Effects of epidural anaesthesia on intestinal oxygenation in pigs

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Background. Perioperative intestinal hypoperfusion is a major contributing factor leading to organ dysfunction. It can be caused by stress as a result of surgical manipulation or hypoxia. Additionally, anaesthesia can affect intestinal oxygenation. This animal study was designed to assess the effects of reduced regional sympathetic nervous activity induced by thoracic epidural anaesthesia on intestinal oxygenation.

Methods. After ethical approval, 16 anaesthetized and acutely instrumented pigs were randomly assigned to two groups (epidural anaesthesia alone vs epidural anaesthesia plus volume loading). The epidural anaesthesia aimed for a T5–T12 block. Measurements were at baseline and after 1 and 2 h.

Results. Epidural anaesthesia was associated with a decrease in mean arterial blood pressure and pronounced mesenteric vasodilatation. Mesenteric blood flow did not change. Intestinal oxygen uptake, mucosal tissue oxygen partial pressure and tissue carbon dioxide partial pressure remained unchanged.

Conclusions. Despite marked systemic hypotension, epidural anaesthesia did not affect intestinal oxygenation. There was no benefit obtained from volume loading.

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Recently the splanchnic region has become of growing interest because of its possible function in the development of systemic inflammatory response syndrome, sepsis and multiple organ failure. Perioperative hypoperfusion and impaired oxygenation of the gut, especially of the intestinal mucosa, which are major factors contributing to organ dysfunction, must be avoided. Splanchnic hypoperfusion can be caused by anaesthesia or enhanced sympathetic nervous activity as a result of surgical manipulation, stress and pain. Additionally, hypovolaemia and endotoxaemia are major contributing factors to reduced intestinal blood flow.

In the past, much research has been done on the effects of different anaesthetics and of surgical manipulation on splanchnic circulation. However, detailed knowledge of the effects of regional anaesthesia, such as thoracic epidural anaesthesia, on intestinal perfusion and oxygenation is still lacking. Results of one small prospective study in humans for the first time indicated beneficial effects of epidural anaesthesia on outcome after emergency abdominal surgery. In dogs and rabbits, a decrease in mortality from 80 to 20% obtained by surgical denervation of the splanchnic viscera before induction of endotoxic shock was demonstrated as early as 1964.

Results were presented in part at the First International Symposium on Problems of the Gastrointestinal Tract in Anaesthesia, the Perioperative Period, and Intensive Care, Würzburg, Germany, October 1–3, 1998.
In clinical practice, epidural anaesthesia is frequently associated with systemic hypotension, which is normally counteracted by volume loading with crystalloids or colloids. This volume loading is believed to be beneficial for the patient, but no data exist about the effects on intestinal oxygenation during thoracic epidural anaesthesia and concomitant volume loading.

Therefore, the present study was performed to characterize intestinal perfusion, the oxygen supply–uptake relationship of the gut, and mucosal tissue oxygenation during regional reduction of sympathetic nervous activity induced by epidural anaesthesia with and without volume preloadings in an intact animal model.

### Methods

**Anaesthesia**

After approval of the study by the local Ethics Committee on Animal Research, 19 male and female German domestic pigs were premedicated i.m. with flunitrazepam 0.2 mg kg⁻¹ body weight (Rohypnol®; Hoffmann-La Roche, Grenzach-Wyhlen, Germany) and ketamine 15 mg kg⁻¹ (Ketanest®; Parke-Davis, Freiburg, Germany) after overnight fasting, and the animals received water *ad libitum*. Anaesthesia was induced i.v. via an ear vein with ketamine 1.6–3.3 mg kg⁻¹ and fentanyl 3 μg kg⁻¹ (Fentanyl-Janssen®; Janssen-Cilag, Neuss, Germany). Anaesthesia was maintained by continuous i.v. infusion of flunitrazepam 0.07–0.1 mg kg⁻¹ h⁻¹, ketamine 7–10 mg kg⁻¹ h⁻¹ and vecuronium 0.5–0.7 mg kg⁻¹ h⁻¹. Mechanical ventilation was provided volume-controlled with intermittent positive-pressure ventilation using a Cato ventilator (Dräger, Lübeck, Germany).

