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LABORATORY INVESTIGATION

Continuous measurements of microcirculatory blood flow in gastrointestinal organs during acute haemorrhage

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Hypoperfusion of splanchnic organs is an important contributor to the development of multiple organ failure after major surgery and trauma. During general anaesthesia and surgery we compared changes in systemic haemodynamics and regional blood flow with changes in the distribution of microcirculatory flow (MBF) in multiple splanchnic organs in pigs exposed to acute haemorrhage. Seven pigs (25 kg) were bled to a mean arterial pressure of 40 mm Hg; 180 min later the shed blood was retransfused. MBF was measured in the intestinal mucosa (stomach, jejunum, colon), pancreas, liver and kidney using a six-channel laser Doppler flowmeter. Cardiac output was measured by thermodilution and superior mesenteric artery flow by ultrasonic flowmetry. During haemorrhage, MBF in the gastric and colon mucosa and flow in the liver and kidney decreased to a similar extent to regional and systemic flows (30–50%). In contrast, MBF in the jejunal mucosa remained virtually unchanged and flow in the pancreas decreased significantly more than systemic and regional flows (60%, $P<0.05$). We conclude that: (1) changes in the distribution of MBF in the gastrointestinal tract during acute haemorrhage are heterogeneous and cannot be predicted from changes in systemic or regional haemodynamics; (2) MBF in the jejunal mucosa did not decrease during haemorrhage, indicating that autoregulation of blood flow in the mucosa remained intact during shock; and (3) MBF in the pancreas decreased significantly more than systemic and regional flows during shock, suggesting that the pancreas is particularly vulnerable to haemorrhage.

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Multiple organ failure syndrome remains a major cause of morbidity and mortality in critically ill patients.[1 2] It is believed that hypoperfusion of splanchnic organs,[3–5] resulting from trauma, haemorrhage or disease, is an important contributor to the development of multiple organ failure (MOF) and death.[6 7] Although blood flow in the gastrointestinal tract has received increased attention from scientists in recent years, the difficult access to the gut in humans has hampered clinically relevant studies.[8] Therefore, most controlled studies have been performed in animal models. However, very few have studied the distribution of flow within different regions and different organs of the gastrointestinal tract during acute haemorrhage.[9] Furthermore, many of the studies on blood flow in the gastrointestinal tract in shock have been performed in rodents,[10] which are known to differ from larger animals (such as pigs) and humans in the microvascular architecture in the intestinal wall.[11]

During acute haemorrhage, the splanchnic circulation is greatly affected by local and systemic regulatory mechanisms, which may cause immediate and sustained hypoperfusion of the gastrointestinal tract.[12] Although measurements of superior mesenteric artery blood flow or analysis of lactate in portal blood may give some information about splanchnic perfusion, very little is known about dynamic changes within different organs of the gastrointestinal tract during haemorrhage. With the recent availability of multichannel laser Doppler flowmetry (LDF) systems, continuous and simultaneous measurements of microcirculatory blood flow (MBF) from several organs has become possible.[13]

The objectives of the present study were to measure

changes in dynamic distribution of MBF in multiple gastrointestinal organs (gastric, jejunal and colon mucosa, pancreas, liver) and the kidney and to compare it with systemic haemodynamics and regional blood flow during acute haemorrhage in anaesthetized pigs.

Materials and methods

This study was performed according to NIH guidelines for the use of experimental animals and the protocol was approved by the Animal Ethics Committee of Canton Berne. Twelve pigs (24–30 kg) were given ketamine 10 mg kg^{-1} i.m. followed 10 min later by metomidate 5 mg kg^{-1} and azaperone 2 mg kg^{-1} i.v. for tracheal intubation. Anaesthesia was maintained with 0.5–0.6% halothane (end-tidal concentrations) in nitrous oxide–oxygen (ratio 2:1) together with an i.v. infusion of fentanyl 15 μg kg^{-1} h^{-1} and pancuronium 0.3 mg kg^{-1} h^{-1}. Inhaled and exhaled concentrations of nitrous oxide and halothane were monitored continuously with a multi-gas analyser (Hellige SMU 611; Hellige, Freiburg, Germany). The animals were ventilated with a volume-controlled ventilator with a positive end-expiratory pressure (PEEP = 4–5 cm H_2O) (Tiberius 19; Drägerwerk, Lübeck, Germany). Tidal volume was kept at 10 ml kg^{-1} and the respiratory rate adjusted (13–18 min^{-1}) to maintain Pa_{CO_2} between 4.5 and 5.5 kPa.

