Effect of thoracic epidural anaesthesia on colonic blood flow

T. H. Gould¹*, K. Grace², G. Thorne³ and M. Thomas²

¹Sir Humphrey Davy Department of Anaesthesia, ²University Department of Surgery and ³University Department of Medical Physics, Bristol Royal Infirmary, Marlborough Street, Bristol BS8 2HW, UK

*Corresponding author

Background. The effect of thoracic epidural block on splanchnic blood flow is unclear. It remains to be resolved if sympathetic block, increases or decreases regional splanchnic blood flow and whether regional splanchnic flow becomes dependent on cardiac output or perfusion pressure. A clear understanding of the regional haemodynamic consequences of an epidural block may modify practice with respect to epidural anaesthesia.

Methods. Fifteen patients, who underwent anterior resection for rectal cancer, had invasive intraoperative monitoring of arterial pressure, central venous pressure, cardiac output, inferior mesenteric artery flow (Doppler flow probe), and colonic serosal red cell flux (laser Doppler probe), while an epidural block was established with local anaesthetic. In three consecutive time periods, arterial pressure was first allowed to fall (to a mean arterial pressure of 60 mm Hg), then treated with colloid fluid resuscitation and finally by vasopressors until the pre-epidural arterial pressure had been restored.

Results. On induction of epidural block, there was a reduction in mean colonic serosal red cell flux to 65% and inferior mesenteric artery flow to 80% (mean) of pre-epidural levels. There was a strong association between mean arterial pressure and both measured inferior mesenteric artery blood flow (P<0.004) and colonic serosal red cell flux (P<0.0001). Changes in cardiac output were poorly associated with either inferior mesenteric artery blood flow (P=0.638) or colonic serosal red cell flux (P=0.265). Inferior mesenteric artery blood flow and colonic serosal red cell flux were restored to pre-epidural levels after arterial pressure had been improved with a vasopressor.

Conclusion. Once intraoperative epidural block has been established, colonic serosal red cell flux and inferior mesenteric artery flow are more closely associated with changes in mean arterial pressure than changes in cardiac output. The measured reduction in colonic flow does not respond to an increase in cardiac output with fluid resuscitation, but requires the use of a vasopressor to increase arterial pressure, before colonic blood flow is improved.

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Three arteries from the aorta supply the gastrointestinal system in man: the coeliac artery supplies blood to the stomach, liver and spleen; the superior mesenteric artery supplies the entire small intestine and the right side of the colon; the inferior mesenteric artery delivers blood to the hindgut (distal colon and rectum). Typically, blood flow through these arteries is 20–25% of the cardiac output, but the distribution of blood flow within the tissue layers of the intestine is not uniform.¹ In unfed animals at rest, blood flow to the mucosal layer is 70–80% of total flow at the expense of the sub-mucosal, muscular, and serosal layers. After a meal, blood flow to the intestine increases by as much as 200%, and most of this increase is shifted to the mucosal layer by recruitment of previously closed capillaries.¹ The exact mechanism for this recruitment is unknown, but paracrine (e.g. vasoconstrictors—endothelin-1, platelet aggregating factor; vasodilators—endothelium-derived releasing factor, prostacyclin) and metabolic mediators (pH, PₐCO₂, PₐO₂) predominantly influence small vessels and hence may moderate changes in local mucosal flow. Larger vessels are under the influence of humoral (catecholamines, angiotensin II, vasopressin, serotonin)
and neural mediators (constriction; increased sympathetic, decreased parasympathetic tone and dilatation; decreased sympathetic tone and increased parasympathetic tone). These multifactorial control mechanisms are inter-related and the relative balance helps determine regional and local blood flow.

To understand and possibly manipulate splanchic blood flow may be clinically useful. It has been suggested that vasodilatation of the splanchic vascular bed will improve splanchic blood flow.2-4 This could be achieved by an injection of local anaesthetic into the thoracic epidural space, which would produce a dense sympathetic block (and a block of C and Aδ pain fibres). A fall in arterial pressure usually follows, concomitant with peripheral arterial and venous vasodilatation. Vasodilatation of the splanchic vascular bed would be part of this response.