Ventilatory frequency and tidal volume were adjusted to maintain arterial carbon dioxide tension (PaCO₂) between 5.1 and 5.6 kPa. Inspired oxygen fraction was adjusted to maintain arterial oxygen partial pressure (PaO₂) at 12.6–15.3 kPa. Inspired gases were warmed with a Cascade II (Bennett, Puritan Corporation, Los Angeles, CA, USA).

**Instrumentation**

After induction of anaesthesia, the animals were placed in the right lateral position for insertion of an epidural catheter. After induction of anaesthesia via an ear vein with ketamine 15 mg kg⁻¹ (Ketanest®; Schering, Berlin, Germany) under x-ray control.

After insertion and careful fixation of the epidural catheter, animals were placed in the supine position on a heating pad to keep body temperature constant.

A two-lumen catheter (7 F Two-Lumen Central Catheterization Set; Arrow, Reading, PA, USA) and an 8.5 F introducer (Arrow Percutaneous Sheath Introducer Set; Arrow) were inserted into the right internal jugular vein. Both catheters were advanced 11–13 cm to guarantee correct positioning of the tip in the superior vena cava. A Swan–Ganz thermodilution catheter (model 93A-131-7F; 7F Swan–Ganz Thermodilutions Catheter; American Edwards Laboratories, Irvine, CA, USA), was introduced into the pulmonary artery. Body temperature was monitored continuously with a thermistor in this flow-directed catheter.

The right femoral artery was cannulated with a 4.5 F introducer set (Arrow Percutaneous Sheath Introducer Set). After median laparotomy, the cranial mesenteric vein (corresponding to the superior mesenteric vein in humans) was cannulated with a 16G single-lumen catheter. A Trip® gastric tube (Baxter, Unterschleissheim, Germany) and a Paratrend® catheter (Paratrend Intravascular Blood Gas Monitoring Systems, Diametrics Medical, High Wycombe, UK) were placed intraluminally into the jejunum. An ultrasonic perivascular flow probe (Transonic Systems, Ithaca, NY, USA) of appropriate size was placed around the superior mesenteric artery (vessel filling 75–100% of the probe’s acoustic window). Care was taken to preserve the periarterial nerve plexus. The flow probe consists of two ultrasonic transducers and a fixed acoustic reflector. It does not produce heat and the measurement is independent of the corpuscular content of the blood. The flow probe has no effect on flow.

A multiwire surface electrode to measure tissue surface PO₂ was placed intermittently on the intestinal serosa and mucosa of a segment of the jejunum. For the latter, a 1 cm transmural antimesenteric incision was made and a spacer was introduced to get uncompromised access to the mucosa. After each measurement, the incision in the gut was sutured.

At the end of the surgical preparation the abdomen was sutured except for a cleft of 10 cm to allow intermittent measurements of surface oxygen partial pressure on the mucosa and serosa tissue of the small intestine. The gap was covered with wet and warm swabs.

For maintenance of normovolaemia, all animals received full-electrolyte solution at 12 ml kg⁻¹ h⁻¹ i.v. (Jonosteril®; Fresenius-Klinik, Bad Homburg, Germany) before laparotomy and 15–20 ml kg⁻¹ h⁻¹ i.v. during laparotomy to maintain blood pressure, central venous pressure, haemoglobin and haematocrit values at the level measured shortly after insertion of the femoral artery and central venous catheters.
Measurements and calculations

Before laparotomy, arterial blood gas values were taken to adjust inspired oxygen concentration and ventilation to maintain predetermined $P_{aO2}$ and $P_{aCO2}$ values, and to measure initial haematocrit values. Blood gases, serum electrolytes, glucose and lactate concentrations were measured using an ABL3 Autoanalyzer (Radiometer, Copenhagen, Denmark).

Haemodynamics

All intravascular catheters were connected to pressure transducers. A multichannel recorder (Hugo-Sachs, March, Germany) and PO-NE-MAH® (Digital Acquisition Analysis and Archive Systems; Plugsys®, Simsbury, USA) was used for online recording. Cardiac output was determined with a thermodilution technique (CO computer, model 404-1; Siemens, Erlangen, Germany). The mean value, calculated from the results of three injections of 5 ml ice-cooled saline, was considered to estimate actual cardiac output if the measurements were within $\pm 5\%$ of the calculated mean. Systemic and regional vascular resistances were calculated using the equations listed in the Appendix. Heart rate was derived from an R-R interval of an extremity ECG. Systemic and regional intestinal oxygen supply (i.e. oxygen supply via the superior mesenteric artery to the gut), oxygen uptake and lactate production were calculated, as shown in the Appendix.