During surgery the animals received Ringer's lactate 15–20 ml kg^{-1} h^{-1}, which kept central venous and pulmonary capillary wedge pressures constant. After surgery the rate of infusion of Ringer's lactate was reduced to 7 ml kg^{-1} h^{-1}. The animals' body temperature was kept at 38.2±0.25°C using two heating blankets.

A gastric tube (Tonometrics Inc., Worcester, MA, USA) was inserted orally into the stomach, and the balloon was prepared according to the manufacturer's recommendations to completely evacuate excess air and filled with 2.5 ml of 0.9% NaCl. Correct position of the tonometry tube was verified after laparotomy. Abdominal aortic and pulmonary artery (Arrow, Reading, PA, USA) catheters were inserted via the femoral artery and veins and a large-bore central venous catheter was inserted via the internal jugular vein.

After midline laparotomy, the spleen was removed to prevent autotransfusion as splenic contraction can contribute up to 25% of the red cell volume in pigs,[14] and a urinary bladder catheter was inserted. Small antimesenteric incisions were made on stomach, small intestine and colon, to allow small-angled LDF probes (Oxford Optronix, Oxford, UK) to be sutured on to the mucosal surface. Six microsutures per probe were used to prevent motion artefacts from respiration and bowel movement. The incisions on the intestinal wall were closed with sutures. Additional probes were sutured on the surface of the left kidney and the pancreas. One probe was attached to the surface of the left liver lobe using six special blunt needles.

The signals from the LDF device were observed continuously on a computer monitor during probe installation; the position of the probes could be corrected immediately if there was inadequate signal or if motion artefacts occurred. Once the experiment was started, manipulation was avoided to minimize the possibility of probe displacement.

An ultrasonic transit time flow-probe (Transonic Systems Inc., Ithaca, NY, USA) of appropriate size (1.5–3 mm) was placed around the superior mesenteric artery. A catheter for blood sampling was inserted in the mesenteric vein. The abdomen was then flushed with warm saline (38°C) and the laparotomy was closed with sutures and clamps before the experiment was started.

Experimental protocol

After completion of surgery the animals were allowed to stabilize for 30–60 min before baseline measurements were performed. The conditions were considered stable when all measurement values remained within 10% for 30 min. Five animals served as controls. Controls were treated as the test animals, except that they were not subject to haemorrhage/resuscitation. Seven animals underwent haemorrhagic shock and subsequent retransfusion of shed blood. Following the baseline measurements, blood was withdrawn from the central venous catheter into a heparinized bag until the mean arterial pressure reached 40 mm Hg. After 180 min of hypovolaemic shock, the shed blood was retransfused over 30 min and the animals were observed for another 90 min.

Gas measurements (end-tidal carbon dioxide, end-tidal halothane and inspired oxygen concentrations), systemic haemodynamics (heart rate, mean arterial blood pressure, central venous pressure, pulmonary artery pressure, pulmonary artery wedge pressure), superior mesenteric artery flow, MBF in the liver, pancreas, kidney and mucosa of the stomach, jejunum and colon were measured continuously throughout the experiment. Cardiac index measurements and blood samples were taken at 30, 60, 120 and 180 min after haemorrhage and at 210, 240, 170 and 300 min (30, 60, 90 and 120 min after retransfusion, respectively). At the end of the experiment the animals were killed with an overdose of i.v. potassium.

Haemodynamic monitoring

Mean arterial blood pressure (MAP), central venous pressure (CVP), mean pulmonary artery pressure (PAP) and pulmonary capillary wedge pressures (PCWP) were recorded with quartz pressure transducers (129A; Hewlett-Packard, Andover, MA, USA) and displayed continuously on a multimodular monitor (Hellige SMU 611) and recorder (Hellige SMR 821). ECG was monitored continuously, and heart rate was estimated from the ECG. Cardiac index was measured by a thermodilution technique (mean of three measurements, Hellige SMU 611 cardiac output module). Central venous blood temperature was recorded from a thermistor in the pulmonary artery catheter. Blood samples for haemoglobin and haematocrit analysis were withdrawn from the aortic artery catheter.