Epidural anaesthesia and analgesia are techniques commonly used in association with major surgery to improve patient outcome.5 However, there are divergent views on the true effect of epidural block on splanchic blood flow.6-10 Previous studies have relied on only two or three single time point measures, and thus have failed to combine continuous measurement of splanchic blood flow with real time changes in arterial pressure, central venous pressure, and cardiac output. Recent studies8-10 have used the less invasive technique of gastric tonometry to measure gastric mucosal Pco2 as an indirect assessment of splanchic blood flow.

It is particularly difficult to study patients in the postoperative period with invasive techniques for splanchic blood flow measurement. We therefore designed an intraoperative study to directly measure the changes in inferior mesenteric artery blood flow and colonic serosal red cell flux, resulting from the initiation of epidural anaesthesia and the subsequent manipulation of arterial pressure and cardiac output with fluid and vasopressors.

**Patients and methods**

Fully informed written consent was obtained from 15 patients (nine male, six female), age 46—85 yr (mean 66, median 72), who underwent anterior resection for rectal malignancy. This study was approved by the local ethics committee. Patients were excluded from the study if they had any pre-existing cardiovascular disease or were taking cardiovascular medication. All patients had 2 litres of normal saline with potassium chloride in the preoperative 18 h to replace the fluid loss that occurred with the bowel preparation before surgery.

After a standardized induction (propofol, fentanyl, atracurium) and maintenance of anaesthesia (ventilation, oxygen, air, isoflurane), an arterial line (for invasive arterial pressure monitoring), an internal jugular central venous catheter and a transoesophageal cardiac output probe (TECO1, Medicina) were inserted, followed by a thoracic epidural catheter at T9—10. Once surgery commenced, a laser Doppler probe (DRT4, Moor Instruments) was attached to the serosal surface of the sigmoid colon (to measure colonic serosal red cell flux) using a serosal suture and a Doppler ultrasound probe (OpDop) was positioned around the inferior mesenteric artery (to measure flow in the inferior mesenteric artery) following careful dissection of the artery and vein. From induction of anaesthesia to the beginning of the study, 1000 ml of Hartmanns solution was given to all patients. When all the monitors were in place and collecting data, the surgery was halted and the study commenced. The study composed of four consecutive time periods.

- **Period 0:** 5 min of steady-state physiological data were collected.
- **Period 1:** 0.5 mg kg⁻¹ (6—8 ml) of 0.5% bupivacaine was then injected down the epidural catheter. Arterial pressure was allowed to fall to a mean arterial pressure of 60 mm Hg (systolic/diastolic approximately 95/50).
- **Period 2:** a rapid fluid infusion of gelofusin was then commenced fast enough to prevent the mean arterial pressure falling below 60 mm Hg. The infusion was stopped when the central venous pressure and cardiac output had both returned to at least pre-epidural levels.
- **Period 3:** up to three 2 mg bolus doses of methoxamine were then used over a 6—9 min period to return the arterial pressure to the pre-epidural level. Once this steady state had again been reached, data collection was terminated and surgery then completed.

Physiological measurements from the monitors were recorded for the duration of the study period (29—40 min).

The position of the probe for laser Doppler (DRT4, Moor Instruments) was adjusted to obtain the optimum signal strength and was then sutured onto the serosal surface of the bowel. Movement artifact is then eliminated by built-in software, which averages recorded values over 0.1 s time intervals. Continuous data of colonic serosal red cell flux was directly downloaded to a personal computer. During this study, red cell flux was measured continuously in 14 of the 15 patients. In one patient, data collection was unusable because of a failure of the event logging of therapeutic interventions.

The measurements of inferior mesenteric artery blood flow were recorded every 15 s and averaged to give a figure for each minute time point of the study. Complete data were collected for 11 patients of the 15 patients in the study. In two patients, difficulty was encountered obtaining an initial signal because of arterial spasm after manipulation of the vessel as it was dissected to attach the probe. In a further two patients, an inability to measure flow was thought to be a result of atheromatous disease.