Tissue oxygenation

Tissue surface oxygen partial pressure ($P_{O2}$) was measured using an eight-channel multiwire platinum surface electrode (Eschweiler, Kiel, Germany) as described previously. The electrode was placed on the serosa or mucosa of the gut. During each measurement a total of approximately 200 individual $P_{O2}$ values were registered at 10 electrode locations to obtain data representative of $P_{O2}$ distribution.

Experimental procedure

At the end of surgical preparation at least 90 min was allowed for stabilization before baseline readings ($t_0$) were obtained in all animals. Subsequently, the animals were randomly divided into two groups that differed in fluid management and one group that served as control group: Group 1 (eight animals, basic fluid) received constant maintenance fluid management as described above; Group 2 (eight animals, volume-loaded) received maintenance fluid management and were additionally volume-loaded; Group 3 (three animals) was the control group.

After baseline readings ($t_0$) had been obtained, the animals of Group 1 received bupivacaine 0.5%, 0.75 ml per segment (Carbostesin® 0.5%; Astra, Wedel, Germany) into the epidural catheter to block segments T5–T12. Measurements were made 1 h ($t_{1h}$) and 2 h ($t_{2h}$) after epidural injection. During the whole procedure, i.v. fluid was given in amounts necessary to keep filling pressures constant during the stabilization period.

After baseline measurements, animals in Group 2 received basic fluid management and additionally hydroxyethyl starch solution 15 ml kg$^{-1}$ (HAES® 6%, 200/0.5;
Fresenius-Klinik, Bad Homburg v.d.H., Germany) i.v. 30 min before epidural anaesthesia. Subsequently bupivacaine 0.5% was injected into the epidural catheter at 0.75 ml per segment. Infusion of hydroxyethyl starch was continued at 10 ml kg⁻¹ h⁻¹. Again, measurements were made 1 h (t₁h) and 2 h (t₂h) after epidural catheter injection.

Three control animals were studied to confirm the stability of the experimental model over time. Animals were instrumented as described above. After baseline readings had been performed, no further interventions were made. Measurements of all parameters were repeated 1, 2 and 3 h later.

All animals were killed by infusion of potassium chloride at the end of the experiment.

**Sympathetic activity**

To demonstrate reduced regional sympathetic activity, plasma concentrations of epinephrine and norepinephrine were determined in arterial blood. Catecholamines were extracted from 1 ml plasma by alumina chromatography, separated by high-performance liquid chromatography and quantified by electrochemical detection.¹⁰

At the end of the experiment, cranial spread of epidural block higher than T5 was excluded by inducing cardioacceleration with glyceryl trinitrate 0.3 mg kg⁻¹ i.v. This was done before and after i.v. injection of atropine 30 µg kg⁻¹. The persistence of the reflex cardioacceleration in animals without and with blocked vagal transmission was interpreted as a sign of unblocked sympathetic innervation of the heart (Nn. accelerantes, T4).¹¹

**Statistical analysis**

Statistical analysis was performed with the JMP® software package (SAS, Cary, NC, USA). Medians are given throughout, with interquartile range (25th–75th percentiles).¹² Differences between experimental periods within the two groups were analysed using Friedman’s statistic followed by the Wilcoxon signed rank test. Differences between the two groups were analysed with the Mann–Whitney test. The level of significance was set at P<0.05. All results were indexed to compensate for differences in body weight.

**Results**

Biometric data of the 19 pigs used were comparable. The mean weight of animals was 31.0 (SD 2.5) in the basic fluid group, 30.0 (1.8) in the volume-loaded group and 30.6 (4.5) kg in control animals.