Table 1 Systemic haemodynamics in animals exposed to haemorrhagic shock. MAP, mean arterial blood pressure; CVP, central venous pressure; PAP, pulmonary artery pressure; PWP, pulmonary artery wedge pressure; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance. *$P<0.05$ compared with baseline

	Baseline mean (SEM)	Change as per cent of baseline, mean (SEM)						
		Time after haemorrhage				Time after retransfusion		
		30 min	60 min	120 min	180 min	30 min	60 min	120 min
Cardiac index	204 (18) ml kg^{-1} min^{-1}	53 (6)*	55 (5)*	54 (5)*	55 (5)*	84 (8)	95 (8)	97 (8)
Heart rate	90.6 (4.8) beats min^{-1}	125 (14)	156 (12)*	167 (8)*	187 (9)*	134 (5)*	139 (10)*	145 (9)*
MAP	95.4 (5.2) mm Hg	43 (3)*	43 (3)*	43 (3)*	42 (3)*	75 (8)	74 (7)*	72 (7)*
CVP	7.71 (0.92) mm Hg	44 (6)*	47 (12)*	49 (11)*	54 (9)*	124 (21)	101 (15)	89 (21)
PAP	21.3 (1.3) mm Hg	68 (4)*	74 (6)*	80 (9)	86 (7)	135 (7)*	111 (7)	110 (4)
PWP	7.71 (0.84) mm Hg	39 (5)*	47 (8)*	48 (9)*	46 (8)*	118 (13)	94 (11)	91 (10)
SVR	1644 (169) dyn s^{-1} cm^{-5}	85 (5)	81 (6)*	82 (7)*	77 (7)*	86 (9)	77 (7)	74 (6)*
PVR	253 (28) dyn s^{-1} cm^{-5}	173 (19)*	176 (19)*	192 (28)*	209 (27)*	181 (20)*	132 (9)*	129 (8)

Respiratory monitoring

Expired minute volume ventilation, tidal volume, respiratory rate, PEEP, peak and end inspiratory pressures, inspired and end-tidal carbon dioxide concentration ($ETCO_2$), and inspired and expired oxygen concentrations were monitored continuously throughout the study. Respiratory compliance (chest wall and lung; C_T) was calculated as expiratory tidal volume (TV) divided by end-inspiratory airway pressure minus PEEP (P_{aw}). Both values were recorded simultaneously from the ventilator. Blood samples for arterial blood gas analysis were withdrawn from the aortic artery catheter and analysed immediately (temperature corrected) in a blood gas analyser (ABL 620; Radiometer, Copenhagen, Denmark).

Gastric tonometry

The tonometer balloon was filled with 2.5 ml of 0.9% NaCl. After 30 min of equilibration, 1 ml of NaCl (dead space) was discarded and PCO_2 was measured in the remaining 1.5 ml in a blood gas analyser (ABL 620, Radiometer) and corrected with a time-dependent correction factor provided by the manufacturer. Intramucosal pH was calculated from arterial bicarbonate and corrected PCO_2 using the Henderson–Hasselbach equation.

Oxygen delivery and oxygen consumption

Global and splanchnic oxygen delivery and consumption were calculated from blood flow and from arterial, mixed venous and mesenteric venous blood gases using standard formulae.

Ultrasonic transit time flowmetry

Blood flow in the mesenteric artery was continuously measured throughout the experiment with ultrasonic transit time flowmetry (TTF) using an HT 206 flowmeter (Transonic Systems Inc.).

Laser Doppler flowmetry

MBF was measured continuously with a six-channel laser Doppler flowmeter system (Oxford Array, Oxford Optronix). The suturable miniature surface probes used (SP 300, Oxford Optronix) were designed to measure MBF to a depth of 0.7 mm into the tissue. The multichannel laser Doppler unit and probes were calibrated by the manufacturer using a motility standard (suspension of latex particles) and an appropriate calibration key for a specific set of laser Doppler probes was attached to the unit. The LDF signals and the TTF signal were exported via analogue outputs and acquired on-line via a multichannel interface (Mac Paq MP 100; Biopac Systems Inc., Goleta, CA, USA) with acquisition/analysis software (Acqknowledge 3.0; Biopac Systems Inc.) to a portable computer.