Cardiac output data were averaged every six beats by the oesophageal Doppler and displayed. The data were stored within the software of the TECO1 and manually recorded at 1 min time point intervals. Heart rate, central venous pressure, systolic, diastolic, and mean arterial pressure were...
manually recorded at 1 min time point intervals contiguous with the other data throughout the study period.

The patient end tidal carbon dioxide (5–5.3 kPa) and end tidal isoflurane (0.8%) were maintained in all patients for the study period. Temperature was maintained at 36.5°C in all of the patients by use of heated under mattress and a heated over blanket, together with warming of i.v. fluids, commenced in the anaesthetic room.

The study design reflected the local management for the commencement of an epidural anaesthetic and the treatment of a subsequent fall in arterial pressure. The hospital ethical committee had granted approval for all aspects of this study.

**Statistical analysis**

The values for heart rate, central venous pressure, arterial pressure, cardiac output, colonic serosal red cell flux, and inferior mesenteric artery blood flow were all transformed to a percentage of the mean value obtained from the steady state 5 min in period 0. The transformation of the data to a percentage of the mean value in period 0 was made because of the variation between the 15 patients in the actual measured base line blood flow using the two techniques. Because of the difference between patients in the duration of each of the time periods, the data selected for analysis were the mean of the last 5 min of each of the study periods 0, 1, 2, and 3 for each physiological variable.

Multiple regression was used to explore the associations between the independent variables heart rate, central venous pressure, mean arterial pressure, cardiac output and the dependant variables colonic mucosal serosal blood flow and inferior mesenteric artery blood flow. This analysis was performed using the robust regression option in Stata 7.0. Using this option the standard errors of the coefficients in the regression model are estimated using the Huber–White estimator of variance. This allows one to relax the assumption of the independence of the observations. That is to say a valid estimate of the standard errors is obtained even if the observations are correlated. The current analysis was conducted on the basis of the observations being clustered by patient (i.e. observations from the same patient were not assumed to be independent).

The ‘robust multiple regression’ was first performed for colonic serosal red cell flux (14 patients) with the variable heart rate, central venous pressure, mean arterial pressure, and cardiac output. A separate ‘robust multiple regression’ was then performed for inferior mesenteric artery flow (11 patients) with the same variables, because of the different number of completed patient data sets for each of the two measurements of flow.

This study was intended to be a pilot study of 20 patients. No power calculation was made because the changes in colonic blood flow were not predictable or consistent from previous studies.3–10 Interim analysis showed consistent data, which were statistically significant after 15 patients.

**Results**

The median duration (95% confidence intervals (CI)) of period 0 was 5 min; period 1, 12 (8–16) min; period 2, 9 (5–13) min; and period 3, 8 (7–11) min.

The objectives of the study to manipulate mean arterial pressure, cardiac output, and central venous pressure as described in the method section were achieved. In period 1, mean arterial pressure fell to 60 mm Hg in all of the patients, 69% of the mean arterial pressure in period 0. At the end of period 2, cardiac output was 110% and central venous pressure was 107% of the values in period 0 in response to fluid therapy. The median (95% CI) volume of gelofusin given during period 2 for the 15 patients was 875 (700–1050) ml. At the end of period 3, in response to the vasopressor, central venous pressure had increased further, mean arterial pressure and cardiac output had returned to their pre-epidural levels. Of particular interest are the changes in colonic serosal red cell flux and inferior mesenteric artery blood flow measurements. In period 1, both measures of flow had a fall in association with the fall in mean arterial pressure. In period 2, there was minimal change in either flow measurement despite the increases in cardiac output and central venous pressure. Finally, in period 3, colonic serosal red cell flux and inferior mesenteric artery blood flow measurements increased with mean arterial pressure in response to the vasopressor (Figs 1 and 2).