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**Table 1** Systemic haemodynamic and oxygen transport variables. Results are given as median (interquartile range). *P<0.05 vs t₀ within groups; †P<0.05 between basic fluid and volume-loaded group at the same time

<table>
<thead>
<tr>
<th>Variable</th>
<th>Basic fluid group</th>
<th>Volume-loaded group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t₀</td>
<td>t₁h</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>130 (121–135)</td>
<td>93 (88–100)*</td>
</tr>
<tr>
<td>Systemic vascular resistance (dyn s cm⁻³ kg⁻¹)</td>
<td>120 (95–137)</td>
<td>76 (70–84)*</td>
</tr>
<tr>
<td>Heart rate (beats min⁻¹)</td>
<td>82 (70–95)</td>
<td>68 (62–87)</td>
</tr>
<tr>
<td>Cardiac output (ml min⁻¹ kg⁻¹)</td>
<td>98 (81–107)</td>
<td>95 (89–107)</td>
</tr>
<tr>
<td>Central venous pressure (mm Hg)</td>
<td>3 (2–4)</td>
<td>4 (3–5)</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure (mm Hg)</td>
<td>6 (5–1.0)</td>
<td>6 (5–7)</td>
</tr>
<tr>
<td>Arterial haemoglobin concentration (mg dl⁻¹)</td>
<td>11.8 (11.1–12.5)</td>
<td>11.1 (10.9–11.8)</td>
</tr>
</tbody>
</table>

**Table 2** Intestinal haemodynamic and oxygenation variables. Results are given as median (interquartile range). *P<0.05 vs t₀ within groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Basic fluid group</th>
<th>Volume-loaded group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t₀</td>
<td>t₁h</td>
</tr>
<tr>
<td>Superior mesenteric arterial vascular resistance (dyn s cm⁻³ kg⁻¹)</td>
<td>1.0 (0.95–1.21)</td>
<td>1.0 (0.77–1.05)</td>
</tr>
<tr>
<td>Superior mesenteric arterial blood flow (ml min⁻¹ kg⁻¹)</td>
<td>9.6 (9.3–10.4)</td>
<td>8.5 (6.6–9.5)</td>
</tr>
<tr>
<td>Small intestinal oxygen delivery (ml min⁻¹)</td>
<td>48 (45–49)</td>
<td>39 (34–45)</td>
</tr>
<tr>
<td>Small intestinal oxygen uptake (ml min⁻¹)</td>
<td>11.7 (9.5–12.7)</td>
<td>12.6 (11.3–13.8)</td>
</tr>
<tr>
<td>Mesenteric venous oxygen saturation (%)</td>
<td>76 (66–83)</td>
<td>66 (65–68)</td>
</tr>
<tr>
<td>Small intestinal lactate flux (µmol min⁻¹)</td>
<td>67 (30–91)</td>
<td>79 (51–104)</td>
</tr>
<tr>
<td>Pco₂ (Paratrend) (kPa)</td>
<td>7.33 (7.20–7.73)</td>
<td>7.07 (6.80–8.0)</td>
</tr>
<tr>
<td>Pco₂ (Tonocap) (kPa)</td>
<td>6.0 (5.20–6.67)</td>
<td>6.13 (5.47–7.20)</td>
</tr>
</tbody>
</table>

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**Effects of epidural anaesthesia on intestinal oxygenation**

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Basic fluid group

In animals of Group 1, epidural anaesthesia resulted in a pronounced decrease in mean arterial pressure and systemic vascular resistance (Table 1). Heart rate, cardiac output and central venous and pulmonary capillary wedge pressure remained unchanged (Table 1).

Superior mesenteric arterial vascular resistance had decreased significantly at 2h, but superior mesenteric arterial blood flow was maintained (Table 2). The fraction of superior arterial mesenteric blood flow from cardiac output (~10%) remained constant.

Both oxygen transport to the jejunum via the superior mesenteric artery and oxygen uptake by the jejunum did not change (Table 2). Mesenteric venous haemoglobin oxygen saturation was maintained. Intestinal oxygen supply and lactate production in the gut did not change (Table 2).

There was a marked gradient between intestinal mucosal and serosal surface $P_O_2$ values (Fig. 1). At baseline the mean mucosal surface $P_O_2$ was considerably lower than mean serosal surface $P_O_2$. Epidural anaesthesia did not influence the mucosal and serosal surface $P_O_2$ values or their distribution (Fig. 1).

Intestinal mucosal carbon dioxide pressure values, measured tonometrically or with the Paratrend remained unchanged for the whole experiment (Table 2). As in Group 1, the gap between intestinal and arterial mucosal carbon dioxide pressure (Fig. 2) did not change.