A detailed description of the theory of LDF operation and practical details of LDF measurements have been described before.[15 16] Briefly, low energy laser light from a solid-state diode laser operating at 780 ± 10 nm is guided to the measurement site via an optical fibre. Two identical adjacent fibres receive back-scattered light from the tissue which is then transmitted to independent photodetectors. This back-scattered portion consists of light scattered from the static tissue matrix which has not been Doppler shifted and a spectrally broadened component resulting from interactions with moving blood cells. Optical mixing of these components at the photodetector surface produces an electrical signal containing all the Doppler frequency shift information. Further processing within the frequency range of 20–12 kHz produces an output voltage which varies linearly with the product of mean blood cell velocity and concentration. The product of mean blood cell velocity and concentration is correctly referred to as the blood cell flux, but since flow rate may also be defined as volume flux then, as long as the number of red cells within a volume of blood remains constant, the blood cell flux will be proportional to the volume flux or flow of blood.

Laser Doppler devices are not calibrated to measure absolute blood flow, as different tissues have different optical properties. Instead, they indicate MBF in arbitrary perfusion units. Baseline values are very variable, so results are usually expressed as changes relative to baseline.[16 17] The quality of the LDF signal was controlled on-line by visualization on a computer screen, so that motion artefacts and noise due to inadequate probe attachment could be

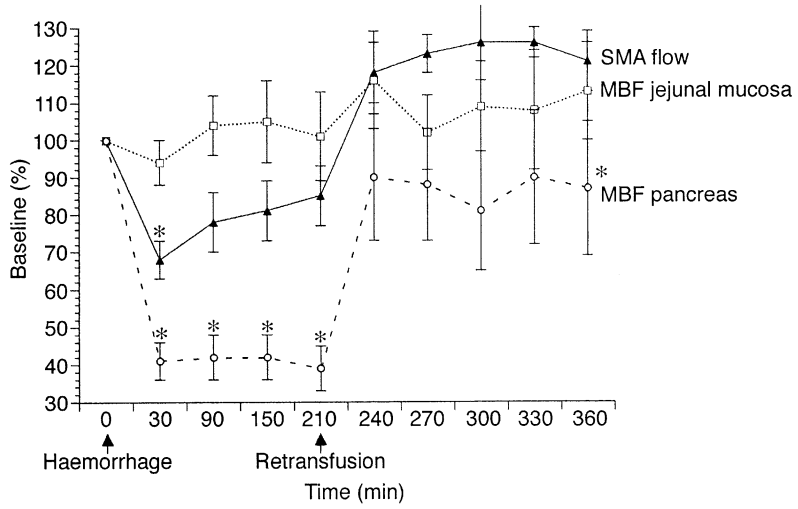

Fig 1 Changes (mean (SEM)) in the superior mesenteric artery flow (SMA flow) and in microcirculatory blood flow (MBF) in the jejunal mucosa and in the pancreas after haemorrhage and after retransfusion of shed blood. Baseline values were: SMA flow, 47 (12) ml min^{-1}; MBF of jejunal mucosa, 259 (9) perfusion units (PU); MBF of pancreas, 753 (257) PU. The SMA flow decreased after blood loss to a similar extent to cardiac index and recovered after retransfusion. MBF in the pancreas decreased more after haemorrhage and failed to recover fully after retransfusion. In contrast, MBF in the jejunal mucosa was not affected by blood loss or by retransfusion. *$P<0.05$ compared with baseline.

immediately detected and corrected before the measurements started.

Statistical analysis and data presentation

Data are presented as mean (SEM). Nonparametric Wilcoxon rank sum test was used to describe changes relative to baseline. For correlation of measurements nonparametric Spearman correlation was used. $P<0.05$ was considered statistically significant. A computer program for statistical analysis (InStat 2.03 for Macintosh; GraphPad Software, San Diego, CA, USA) was used for all calculations.

