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## ORIGINAL ARTICLE

# Effectiveness of epidural analgesia following open liver resection

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## Abstract

**Objectives:** Epidural analgesia is often considered the reference standard for pain relief following major abdominal surgery; however, the provision of analgesia in the context of liver surgery raises unique challenges. This study investigated the effectiveness of analgesia and the postoperative course of patients who did or did not receive epidural analgesia following liver resection.

**Methods:** Data were collected retrospectively on 177 patients who underwent open liver resection between June 2007 and June 2009. Patients were divided into two groups consisting, respectively, of those who received epidural analgesia (Epidural group,  $n = 148$ ) and those who did not (No-Epidural group,  $n = 29$ ).

**Results:** In the Epidural group, 27 patients (18%) required i.v. opiate analgesia on the day of surgery (DoS) or the first postoperative day (POD1). The Epidural group received significantly more i.v. colloid solution on the DoS (median: 1500 ml vs. 750 ml, range: 0–12 000 ml vs. 0–3500 ml;  $P = 0.004$ ) and POD1 (median: 0 ml vs. 0 ml, range: 0–5000 ml vs. 0–1000 ml;  $P = 0.018$ ), and total fluid on the DoS and POD1 combined (median: 6522 ml vs. 5453 ml, range: 2150–21 300 ml vs. 2875–15 886 ml;  $P = 0.032$ ).

**Conclusions:** Epidural analgesia provided inadequate postoperative pain relief in approximately 20% of liver resection patients and was associated with the administration of significantly greater volumes of i.v. colloid solution.

## Keywords

liver resection, epidural, pain control, analgesia

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## Introduction

In the UK, mid-thoracic epidural analgesia is used widely for the provision of pain relief following major upper abdominal surgery. It is considered by many to be the reference standard for postoperative analgesia and is recommended as part of enhanced recovery programmes.<sup>1</sup> Compared with patient-controlled opiate analgesia (PCA), epidural analgesia has been shown to provide

superior postoperative analgesia following intra-abdominal surgery.<sup>2</sup> However, despite numerous randomized, controlled trials (RCTs) and meta-analyses, the effects of epidural anaesthesia and analgesia on other important outcomes, such as mortality and major morbidity, remain unclear. The largest meta-analysis to date, performed by Rodgers and colleagues, concluded that the use of intraoperative neuraxial blockade was associated with significant reductions in postoperative morbidity and mortality.<sup>3</sup> However, two subsequent large RCTs failed to confirm these findings.<sup>4,5</sup>

Although an optimally functioning epidural may provide unrivalled dynamic analgesia in the immediate postoperative period, it is widely recognized that a significant proportion of epidurals function suboptimally or not at all.<sup>6,7</sup> In those patients in whom

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the technique fails, very poorly controlled pain may be experienced for a variable period of time, before an alternative analgesic method is commenced. It follows that respiratory morbidity, in particular, is likely to be more prevalent in patients who experience a prolonged period of extreme pain at this early stage in their recovery.

Epidural-associated hypotension is commonly seen as a result of sympathetic blockade. Intraoperatively, this feature can be useful for the maintenance of low central venous pressure (CVP) during hepatic transection, which has been shown to reduce blood loss and transfusion requirements.<sup>8</sup> However, in the postoperative period, attempts to ensure adequate circulating volume may lead to the administration of excessive volumes of i.v. fluids. The complications of gross fluid overload are well known.<sup>9</sup> Two randomized trials in patients undergoing elective colorectal surgery have demonstrated that the administration of only moderately excessive volumes of i.v. fluids is associated with poorer outcome in terms of complication rate and length of hospital stay, compared with more restricted regimes.<sup>10,11</sup> Judicious use of vasoactive drugs may circumvent the problem of epidural-associated hypotension, but in practice it is not uncommon for patients to receive significant volumes of i.v. fluids before these are commenced. Epidural-associated hypotension is known to often limit the mobilization of patients in the immediate postoperative period.<sup>12</sup>

Finally, the most serious potential complications of epidural insertion are epidural haematoma or abscess formation and their associated neurological sequelae. Although these complications are fortunately extremely rare,<sup>13</sup> they can be disastrous for affected individuals. In the context of liver resection, in which a period of postoperative coagulopathy is commonly seen, this issue merits special consideration.

The aims of this audit were: to determine the rate of epidural catheter insertion in patients undergoing open liver resection at the Royal Infirmary of Edinburgh; to evaluate the effectiveness of the technique in providing postoperative analgesia in these patients; to establish whether the use of epidural analgesia has any influence on postoperative fluid administration, and, finally, to determine the frequency with which coagulopathy impacts on the management of epidurals in the postoperative period.