Verification of epidural anaesthesia

In all animals, the tip of the epidural catheter was localized at T8, which was verified radiographically. After injection of bupivacaine into the epidural space, the plasma concentrations of both norepinephrine and epinephrine in arterial blood decreased in all animals compared with baseline values. After 1 h of epidural anaesthesia, plasma norepinephrine concentration was reduced by 60% (74–36%) [median, (interquartile range)] of baseline and epinephrine concentration by 77% (86–64%). This level was maintained until the end of the experiment.

I.V. glyceryl trinitrate 0.3 mg kg$^{-1}$ elicited cardioacceleration by 33 (14) beats min$^{-1}$ in animals of Group 1 and by 25 (13) beats min$^{-1}$ in the volume-loaded group (Group 2). Atropine increased heart rate by 38 (20) and 29 (11) beats min$^{-1}$ in the two groups respectively. Application of glyceryl trinitrate after atropine further increased heart rate by 23 (12) beats min$^{-1}$ in Group 1 and 17 (7) beats min$^{-1}$ in Group 2.

Control animals

In the three control animals, differences between baseline values and those obtained hourly during the subsequent 3 h did not exceed 10%.

Heart rates increased by 49 (22) beats min$^{-1}$ after glyceryl trinitrate, 39 (17) beats min$^{-1}$ after atropine and 21 (7) beats min$^{-1}$ after glyceryl trinitrate after atropine.
Discussion

The principle findings of this study are as follows. (i) Epidural anaesthesia (T5–T12) was associated with pronounced systemic hypotension, which was made less pronounced but could not be prevented by volume loading. In spite of hypotension, cardiac output and superior mesenteric arterial blood flow remained unchanged because of significant systemic and mesenteric arterial vasodilatation. The intestinal oxygen supply–uptake relationship did not change during epidural anaesthesia. Intestinal mucosal tissue $P_{O_2}$ and $P_{CO_2}$ were maintained at baseline levels. (ii) Volume loading before and during epidural anaesthesia partly attenuated the decrease in mean arterial pressure, but this was not reflected in any beneficial effect on intestinal microcirculation and oxygenation.

Perioperative hypoperfusion and impaired oxygenation of the gut are major factors leading to organ dysfunction. This is because the mucosal villi are very vulnerable, suffering from oxygen shunting as a result of countercurrent microcirculatory blood flow during low-flow states. Mucosal hypoxia increases gut permeability, induces bacterial translocation and impairs immune function of the body. Perioperative vasoconstriction can be caused by enhanced sympathetic nervous activity and increased plasma levels of catecholamines as a response to surgical manipulation, stress, pain and hypoxia. In clinical practice, one method of reducing sympathetic activity is epidural anaesthesia. Frequently this procedure is associated with a marked decrease in mean arterial perfusion pressure. The mechanisms of this decrease in mean arterial pressure are increased splanchnic venous capacitance as a result of markedly decreased splanchnic nerve sympathetic activity, and relaxation of precapillary arterioles and sphincters.

Few data exist regarding the effects on intestinal blood flow and mucosal oxygenation resulting from the decrease in mean arterial pressure induced by epidural anaesthesia. Therefore this study was performed to investigate whether regional epidural anaesthesia affects intestinal perfusion and oxygenation in acutely instrumented pigs during laparotomy. Additionally, there was a need to examine whether decreases in mean arterial pressure can be modulated by volume loading before and during epidural anaesthesia.

In the basic fluid group (Group 1), epidural anaesthesia induced a decrease in systemic vascular resistance of 28–32% without changes in cardiac output, which resulted in a pronounced reduction in mean arterial pressure of 30–32%. The decrease in mean arterial pressure is in general agreement with previous findings in anaeasthetized animals during mechanical ventilation. The changes in cardiac output, mean arterial pressure and heart rate are exactly the same as those described in humans.

No changes in mean arterial pressure, systemic vascular resistance and cardiac output and a significant increase in heart rate were described by Bonica and colleagues in human volunteers with lumbar epidural block to T4. The missing haemodynamic changes for blocks to T4 were explained by compensation for vasodilatation by vasoconstriction in non-anaesthetized parts of the body. In the same study, a 15% decrease in mean arterial pressure and systemic vascular resistance and a 23% increase in cardiac output were observed if the block extended above T4.