Results

Systemic and regional haemodynamics

The main results are presented in Table 1. After haemorrhage, filling pressures (PCWP and CVP), MAP, cardiac index and SVR decreased, while PVR increased ($P<0.05$). Retransfusion of shed blood restored filling pressures and cardiac index. MAP also increased but it remained 28% below baseline ($P<0.05$). SVR also remained low (26% below baseline) but PVR decreased after retransfusion. At the end of haemorrhage, SMA flow was 32% below baseline ($P<0.05$), but after 3 h of shock it was 15% below baseline. After retransfusion of the shed blood, SMA flow increased to 21% above baseline (Fig. 1, $P<0.05$). The changes in SMA flow correlated well with changes in cardiac index ($r=0.91$, $P<0.05$)

MBF in the intestinal mucosa

After haemorrhage the MBF in the gastric and colon mucosa decreased by 28% ($P<0.05$) and 23% respectively. After retransfusion of shed blood, MBF increased to 16% above baseline in the gastric mucosa and returned to baseline in the colon mucosa (Table 2). MBF in the jejunal mucosa was virtually unaffected by haemorrhage and retransfusion (Fig. 1)

MBF in the pancreas, liver and kidney

After haemorrhage, MBF in the liver decreased by 36% ($P<0.05$) and in the kidney by 40% ($P<0.05$). After retransfusion of shed blood, MBF in the liver returned to baseline in both organs (Table 2). MBF in the pancreas decreased by 61% during haemorrhage and remained 13% below baseline after retransfusion (Fig. 1).

Gastric tonometry

Gastric intramucosal pH (pH_i) was 7.27 (0.02) at baseline and decreased to 7.15 (0.03) after 180 min of haemorrhagic shock ($P<0.05$). After retransfusion of shed blood, pH_i increased slightly but did not reach baseline values (7.20 (0.03); $P<0.05$). The difference between arterial P_{CO_2} and the P_{CO_2} measured by gastric tonometry was 1.73 (0.39) kPa at baseline and increased to 2.63 (0.54) kPa ($P<0.05$) after haemorrhage. After retransfusion it was 1.72 (0.56) kPa (Table 3).

Oxygen transport and oxygen consumption

Systemic oxygen delivery decreased by 60% and splanchnic oxygen delivery by 40% after haemorrhage. Systemic oxygen extraction increased from 31% to 75% and splanchnic oxygen extraction from 36% to 65%. After retransfusion these parameters returned to baseline values except for global oxygen extraction which decreased, but remained 30% above baseline. Oxygen consumption remained unchanged throughout the experiment both globally and in the splanchnic region (Table 4).

Table 2 Microcirculatory blood flow (MBF) measured with laser Doppler flowmetry in animals exposed to haemorrhagic shock. Baseline data are presented as mean (SEM) perfusion units (PU). Changes after haemorrhage and retransfusion are expressed as mean (SEM) per cent of the baseline. *$P<0.05$ compared with baseline

	Baseline MBF (PU) mean (SEM)	Change in MBF, mean (SEM) per cent of baseline						
		Time after haemorrhage				Time after retransfusion		
		30 min	60 min	120 min	180 min	30 min	60 min	120 min
Gastric mucosa	224 (22)	65 (10)*	79 (12)	73 (10)*	72 (11)*	107 (18)	121 (19)	116 (21)
Colon mucosa	243 (22)	84 (9)	83 (11)	82 (10)	77 (11)	123 (17)	103 (12)	105 (8)
Liver	924 (268)	71 (8)*	70 (11)	67 (12)	64 (14)	85 (11)	106 (6)	101 (7)
Kidney	640 (115)	72 (9)*	60 (9)*	62 (11)*	60 (11)*	84 (13)	95 (22)	107 (21)

Table 3 Arterial blood gases and gastric tonometry data. Hb=haemoglobin; Sa_{O_2}, arterial oxygen saturation; Pa_{O_2}, arterial oxgen partial pressure; Pa_{CO_2}, arterial carbon dioxide partial pressure; pH_a, arterial pH; BE, arterial base excess; pH_i, gastric intramucosal pH; Pi_{CO_2} gastric intramucosal carbon dioxide partial pressure measured by gastric tonometry. All values are presented as mean (SEM). *$P<0.05$ compared with baseline