## Materials and methods

Data were collected retrospectively from case notes of patients who underwent liver resection at the Royal Infirmary of Edinburgh between June 2007 and June 2009 as part of an ongoing clinical audit. A standardized data collection form was used. Variables recorded included patient characteristics (age, gender, diagnosis, co-morbidities), surgical, anaesthetic and intraoperative details, postoperative analgesia and i.v. fluids received, reasons for delay in epidural catheter removal, complications, and overall length of hospital stay. Diabetes, hypertension, ischaemic heart disease, cerebrovascular disease, peripheral vascular disease, chronic obstructive airways disease, cirrhosis and obesity were all

considered major co-morbidities, and the presence of any of these in each patient was noted. All patients underwent a right subcostal incision which was extended upwards to the midline or across the midline to the left subcostal region depending on the type of resection and the patient body habitus. Resection was defined as major or minor, with minor resections comprising one or two segments, and major resections comprising three or more segments. Intravenous fluid administration in the early postoperative period was intended to maintain fluid balance and patients received 100 ml i.v. fluid per hour. However, there was no standard protocol in our high-dependency unit (HDU) regarding the type and volume of fluid administered to manage oliguria and hypotension. Hypotension was defined as a systolic blood pressure of <100 mmHg. Pneumonia was defined by clinical or radiographic evidence of consolidation, with a positive sputum culture. Microbiological confirmation was required for all types of infectious complications.

A mid-thoracic epidural was inserted, aimed at placement at the T7–8 interspace by reference to C7. All attempts at epidural insertion were noted, including those that were unsuccessful. Reasons for not attempting epidural insertion were documented where available. In the postoperative period, epidural analgesia was continued with an epidural infusion of bupivacaine and fentanyl. In the HDU, care and monitoring includes regular pain scoring and block height checks, and standing orders exist for response to ascending block/increasing motor block and poor pain scores.

Epidural failure was defined by the requirement for opiate PCA to commence on the day of surgery (DoS) or the first postoperative day (POD1). Institutional protocol requires that patients with epidurals must be nursed within a level 1 facility. For operational reasons this means that epidurals are run for a maximum of 48–72 h postoperatively. After discontinuation of epidural administration, step-down analgesia is managed with a combination of oral and parenteral opiates as required. Therefore, the commencement of PCA within 48 h of surgery is a reliable marker of epidural failure.

The majority of patients in whom epidural insertion was not attempted or was unsuccessful were managed with opiate PCA for the first 48–72 h postoperatively, before being stepped down to oral opiate analgesia. Opiate analgesia was deemed necessary to provide adequate analgesia for large upper abdominal incisions, but the i.v. route was preferred until the oral route was established. In a number of these patients, continuous wound infiltration with local anaesthetic was used to complement opiate PCA. A small number of patients were managed with oral opiate analgesia alone from the DoS.

In the analysis of postoperative course, patients were grouped into those with a functioning epidural at the start of the surgical procedure (Epidural group), and those without (No-Epidural group); analysis was undertaken on an intention-to-treat basis. Postoperative days were defined as beginning and ending at 08.00 h each day.

At the end of infusion, epidural catheters were removed according to local protocol, when the INR (international normalized ratio) was  $\leq 1.5$ . Any delay in epidural catheter removal was documented.

All data were entered into a database using Microsoft Access 97. Data were analysed using SPSS for Windows Version 15.0 (SPSS, Inc., Chicago, IL, USA). Mann–Whitney and Fisher's exact tests were used as appropriate. Data are presented as medians (ranges) except where stated otherwise.

## Results

### Epidural insertion rate

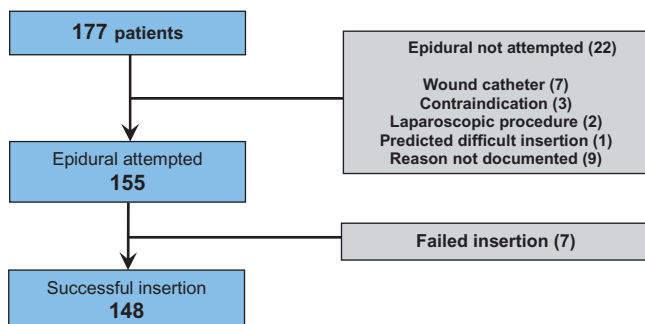
During the 2-year study period, 190 patients were submitted to liver resection. Complete data were available for 177 (93%) of these. Of these 177 patients, epidural insertion was attempted in 155 (88%) and was unsuccessful in seven (5%) (Fig. 1). Reasons for not attempting epidural insertion included contraindications to the technique and the piloting of alternative techniques (e.g. local anaesthetic wound catheter). For nine patients, no contraindications or explanations for the lack of epidural attempt were documented in the case records.