Differences between the results of Bonica and colleagues and our findings might be because of differences in species and to different levels of consciousness—awake volunteers vs anaesthetized pigs. In comparison with our results, Greitz and colleagues found far more pronounced decreases in mean arterial pressure, cardiac output and systemic vascular resistance during high epidural anaesthesia in dogs. This might be attributable to their use of a different species (dog rather than pig) and to the epidural block, which included cardiac nerves.

Superior mesenteric arterial blood flow was maintained despite a marked decrease in mean arterial pressure in the basic fluid group. This was a result of a decrease of more than 35% in superior mesenteric arterial vascular resistance. These data demonstrate regional vasodilatation as a consequence of reduced regional sympathetic activity attributable to epidural anaesthesia. The fraction of superior mesenteric arterial blood flow from cardiac output remained unchanged, indicating that there was no redistribution of systemic blood flow to the gut.

As could be expected from unchanged intestinal blood flow, maintained arterial haemoglobin concentration and saturation, there was no significant effect on oxygen delivery to the gut. Oxygen uptake of the gut was constant, thus maintaining the oxygen extraction ratio. The tendency towards a slightly higher oxygen demand might have been a result of increased intestinal motility and therefore increased oxygen utilization, which was an obvious effect of epidural anaesthesia.

As a result of the unchanged oxygen supply–uptake relationship, intestinal oxygenation was not affected. This was reflected by no changes in either serosal or mucosal surface oxygen partial pressure. The lower surface oxygen partial pressure of the mucosa compared with the serosa at baseline is an obvious finding which had been demonstrated in previous studies. This can be explained by the specific anatomical and physiological conditions of the mucosal villi. These are characterized by oxygen shunting via countercurrent microcirculatory blood flow, by plasma skimming as a result of right-angle spread of the vessels, and by higher metabolic activity and concomitant higher oxygen demand.

If the observed decrease in mean arterial pressure during epidural anaesthesia had had a detrimental effect on intestinal microcirculation, this would have been noted as a decrease in mucosal tissue oxygen partial pressure. However, unchanged levels of mucosal oxygen partial pressure and unchanged distribution of these values indicate that intestinal oxygenation is preserved during epidural anaesthesia. This is
underlined by the results of intestinal tonometry. Neither mucosal \( PCO_2 \) nor the difference between tissue and arterial \( PCO_2 (\Delta PCO_2) \), which is the most useful marker for the detection of splanchnic hyperperfusion, was influenced by the decrease in mean arterial pressure caused by epidural anaesthesia. The \( \Delta PCO_2 \) of about 2.0 kPa over the whole period of the experiments is in general agreement with previously estimated values and represents undisturbed intestinal mucosal microcirculation.

We conclude that in this setting with healthy, normovolaemic pigs there was optimal, physiological perfusion of the intestinal mucosa already at baseline, which could not be improved by epidural anaesthesia. However, these findings are not necessarily transferable to low-flow states.

In general, our results are in agreement with previous findings that epidural anaesthesia at least does not harm perfusion and oxygen delivery to the gut. A study presented recently indicated that thoracic epidural anaesthesia could be useful for preserving visceral perfusion during major abdominal surgery. Unfortunately this study only reported the pH\text{i} value, which is no longer the accepted parameter for quantifying intestinal oxygenation, and gave no information about the volume status and fluid balance of the patients or the effects of high epidural anaesthesia (including cardiac nerves) on cardiac output. Together with this study, our results are able to deliver the missing information on both mucosal oxygenation and intestinal perfusion.

As a consequence of maintained microcirculation of the gut, lactate production did not increase.

To compensate for the decrease in blood pressure seen clinically in response to epidural anaesthesia, volume loading is undertaken. Therefore, we compared animals that received epidural anaesthesia and basic fluid management with a volume-loaded group of animals. For volume loading, we used 6% hydroxyethyl starch, in accordance with clinical practice in humans.

Volume loading and epidural anaesthesia increased cardiac output by 14–18% by maintaining heart rate and increasing stroke volume. The increase in cardiac output in volume-loaded animals was a result of hypervolaemic haemodilution. This is in agreement with previous work regarding the effects of haemodilution. In spite of volume loading, mean arterial pressure still fell significantly, by 16%. As reported by several other investigators, in thoracic epidural anaesthesia it was not possible to maintain mean arterial pressure by volume loading, especially during generally anaesthesia. Systemic vascular resistance decreased much less.