	Baseline	Time after haemorrhage				Time after retransfusion		
		30 min	60 min	120 min	180 min	30 min	60 min	120 min
Haemoglobin (g litre^{-1})	97 (5)	83 (5)*	74 (6)*	74 (5)*	70 (5)*	90 (5)*	90 (3)	87 (3)
Sa_{O_2} (%)	94.6 (0.1)	94.8 (0.1)*	94.8 (0.2)	94.9 (0.1)*	94.9 (0.1)*	94.5 (0.2)	94.3 (0.3)	94.4 (0.3)
Pa_{O_2} (kPa)	18.0 (0.6)	17.0 (0.8)	18.4 (1.2)	17.4 (0.9)	18.2 (1.4)	17.2 (0.9)	16.1 (1.0)	15.8 (1.1)
Pa_{CO_2} (kPa)	5.0 (0.1)	5.0 (0.2)	5.6 (0.3)	5.2 (0.2)	5.2 (0.1)	5.2 (0.1)	5.1 (0.1)	5.1 (0.2)
pH_a	7.45 (0.01)	7.43 (0.02)	7.39 (0.04)	7.39 (0.02)	7.38 (0.02)*	7.39 (0.03)	7.41 (0.01)	7.42 (0.02)
BE (mmol litre^{-1})	1.7 (0.9)	0.8 (0.5)	–0.6 (1.3)	–1.4 (1.4)*	–1.8 (1.5)*	–1.4 (1.5)*	–0.2 (1.2)	–0.1 (1.0)*
pH_i	7.23 (0.02)	7.20 (0.03)*	7.16 (0.03)*	7.17 (0.02)*	7.15 (0.03)*	7.17 (0.02)	7.20 (0.03)*	7.20 (0.03)*
Pi_{CO_2}–Pa_{CO_2} (kPa)	1.73 (0.39)	2.14 (0.50)	2.56 (0.59)*	2.47 (0.26)	2.63 (0.54)*	1.75 (0.72)	1.68 (0.52)	1.72 (0.56)

Table 4 Oxygen delivery and consumption in animals exposed to haemorrhagic shock. After haemorrhage, systemic oxygen delivery (Do_2 systemic) decreased in parallel with flow (cardiac index). Total body oxygen extraction (ER systemic) and splanchnic oxygen extraction (ER splanchnic) increased during shock, keeping systemic (Vo_2 systemic) and splanchnic (Vo_2 splanchnic) oxygen consumption unchanged. Baseline values are presented as mean (SEM). Changes after haemorrhage and retransfusion are expressed as mean (SEM) per cent of the baseline except for ER values which are presented as absolute values. *$P<0.05$ compared with baseline

	Baseline	Change in parameter as per cent of baseline						
		Time after haemorrhage				Time after retransfusion		
		30 min	60 min	120 min	180 min	30 min	60 min	120 min
Do_2								
systemic	26 (3) ml kg^{-1} min^{-1}	45 (5)*	42 (4)*	42 (4)*	41 (5)*	78 (8)	89 (10)	88 (8)
splanchnic	0.24 (0.05) ml kg^{-1} min^{-1}	58 (4)*	60 (5)*	62 (6)*	62 (7)*	110 (9)	118 (12)	109 (6)
Vo_2								
systemic	7.9 (0.5) ml kg^{-1} min^{-1}	88 (5)*	95 (5)*	92 (5)*	93 (5)*	97 (3)*	102 (5)	108 (5)
splanchnic	0.09 (0.02) ml kg^{-1} min^{-1}	99 (8)*	107 (10)*	115 (12)	119 (19)	94 (13)	86 (7)	95 (10)
ER								
systemic	31 (2) %	65 (1)*	73 (1)*	71 (1)*	73 (1)*	47 (3)	44 (4)	46 (5)
splanchnic	36 (3) %	65 (2)*	68 (3)*	69 (3)*	67 (4)*	40 (5)	35 (3)*	40 (5)

Control group

There were no significant changes in any of the parameters measured in the control group. Some of the main parameters are summarized in Table 5.