### Epidural efficacy

Of the 148 patients in whom an epidural was inserted successfully, nine (6%) experienced inadequate analgesia and required i.v. opiate PCA to be commenced on the DoS; a total of 27 patients (18%) required i.v. opiate PCA by POD1 (Fig. 2). The reasons for epidural failure were inadequate block ( $n = 10$ ), dislodged or leaking catheter ( $n = 7$ ), and not documented ( $n = 10$ ).

### Postoperative course

In the analysis of the postoperative course, the study group comprised 145 patients in whom epidural insertion was successful at the start of surgery. Three (2%) patients were excluded from this group as unusual circumstances precluded a 'standard' postoperative course: two patients underwent liver resection combined with a partial gastrectomy or right hemicolectomy, and one patient suffered an on-table cardiac arrest related to resuscitation for haemorrhage. In 29 of the original 177 patients (16%), epidural



**Figure 1** Flow diagram demonstrating outcome following attempted epidural catheter insertion in patients undergoing liver resection

analgesia was either not attempted or was unsuccessful at the start of surgery; these patients represented the control group. Both groups were well matched in terms of patient characteristics and intraoperative details (Table 1). Although a greater proportion of patients in the Epidural group underwent major resection, no difference was demonstrated in estimated blood loss or the volume of intraoperative i.v. fluids administered (Table 1).

### Hypotension

In the early postoperative period, patients in the Epidural group were three times more likely to suffer one or more hypotensive episodes requiring i.v. fluid bolus administration on the DoS or POD1 than those in the No-Epidural group ( $n = 111$ , 77% vs.  $n = 7$ , 24%;  $P < 0.001$ ).

### Intravenous fluid administration

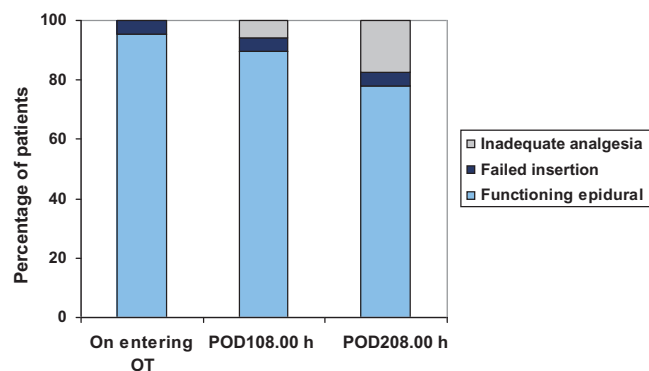
Analysis of i.v. fluid administration demonstrated that patients who received epidural analgesia were given significantly more i.v. colloid solution on the DoS (median: 1500 ml vs. 750 ml, range: 0–12 000 ml vs. 0–3500 ml;  $P = 0.004$ ) and POD1 (median: 0 ml vs. 0 ml, range: 0–5000 ml vs. 0–1000 ml;  $P = 0.018$ ), and total fluid on the DoS and POD1 combined (median: 6522 ml vs. 5453 ml, range: 2150–21 300 ml vs. 2875–15 886 ml;  $P = 0.032$ ) (Fig. 3). There was no significant difference in volumes of i.v. crystalloid solution received between the Epidural group and the No-Epidural group on the DoS (median: 3125 ml vs. 3000 ml, range: 1079–7840 ml vs. 1625–4750 ml;  $P = 0.782$ ) or POD1 (median: 1920 ml vs. 1443 ml, range: 0–4625 ml vs. 250–2975 ml;  $P = 0.265$ ).

### Epidural catheter removal

Epidural catheter removal was delayed for 1–3 days as a result of coagulopathy in 22 (15%) patients. No patients developed an epidural haematoma or abscess.