It is clear from the multiple regression analysis that mean arterial pressure is the variable most closely associated with colonic serosal red cell flux ($P<0.0001$) (Table 1) and inferior mesenteric artery blood flow ($P=0.004$) (Table 2). Both colonic serosal red cell flux and inferior mesenteric artery blood flow are poorly associated with cardiac output ($P=0.64$, Table 1 and $P=0.27$, Table 2). There was one other significant association, inferior mesenteric artery flow with central venous pressure ($P=0.015$, Table 2). This could be accounted for by the continued increase in central venous pressure seen in period 3 in response to systemic vasoconstriction at the same time as there is an increase in inferior mesenteric artery flow.

Diagnostic tests were performed subsequent to the multivariate analysis, the residuals were found to be normally distributed and these values were found to be independent of the predicted values.

Although the results for arterial pressure have been presented as mean arterial pressure, similar associations exist for systolic and diastolic values.

**Discussion**

In previous published studies, splanchnic blood flow in patients is usually measured by indirect techniques which are then extrapolated to infer changes in actual blood flow. Methods commonly used are gastric tonometry (measures gradient between arterial and gastric mucosal $P_{\text{ACO}_2}$), and
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indocyanine green (measures hepatic extraction of indocyanine green from the blood). Such indirect measurements have evolved principally because of the practical difficulties of using highly invasive direct techniques in patients. In conducting this study in the operating theatre on patients whose segment of bowel is later removed as part of the surgery, it was possible to use direct measurements of actual colonic blood flow.

The laser Doppler (DRT4, Moor Instruments) was used to measure colonic serosal red cell flux. When light is emitted into tissue that contains moving red blood cells, light is reflected from the stationary tissue and Doppler shifted light is reflected from the red blood cells. The shifted and unshifted light are collected on a photodetector and a beat frequency is generated. In reality, red blood cells move at different velocities and the back scattered light creates a spectrum of Doppler frequencies. The magnitude of the Doppler shift depends on the product of the number of moving cells and their velocity. This measured quantity is a true estimation of blood flow. The relative changes in serosal and mucosal flows measured by laser Doppler are comparable and hence placement of the probe onto the serosa is valid in this study design and technically easier and safer than mucosal measurements.

The Operative Doppler (OpDop: designed in the Department of Vascular Studies, Bristol Royal Infirmary) was used to measure directly flow in the inferior mesenteric artery. The diameter of the artery to be studied is measured and a 10 MHz pencil ultrasound probe is held in the appropriate size cuff against the vessel. Blood flow is calculated from the mean blood velocity and the vessel internal diameter (derived calibration factor to compensate for uneven insonation of the lumen). As reported previously, if the vessel diameter remains constant at the point of measurement, then the mean velocity is directly proportional to blood flow. The transoesophageal cardiac output probe (TECO1, Medicina) has undergone extensive validation studies. A probe 3 mm in diameter is inserted 35–40 cm into the distal oesophagus and is orientated to obtain the characteristic aortic flow signal. The area (integral) under each velocity–time waveform represents the stroke volume flowing in the descending aorta. Applying a nomogram that incorporates patient age, height, and weight enables an estimate of left ventricular stroke volume and hence cardiac output. Intraobserver variability is low and trend following is accurate over a wide range of flow and arterial pressure. A recent study highlighted the overestimation of cardiac output by oesophageal Doppler during lumbar epidural anaesthesia when compared with thermodilution techniques. The investigators in the present study were aware of this from our own preliminary work in preparation for this study. To choose the optimum measurement technique for cardiac output, oesophageal Doppler was compared with thermodilution in eight patients (over 18 months) in whom a pulmonary artery catheter was used for invasive cardiovascular monitoring at laparotomy. After commencement of thoracic epidural anaesthesia and adequate fluid resuscitation a measured increase in cardiac output occurred with both techniques. The increase was greater with the oesophageal method (which measures velocity of flow in the descending aorta), but less so than the magnitude reported by Leather and co-workers who used an epidural placed at L2–3. The phenomenon is probably explained by a relative redistribution of flow between the upper and lower part of the body after the epidural was commenced and vasodilatation occurs. The investigators took the previously discussed observations into account, but selected the oesophageal Doppler, a much less invasive technique to measure cardiac output for the present study, as the main aim of the study was to observe the trend changes after the commencement of an epidural.