Discussion

It is generally recognized that sufficient splanchnic blood flow is vital for positive outcome of patients exposed to major surgery or trauma,[6 7] yet treatment of patients in circulatory shock is still frequently guided by systemic haemodynamic parameters alone. This is a result of the difficulty of access to the gastrointestinal tract. Direct measurements of regional or local splanchnic blood flow are invasive, time consuming and require special skills and instruments that are not readily available at the bedside. In order to evaluate the dynamic relationship between systemic, regional and local splanchnic blood flows during the development of haemorrhagic shock in anaesthetized subjects we, therefore, used an animal model. We chose the pig for this study because of its anatomical and physiological similarity to humans with respect to the cardiovascular system and the digestive tract.[18] The laser Doppler technique, which was used to monitor MBF in this study, has been validated for measuring flow in many organs including the intestinal mucosa,[19] the liver,[15] the pancreas[20] and the

Table 5 Systemic haemodynamics, regional and microcirculatory blood flow (MBF) in control animals, not exposed to haemorrhagic shock. MAP, mean arterial blood pressure; PU, perfusion units; SMA flow, superior mesenteric artery flow. Baseline data are presented as mean (SEM) ($n=5$). *$P<0.05$ compared with the baseline. [a]Except for haemoglobin concentration, which is presented in g litre^{-1}, mean (SEM).

	Baseline	Change, mean (SEM) per cent of baseline[a]						
		30 min	90 min	150 min	210 min	240 min	300 min	360 min
Haemoglobin	95 (4) g litre^{-1}	95 (4)	99 (4)	101 (4)	100 (4)	101 (3)	102 (4)	101 (2)
MAP	87 (6) mm Hg	100 (2)	99 (4)	97 (3)	97 (4)	96 (3)	100 (3)	97 (4)
Cardiac index	191 (21) ml kg^{-1} min^{-1}	92 (3)	87 (3)	90 (3)	95 (6)	94 (7)	93 (11)	93 (10)
SMA flow	40 (11) ml min^{-1}	103 (5)	109 (8)	118 (13)	136 (12)	128 (8)	124 (20)	128 (21)
MBF								
Gastric mucosa	229 (18) PU	98 (6)	94 (5)	103 (7)	101 (8)	104 (8)	115 (14)	107 (9)
Jejunal mucosa	256 (14) PU	101 (3)	102 (4)	107 (8)	114 (10)	120 (7)	109 (13)	117 (15)
Colon mucosa	365 (55) PU	96 (3)	87 (6)	90 (5)	91 (6)	91 (6)	92 (6)	98 (12)
Pancreas	841 (203) PU	100 (8)	94 (9)	90 (11)	95 (14)	96 (17)	105 (20)	95 (17)
Liver	859 (261) PU	95 (9)	93 (12)	99 (11)	109 (13)	106 (17)	117 (21)	102 (14)
Kidney	626 (48) PU	100 (10)	101 (11)	106 (13)	105 (8)	100 (7)	104 (9)	115 (15)

kidney.[21] The technique is based on detecting moving erythrocytes in the microvasculature, and is therefore sensitive to motion artefacts such as respiratory movements, gastrointestinal motility and shivering. By using small, lightweight, custom-made, flexible probes sutured (with microsutures) to the tissue under observation it was possible to prevent such artefacts.

In awake subjects the normal acute response to blood loss includes increased peripheral vascular resistance due in large part to vasoconstriction in splanchnic organs.[22] Indeed splanchnic hypoperfusion may persist for several hours after systemic haemodynamics have been restored.[12] General anaesthesia is known to influence central haemodynamics and regional blood flow and it depresses the normal sympathetic and humoral response to hypovolaemia.[23] In the anaesthetized animals used in our study, systemic vascular resistance fell after haemorrhage and mesenteric blood flow was better maintained than cardiac output. The slight increase of superior mesenteric artery flow during haemorrhagic shock might be explained by decreasing splanchnic vascular resistance over time.[24] Furthermore, after retransfusion of shed blood, mesenteric blood flow rose to above baseline while the recovery of cardiac output was less marked. Thus, the acute response to blood loss may differ between anaesthetized and conscious subjects.

The decrease in MBF in the gastric and colon mucosa (approximately 30%) was similar to the decrease observed in regional blood flow (Table 2). This reduction in gastric mucosal blood flow was accompanied by gastric mucosal acidosis manifested by an increased difference between arterial and mucosal P_{CO_2} ($Pi_{CO_2} - Pa_{CO_2}$; Table 3). After retransfusion of shed blood, gastric mucosal blood flow and the $Pi_{CO_2} - Pa_{CO_2}$ gap returned to baseline. There was a positive correlation between the change in MBF in the gastric mucosa and the $Pi_{CO_2} - Pa_{CO_2}$ gap ($r=0.36$, $P<0.01$). This finding suggests that the laser Doppler flowmeter did indeed measure changes in nutritive blood flow in the gastric mucosa during haemorrhagic shock.