### Complications

Postoperative complications are shown in Table 2. In the No-Epidural group, one patient developed a myocardial infarct-



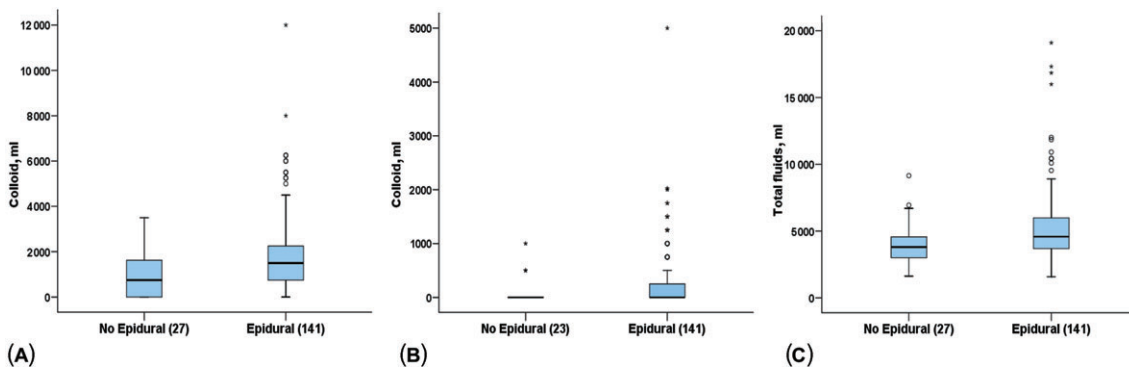
**Figure 2** Adequacy of epidural analgesia in 155 patients following liver resection. OT, operating theatre; POD, postoperative day

**Table 1** Baseline characteristics and intraoperative details of patients who did and did not receive epidural analgesia

	No epidural (n = 29)	Epidural (n = 145)	P value
Patient characteristics			
Median age (range), years	64 (33–80)	61 (19–84)	0.437
Male gender, n (%)	14 (48.3)	76 (52.4)	0.684
ASA physical status, n (%)			
I	1 (3.4)	21 (14.5)	0.034
II	19 (65.5)	96 (66.2)	
III	7 (24.1)	21 (14.5)	
IV	1 (3.4)	0	
Unknown	1 (3.4)	7 (4.8)	
Number of co-morbidities <sup>a</sup> , n (%)			
0	10 (34.5)	78 (53.8)	0.293
1	10 (34.5)	35 (24.1)	
2	6 (20.7)	23 (15.9)	
≥3	3 (10.3)	9 (6.2)	
Indication for surgery, n (%)			
Colorectal metastases	14 (48.3)	92 (63.4)	0.081
Hepatocellular carcinoma	5 (17.2)	17 (11.7)	
Cholangiocarcinoma	0	10 (6.9)	
Other malignancy	2 (6.9)	10 (6.9)	
Benign disease	8 (27.6)	16 (11.0)	
Smoking status, yes, n (%)	3 (13.8)	30 (20.7)	0.608
Intraoperative data			
Median operating time (range), min	180 (50–435)	230 (50–735)	0.041
Extent of hepatic resection, n (%)			
≤2 segments	20 (69.0)	61 (42.1)	
≥3 segments	9 (31.0)	84 (57.9)	
Median blood loss (range), ml	775 (25–2000)	800 (25–15 000)	0.399
Median intraoperative fluids (range), ml	2000 (600–4500)	2100 (500–14 400)	0.068

<sup>a</sup>Diabetes, hypertension, ischaemic heart disease, cerebrovascular disease, peripheral vascular disease, chronic obstructive airways disease, cirrhosis and obesity

ASA, American Society of Anesthesiologists



**Figure 3** Volume of i.v. fluids received following liver resection. (A) Colloid solution administered on the day of surgery (DoS) ( $P = 0.004$ ). (B) Colloid solution administered on postoperative day 1 (POD1) ( $P = 0.018$ ). (C) Total colloid and crystalloid solution administered on the DoS and POD1 ( $P = 0.032$ ). IQR, interquartile range

**Table 2** Postoperative complications following liver resection in patients who did and did not receive epidural analgesia

	No epidural (n = 29)	Epidural (n = 145)
Complications, n (%)		
Any	4 (13.8)	53 (36.6)
General		
Cardiovascular <sup>a</sup>	2 (6.9)	8 (5.5)
Infective <sup>b</sup>		
Pneumonia	1 (3.4)	14 (9.7)
Wound	0	5 (3.4)
Other	0	2 (1.4)
Encephalopathy	0	2 (1.4)
Ascites	0	3 (2.1)
Ileus	0	6 (4.1)
Multi-organ failure (and death)	0	2 (1.4)
Other	1 (3.4)	10 (6.9)
Technical		
Postoperative haemorrhage	0	3 (2.1)
Bile leak/collection	1 (3.4)	9 (6.2)
Other	0	1 (0.7)

<sup>a</sup>Includes arrhythmia, myocardial infarction, pulmonary oedema

<sup>b</sup>Clinical and microbiological diagnosis

tion following air embolus, which occurred as a result of a broken central line port. In the Epidural group, one patient with pulmonary oedema required diuretic administration, and one patient demonstrated epidural-mediated bradycardia. There was no significant difference in the rate of postoperative pneumonia between those who received epidural analgesia, and those who did not ( $n = 14$ , 9% vs.  $n = 1$ , 3%;  $P = 0.471$ ).