Fig 1 Graph of percentage change from period 0 for each parameter mean arterial pressure, cardiac output, central venous pressure, colonic serosal red cell flux (laser Doppler) at the end time points of periods 1, 2, and 3. Mean values, 95% CI.

Fig 2 Graph of percentage change from period 0 for each parameter mean arterial pressure, cardiac output, central venous pressure, inferior mesenteric artery blood flow (OpDop) at the end time points of periods 1, 2, and 3. Mean values, 95% CI.
In addition, the loss of vascular resistance in the peripheral vascular beds increases flow into the lower resistance vascular beds. Cardiac output (e.g. with i.v. fluid resuscitation) preferentially increases flow into the arterioles. Basal tone after a complete sympathetic block would be in the opposite direction, as tissues with the highest density of alpha receptors would be most affected. After epidural anaesthesia at the mid-thoracic level, there will be a loss of sympathetic tone, especially in the skeletal muscle below the level of the block. This loss of tone may lead to a 'steal' phenomenon away from the colonic bed and increased flow into the maximally dilated peripheral vascular beds. At the same time the increase in venous capacitance will reduce cardiac end diastolic volume and cardiac output will normally fall. Any improvement in cardiac output (e.g. with i.v. fluid resuscitation) preferentially increases flow into the lower resistance vascular beds. In addition, the loss of vascular resistance in the peripheral vascular beds decreases the total arterio-venous pressure difference, arterial pressure falls and this may further reduce colonic blood flow.

The results of our intraoperative study demonstrate a strong association between colonic serosal red cell flux and inferior mesenteric artery flow with mean arterial pressure, when an epidural block has been established. The measured reduction in flow did not respond to an increase in cardiac output with fluid resuscitation but to an increase in vascular tone after the use of a vasopressor.

To understand the cardiovascular response to a change in vasomotor tone, it is useful to consider that arterial pressure is a function of flow (cardiac output) and the total resistance of the individual organ and tissue beds arranged in parallel. Effenter sympathetic tone of organ and tissue beds modifies internal flow resistance. The gradation of sympathetic tone (skin/skeletal muscle > kidney > intestine > brain > heart/lungs) is determined by the density of alpha receptors in the arterioles. Basal tone after a complete sympathetic block would be in the opposite direction, as tissues with the highest density of alpha receptors would be most affected. After epidural anaesthesia at the mid-thoracic level, there will be a loss of sympathetic tone, especially in the skeletal muscle below the level of the block. This loss of tone may lead to a 'steal' phenomenon away from the colonic bed and increased flow into the maximally dilated peripheral vascular beds.

The study procedure described in this manuscript was as relevant to clinical practice as possible, but the study is too small to show any detrimental side-effects from a reduction in colonic blood flow and was not designed to do so. Indeed, it is not really possible to take this study model much further because of the intraoperative time limitations and ethical considerations. Further studies with regard to the haemodynamic control of colonic blood flow should probably be pursued in an animal model. Adequate colonic blood flow is critical to gut mucosal integrity and anastomotic healing. A study of pH using tonometry at the site of the anastomosis after anterior resection, showed a decrease in pH after commencement of a thoracic epidural block and then improvement on its cessation. It is also possible that a reduced mean arterial pressure and hence a reduced colonic blood flow for a sustained period, may lead to an ischaemia reperfusion injury to the gut. This could precipitate bacterial infection.