In contrast to MBF in the mucosa of the stomach and colon, flow in the jejunal mucosa was unaffected by haemorrhage despite the significant decrease in systemic and regional flows. This suggests that autoregulation of blood flow in the jejunal mucosa remains intact during acute haemorrhage in anaesthetized pigs. It is possible that, under these circumstances, blood flow is directed away from the muscularis layer towards the mucosa.[25]

It has been suggested that redistribution of blood flow during haemorrhagic shock from tissues with low oxygen demand towards tissues with a high oxygen demand is an important mechanism for maintaining oxygen consumption independent from supply. Increased vascular tone mediated by neurohumoral factors in tissues with a low oxygen demand seems to play an important role in this mechanism.[26] After electric stimulation of splanchnic nerves a decreased blood flow in the intestinal wall is followed by an 'autoregulatory escape' of microcirculatory blood in the small intestinal mucosa, particularly in the villus region[27] but to a much lesser extent in the muscularis. It has also been shown that exposure of the small intestinal mucosa to nutrients leads to mucosal hyperaemia due to autoregulation of blood flow to the absorptive site[28] and, when blood flow to the intestine is reduced, this autoregulation seems to occur at the expense of the intestinal segments not exposed to nutrients.[29] Furthermore, vasoactive drugs influence the distribution of blood flow in the gut. Both isoproterenol and adenosine[30] cause a significant increase in total blood flow to the intestinal wall. However, isoproterenol favours blood flow to the mucosa while adenosine favours flow to the muscularis layer. Both vasodilators depress oxygen uptake in the intestine.

Thus, under certain conditions, redistribution of blood flow from the muscularis layer to the mucosa does occur; however, to our knowledge, intact autoregulation of blood flow in the intestinal mucosa remains to be demonstrated in haemorrhagic shock. Thus, it appears that local control mechanisms of blood flow in the small intestine favour flow to the mucosa at the cost of the muscularis during hypovolaemia.[27] It is possible that this autoregulation is facilitated or even controlled by high oxygen demand[31] in

the mucosa together with very low oxygen tension in the intestinal villi.

During blood loss, the decrease in MBF in the pancreas was greater (–60%) than the changes seen in systemic (–45%) and regional (–30%) flows. Arterial blood pressure also decreased by 60% as compared with baseline, suggesting the absence of autoregulation of blood flow in the pancreas during haemorrhage. After retransfusion of shed blood the pancreas blood flow did not return to baseline values in contrast to the other organs studied. No other organ showed such a profound decrease in local blood flow during haemorrhage or such persistent hypoperfusion after retransfusion of shed blood. This finding is in accordance with studies on anaesthetized dogs exposed to haemorrhagic shock[32] where total blood flow to the pancreas decreased proportionally more than blood flow in the superior mesenteric artery. In a study by Bor and colleagues,[33] pancreatic blood flow, measured using the ^{33}Xe washout technique, decreased to the same extent as systemic blood pressure. Thus, MBF in the pancreas appears to be more susceptible to hypovolaemia than other splanchnic organs. It has also been shown that morphological and functional damage occurs in the pancreas after haemorrhage.[34] Thus, it is likely that pancreatic hypoperfusion may contribute to the development of remote organ dysfunction in critically ill or injured patients.[35]

Conclusions

Changes in the distribution of microcirculatory (local) blood flow in the gastrointestinal tract are heterogeneous during haemorrhagic shock and cannot be predicted from systemic or regional blood flow in anaesthetized pigs. Splanchnic regional blood flow and MBF in the gastric and colon mucosa decrease to a similar extent as systemic flow during haemorrhage and hypoperfusion does not persist after retransfusion of shed blood. It appears that autoregulation of blood flow in the jejunal mucosa is intact in anaesthetized pigs during haemorrhagic shock. MBF in the pancreas appears to decrease more than in any other splanchnic organ during acute haemorrhage.

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