## Discussion

Epidural delivery is a popular choice for the provision of analgesia following liver resection. However, this audit has demonstrated some of the problems associated with the technique. Catheter insertion proved technically impossible in 5% of patients and failed to provide adequate analgesia in a fifth of those in whom it was successful. These results are consistent with previously reported findings in large series of patients.<sup>6,7</sup> All the epidurals in this study were sited by anaesthesia consultants with specialist expertise in hepatobiliary anaesthesia or by senior trainees under their supervision. Unsuccessful epidural insertion by a trainee prompted a further attempt by the consultant. It seems therefore that, despite best efforts, a proportion of epidurals simply will not work.

Hepatic resection inevitably requires a large upper abdominal incision. Although the type of incision used in this study was not standardized, a mid-thoracic epidural would provide a sensory block bilaterally across the upper abdomen for all variations used.

The exact size and orientation of any incision within the upper abdomen is likely to be less important, provided that the quality of the block achieved is good.

Re-siting poorly functioning epidural catheters may allow for the subsequent attainment of excellent pain relief; however, as McLeod *et al.* point out, increasing time pressures imposed on appropriately trained staff outside the normal working day often limit opportunities for replacing catheters.<sup>7</sup> The timing of thromboprophylactic heparin administration may preclude epidural replacement. In addition, in the context of liver resection, in which coagulation may be further disordered postoperatively, the removal and replacement of poorly functioning epidural catheters carries potential risk. Indeed, a small but significant proportion of patients in this study experienced coagulopathy that necessitated a delay in the removal of their epidural catheter, which highlights the unique considerations that must be taken into account in this type of surgery.

The effects of epidural analgesia on the sympathetic nervous system can be both advantageous and disadvantageous. Intraoperatively, epidural analgesia is often used, in combination with other techniques, to maintain a low CVP. This has been shown to reduce blood loss, keep the surgical field dry and reduce transfusion requirements.<sup>8</sup> However, in the postoperative period, if patients are not looked after as intensively by people with the same level of expertise as they are when under anaesthesia, problems may occur.

Postoperative hypotension, requiring fluid bolus administration, has been shown to occur in over 75% of patients with epidural analgesia, which corresponds to the administration of significantly greater volumes of i.v. colloid solution in these patients than in those without an epidural. This study was not adequately powered to assess the effect of this on postoperative complication rates, but the dangers of excessive i.v. fluid administration have been well documented.<sup>9</sup> Suboptimal postoperative fluid prescribing has been recognized as a problem for some time, for which a lack of knowledge and experience on the part of those prescribing the fluids are cited as the most common reasons.<sup>14</sup> No standard protocol was followed for the prescription of fluids in this study. Within the institution in which this study was performed, modern working practices have led to the prescription of i.v. fluids by staff from a mixture of surgical, anaesthetic and medical backgrounds, with varying levels of experience and different degrees of appreciation of normal post-surgical physiology.

Judicious use of vasoactive drugs such as ephedrine may significantly ameliorate the problem of epidural-associated hypotension, but, in reality, these are often only commenced after a significant volume of i.v. fluid has been administered. If these are not used pre-emptively prior to mobilization, attempts to mobilize patients with epidurals in the early postoperative period can be limited by postural hypotension and may often result in the administration of more i.v. fluid.

It should be possible to reduce the incidence of epidural-associated hypotension by improving education about normal

post-surgical physiology and the appropriate use of fluids, by running epidurals at slightly lower rates and by the appropriate use of vasoactive drugs. However, this requires a coordinated effort by surgical and anaesthetic staff, and the pain team service. Many of the problems with epidural-associated hypotension occur at night when emergency team cover and such expertise are not readily available. As might be expected with a study of this small size, there were no recorded cases of epidural haematoma or abscess formation, as both are, fortunately, exceptionally rare. However, risk for these complications does exist and must be borne in mind every time epidural analgesia is offered.

## Conclusions

Mid-thoracic epidural analgesia is advocated by enhanced recovery programmes following major abdominal surgery as it provides superior dynamic analgesia compared with opiate PCA. However, this study has demonstrated that the technique is not without problems. A more co-ordinated approach to the management of epidural-related hypotension might limit excessive fluid administration. Alternative local anaesthetic techniques such as wound catheters might provide the benefits of regional anaesthesia without extensive sympathetic blockade, and could be incorporated into multimodal analgesic regimes as part of enhanced recovery programmes.

## Conflicts of interest

None declared.

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