All effects of epidural anaesthesia on intestinal blood flow and oxygenation were qualitatively and quantitatively comparable to the results in the basic fluid group. Thus, volume loading before and during epidural anaesthesia partly attenuated the decrease in mean arterial pressure, but this was not reflected in any beneficial effect on intestinal microcirculation and oxygenation.

**Methodological critique**

One method of inducing decreased regional sympathetic activity is epidural anaesthesia. Epidural anaesthesia from T5 to T11 blocks splanchnic supply to the stomach (T6–T10), gall bladder and liver (T5–T9), small intestine (T7–T11), pancreas (T6–T10) and adrenal glands (T6–L1).

In this study, the effects of reduced sympathetic activity induced by thoracic epidural anaesthesia on splanchnic oxygenation were investigated. We are aware that evaluating the spread of epidural anaesthesia in animals during general anaesthesia is very difficult and that there is no gold standard. Direct measurement of activity in splanchnic fibres supplying large vascular beds seems to be the best method, but sympathetic system activity is also heterogeneous and fibres to different tissues exhibit specific patterns of basal and reflex activity. Some groups have used a modified pin-prick technique, post-mortem analysis of injected dye or capillary \( PO_2 \) measurement.

We used radiology to keep the position of our catheter correct. Reduced sympathetic activity as a result of epidural anaesthesia was proven by reduced arterial and mesenteric venous plasma norepinephrine concentrations during epidural anaesthesia compared with baseline values. Norepinephrine is produced only locally in peripheral tissues. A reduction in plasma norepinephrine concentration is an index of reduced tissue sympathetic activity. A substantial decrease in plasma epinephrine concentration is an index of sympatholysis at the adrenal glands, which form part of the sympathetic nervous system and are supplied by nerves from T6 to L1. Because the liver and small intestine are supplied from the same autonomic segments as the adrenal glands, this proves sympatholysis of the splanchnic organs. We found a marked reduction in plasma concentrations of both epinephrine and norepinephrine in response to epidural anaesthesia. The extent to which a particular catecholamine is reduced is dependent on the intensity of the sympathetic nervous block and baseline activity of the sympathetic nervous system.

Findings in the literature regarding catecholamines and epidural anaesthesia are not consistent. With segmental epidural anaesthesia from T4 to T11, we not only elicited effects attributable to blocking spinal nerve roots at the epidural space but also blocked the adrenal glands.

To exclude spread higher than T4, we used two pharmacological tests at the end of our experiments: the heart rate response to hypotension was evaluated in animals before vagal transmission was blocked and animals in which cardiac vagal transmission was blocked with atropine. Atropine decreases parasympathetic activity, thus eliciting tachycardia by increased sympathetic effects on the heart. Glyceryl trinitrate, as a short-acting drug, was used to elicit reflex tachycardia attributable to pronounced hypotension, if cardiac nerves were not blocked. Cardioacceleration was maintained in both situations, indicating intact function of cardiac sympathetic nerves. This, in turn, indicates that
spinal segments higher than T4 (the origin of preganglionic cardiac sympathetic neurones) were not blocked by epidural anaesthesia.

It could not be proven that epidural injection of bupivacaine produced a reduction in sympathetic activity by providing anaesthesia. However, after sufficient time for stabilization the monitored values changed promptly after epidural bupivacaine injection.

To assess whether macrocirculatory changes during thoracic epidural anaesthesia were associated with microcirculatory effects in the splanchnic region, three methods were used to characterize intestinal oxygenation. Gastric tonometry is a non-invasive bedside monitor of splanchnic perfusion and detects mucosal acidosis for therapeutic guidance and prediction of outcome in critically ill patients. The tonometric balloon was positioned inside the jejunum to prevent interference with gastric juice and to allow us to compare measurements obtained by different methods within the same anatomical region.

Direct measurement of mucosal surface $\text{PCO}_2$ with the Paratrend is an alternative method. As shown recently, this device is able to provide accurate online measurement of mucosal $\text{PCO}_2$ with a very short equilibration time and an error of $<5\%$. This enables the immediate recognition of changes in mucosal $\text{PCO}_2$ as a marker of intestinal perfusion and oxygenation. Use of this technique was compared with continuous $\text{PCO}_2$ measurement with the Tonocap by automated air tonometry, as reported by other groups. In general, variables moved in the same direction independently of the method of measurement. However, use of the Tonocap was slower and therefore missed acute changes, such as the reproducible decrease in $\text{PCO}_2$ seen initially after starting epidural anaesthesia. The difference between the two systems was consistently 1.3–2.6 kPa (10–20 mm Hg), with the Tonocap values on the lower side.