### Table 1

| Colonic serosal red cell flux | Coefficient (95% CI) | t value | P>|t| |
|-----------------------------|---------------------|--------|------|
| Cardiac output              | -0.17 (-0.93, 0.59) | -0.48  | 0.638|
| Mean arterial pressure      | 10.2 (6.94, 13.55)  | 6.7    | 0.0001|
| Heart rate                  | -0.5 (-1.66, 0.64)  | -0.94  | 0.362|
| Central venous pressure     | 0.93 (-3.23, 3.41)  | 0.06   | 0.952|
| Constant                    | 63.62 (-41.94, 169.19) | 1.3   | 0.216|

### Table 2

| Inferior mesenteric artery blood flow | Coefficient (95% CI) | t value | P>|t| |
|-------------------------------------|---------------------|--------|------|
| Cardiac output                      | 0.68 (-0.60, 1.96)  | 1.18   | 0.265|
| Mean arterial pressure              | 11.78 (4.87, 18.7)  | 3.8    | 0.004|
| Heart rate                          | -1.73 (-3.82, 0.36) | -1.84  | 0.095|
| Central venous pressure             | -0.54 (-0.95, -0.13) | -2.95  | 0.015|
| Constant                            | 144.8 (-5.3, 294.9) | 2.15   | 0.057|

How do the findings reported in this study correlate with the results from other studies that compare splanchnic blood flow after epidural anaesthesia–analgesia? An improvement in splanchnic blood flow has been recorded in a similar study using intraoperative laser Doppler flowmetry measured at the site of the colonic anastomosis and in two studies with tonometry, one postoperative the other in intensive care in septic patients. Using tonometry, in a group of patients after aortic aneurysm surgery, investigators found no change in flow. A further study demonstrated results closest to our reported results, a fall in flow measured by an electromagnetic probe placed on the superior mesenteric artery. Flow then improved after dopamine 4 µg kg⁻¹ min⁻¹. None of these studies involved the combination of two direct invasive measurements of flow and such comprehensive data collection. Neither did the previously reported studies control arterial pressure or manipulate fluid and vasopressors so tightly, compared with data presented in this study.

The variation in the reported studies is still confusing. The level of the epidural and the dose of bupivacaine did, however, vary between studies and in patients within the same study. The only study in addition to our reported results, where a thoracic epidural is placed consistently (T7–8 or T8–9), is the one which showed a fall in flow. This is probably very important; indeed two animal studies (which use direct invasive measurement to measure blood flow) suggest that if the thoracic epidural is placed high (T1–5), or a lumbar epidural is used, sympathetic block is incomplete. Incomplete block may lead to increased sympathetic activity and a lesser decrease in arterial pressure, because baroreceptor stimulation produces increased splanchnic sympathetic activity and mesenteric vеноconstriction. Thus, as splanchnic tone is preserved, there is less change in arterial pressure and splanchnic blood flow is more stable. An epidural placed in the mid-low thoracic region causes a decrease in sympathetic activity, mesenteric vенodilatation, a lower arterial pressure and reduced splanchnic blood flow.

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translocation, endotoxin absorption from the bowel and become a potential trigger of sepsis and septic shock.

A common approach to the perioperative treatment of hypotension and reduced urine output associated with epidural block is i.v. fluid resuscitation. We have demonstrated difficulty in returning colonic blood flow to normal levels with fluid resuscitation alone after a single bolus dose of bupivacaine. In addition, the relative unresponsiveness of the renin–angiotensin system to hypotension and the increase in anti-diuretic hormone after sympathetic block could actually lead to fluid retention and precipitate cardiac failure in susceptible patients, when given excess fluid resuscitation to restore hypotension and improve urine output.

This study was carried out in the operating theatre with a combined general and thoracic epidural anaesthetic. The authors accept that the use of postoperative thoracic epidural analgesia tends to involve lower doses of bupivacaine but postoperative hypotension (systolic <100 mm Hg) can still occur in up to 28% of patients. On the basis of the presented data, we postulate that hypotension associated with epidural analgesia should be dealt with promptly (this recommendation is included in the 2001 Report of the National Confidential Enquiry into Perioperative Deaths) and that vasopressor therapy be considered early if there is no improvement with intravenous fluids. Finally, to minimize haemodynamic consequences, epidural block should be confined to the fewest necessary segments avoiding splanchnic innervation (T8–L1) when possible.

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