates and sodium nitroprusside had no effect on the hepatosplanchnic blood flow despite increased cardiac output, indicating blood flow redistribution [40]. In contrast, sodium nitroprusside increased hepatosplanchnic blood flow in parallel with cardiac output in postoperative cardiac surgery patients [54]. Despite the increase in splanchnic blood flow, gastric pH$_i$ decreased slightly.

Angiotensin converting enzyme inhibitors either had no effect or slightly reduced the hepato-

splanchnic flow in cardiac failure [40]. After cardiac surgery, enalapril had no effect on either cardiac output or hepatosplanchnic blood flow, but reduced the gastric pH$_i$ [52].

The effect of vasodilators on hepatosplanchnic blood flow or gastric pH$_i$ have not been studied in septic patients. Nevertheless, the available data suggest that also the effects of vasodilators are modified markedly by the underlying clinical condition. It seems likely that redistribution of blood flow may occur at the level of both macro- and microcirculation.

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