The technique of measuring surface $\text{PO}_2$ with a multiwire electrode is well established and allows measurement of tissue $\text{PO}_2$ without destroying tissue or interference with microrcirculation.

Conclusions
Thoracic epidural anaesthesia did not improve intestinal oxygen supply. However, despite marked systemic hypotension, mucosal oxygenation was maintained. There seems to be no benefit to splanchic perfusion and oxygenation from maintaining mean arterial blood pressure at pre-epidural anaesthetic levels by volume loading. We assume that this is true as long as mean arterial pressure is above 60 mm Hg.

The benefits of hydroxyethyl starch solution are questionable because of haemodilution and hence decreased oxygen delivery to the gut.

Possible reasons why we did not find a positive effect on splanchic microcirculation are that our procedure did not test for a critical level of oxygen delivery and that we did not reduce blood flow or increase oxygen consumption by endotoxic shock.

Although we did not find a positive effect on splanchic perfusion and oxygenation in healthy pigs, studies on endotoxaemic shock are warranted.

Appendix

$\text{Equations used to calculate vascular resistances}$

\[
\text{SVR} = \frac{\text{MAP} (\text{mm Hg}) - \text{CVP} (\text{mm Hg})}{\text{CO} (\text{litr min}^{-1}) \times 80 \times \text{bw} (\text{kg})^{1.3}}
\]

\[
\text{SMAVR} = \frac{\text{MAP} (\text{mm Hg}) - \text{PVP} (\text{mm Hg})}{\text{SMABF} (\text{litr min}^{-1}) \times 80 \times \text{bw} (\text{kg})^{1.3}}
\]

$\text{SVR=systemic vascular resistance; SMAVR=superior mesenteric arterial vascular resistance MAP=mean arterial pressure; CVP=central venous pressure; PVP=portal venous pressure; CO=cardiac output; SMABF=superior mesenteric artery blood flow; bw=body weight.}$

$\text{Equations used to calculate oxygen supply and uptake}$

\[
\text{O}_2 = \text{Hb} (\text{g dl}^{-1}) \times 1.34 \text{ml O}_2 (\text{g Hb})^{-1} + 0.0031 \text{ml O}_2 \text{dl}^{-1} \text{mm Hg} \text{PO}_2 \times \text{PO}_2 (\text{mm Hg})
\]

\[
\text{DO}_2 = \text{CO}_2 \times \text{flow} (\text{ml O}_2 \text{min}^{-1})
\]

\[
\text{DO}_2 \text{PV} = \text{CO}_2 \text{PV} \times \text{PVBF} \times 10^{-10} (\text{ml O}_2 \text{min}^{-1})
\]

\[
\text{DO}_2 \text{SMA} = \text{CO}_2 \text{A} \times \text{SMABF} \times 10^{-10} (\text{ml O}_2 \text{min}^{-1})
\]

\[
\text{VO}_2 \text{SI} = (\text{CO}_2 \text{A} - \text{CO}_2 \text{PV}) \times \text{SMABF} \times 10^{-10} (\text{ml O}_2 \text{min}^{-1})
\]

\[
\text{EO}_2 \text{SI} = \text{VO}_2 \text{SI} / \text{DO}_2 \text{SMA} (\%)
\]

$\text{CO}_2=$Oxygen content; $\text{DO}_2=$oxygen delivery; $\text{DO}_2 \text{SMA}=$superior mesenteric arterial oxygen delivery; $\text{CO}_2 \text{A}=$systemic arterial oxygen contents; $\text{CO}_2 \text{PV}=$portal venous oxygen content; $\text{VO}_2 \text{SI}=$total small intestinal oxygen uptake; $\text{EO}_2 \text{SI}=$total small intestinal oxygen extraction ratio.

$\text{Lactate production of gut}$

\[
\text{DLACG} (\mu \text{mol min}^{-1}) = -((\text{CLACA} - \text{CLACVM}) \times \text{SMABF})
\]

$\text{CLACA}=$arterial lactate concentration; $\text{CLACVM}=$venous mesenteric lactate concentration.

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