

# Benefit and outcome after epidural analgesia

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## Key points

Epidural analgesia with a combination of local anaesthetic and opioid can provide complete dynamic analgesia.

Epidural analgesia obtunds the stress response to major surgery.

Epidural analgesia can reduce the incidence of postoperative pulmonary, thromboembolic and cardiac complications.

As part of a multimodal recovery programme, epidural analgesia can enhance the quality of patient recovery from major surgery and shorten hospital stay.

With careful patient selection and supervision by an acute pain service, the risk of serious complications from epidural analgesia should be far outweighed by the benefits in high-risk patients undergoing major surgery.

Epidural analgesia is considered by many as the gold standard analgesic technique for major surgery. It has the potential to provide suitable patients with complete analgesia for as long as the epidural is continued. This is usually achieved with a combination of epidural local anaesthetic and an opioid. Epidural techniques are particularly effective at providing dynamic analgesia, allowing the patient to mobilize and resume normal activities unlimited by pain. Parenteral opioids, even with patient-controlled delivery systems, cannot predictably provide the same quality of analgesia. In particular, pain on movement (dynamic analgesia) is generally less well controlled.

One of the major issues of concern to patients presenting for major surgery is analgesia, and an epidural technique can be recommended on these grounds alone. However, the benefits of epidural anaesthesia and analgesia are not limited to pain relief, and this article will discuss the benefits and potential complications of epidural analgesia in high-risk patients presenting for major surgery.

## Potential benefits of epidural analgesia

### Attenuation of the stress response

Morbidity and mortality as a result of apparently uncomplicated major surgery is related to the cascade of effects that result from 'surgical injury' and pain. This 'stress response' results from activation of neural, metabolic and endocrine pathways with initiation of coagulation and inflammatory mechanisms. This can lead to sequelae such as myocardial ischaemia and infarction, thromboembolic phenomena, impaired pulmonary function, ileus, fatigue, muscle catabolism, postoperative infection and postoperative confusional states in susceptible individuals.

The occurrence of postoperative pain is inextricably linked to this inflammatory and stress response. It is postulated that the beneficial effects of epidural analgesia result from attenuation of the stress response and

the provision of good analgesia. High-dose opioid analgesia may also obtund the stress response during operation. However, until remifentanyl became available, the use of this technique resulted in postoperative respiratory depression necessitating ventilation.

Stimulation of the stress response is not limited to the intraoperative period but persists after operation. The continuation of epidural analgesia during this time extends these beneficial effects. Although systemic opioids can provide excellent pain relief in some patients, side-effects, in particular respiratory depression, limit the dose that can be given. This results in suboptimal analgesia for some patients.

### Pulmonary function

Epidural opioids and local anaesthetic infusions have been shown to reduce the incidence of postoperative atelectasis and pulmonary infection and improve postoperative oxygenation. Postoperative pulmonary dysfunction results from a number of factors, including impaired central ventilatory control, deranged pulmonary mechanics and alterations of ventilation/perfusion matching. The improvements resulting from epidural analgesia may be due to a number of factors:

- effective pain relief allowing the patient to take deep breaths, cough and cooperate with physiotherapy;
- blocking of reflexes inhibiting diaphragmatic function, demonstrable after abdominal and thoracic surgery, is likely to have a beneficial effect on pulmonary mechanics;
- avoidance of high-dose systemic opioids should reduce respiratory depression; and
- reduction of the stress response to surgery reduces the level of postoperative immunosuppression, which may contribute to a reduction in pulmonary infection.

### Cardiovascular

Postoperative epidural analgesia reduces the incidence of postoperative myocardial infarction.

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tion. A number of effects should improve the myocardial oxygen supply demand ratio and hence contribute to this effect:

- reduction of sympathetic activity;
- improved postoperative pulmonary function; and
- reduced thrombotic tendency.

### Thromboembolic complications

Epidural analgesia attenuates the hypercoagulable response to surgery and improves fibrinolytic function by attenuating the stress response. Increased postoperative mobility facilitated by effective analgesia will also play a role.

Studies in patients undergoing orthopaedic procedures have shown a reduced incidence of deep venous thrombosis in patients receiving epidural anaesthesia and analgesia rather than general anaesthesia and opioids. This beneficial effect on coagulation/fibrinolysis has also been shown to improve graft outcome after lower limb revascularization procedures under epidural rather than general anaesthesia.

### Gastrointestinal function

Pain, sympathetic activity and systemic opioids all contribute to the maintenance of postoperative ileus. The result is a nauseated patient unable to drink and eat, often with a more prolonged hospital stay attendant on return of normal bowel function. In addition, the catabolic effects of the stress response in conjunction with lack of nutrition results in loss of muscle and postoperative weakness. The catabolic effect is also likely to contribute to postoperative immunosuppression and poor wound healing. Epidural analgesia, by limiting systemic opioid use and improving intestinal motility by blocking nociceptive and sympathetic reflexes, reduces the duration of postoperative ileus, permitting earlier enteral feeding. This in turn has a beneficial effect on postoperative catabolism. The combination of epidural analgesia and early postoperative feeding has been shown to reduce postoperative negative nitrogen balance and muscle wasting and to preserve total body protein. This contributes to improved postoperative exercise tolerance, muscle strength and wound healing.

### Intraoperative blood loss

Intraoperative neuraxial block has been shown to reduce the requirement for blood transfusion. Blood transfusion is associated with several potential problems and possibly an increased risk of recurrence in cancer surgery.

### Evidence of improved outcome

A number of studies have investigated the effect of epidural analgesia on outcome after surgery. In 1987, Yaeger and colleagues undertook a randomized controlled trial of high-risk surgical patients, comparing epidural anaesthesia and analgesia with standard general anaesthesia and systemic opioid analgesia. They demonstrated a reduction in postoperative complications in

the epidural group and a significant reduction in perioperative mortality. The study was terminated early as a result of these findings, and it has been criticized because of the small numbers of patients in each group. The methodology has also been criticized, and subsequent studies have failed to replicate the results.

More recently, a meta-analysis of the effects of neuraxial blocks (spinal and epidural) on postoperative mortality also showed a benefit; postoperative mortality was reduced by 30% in patients receiving blocks. Almost 10,000 patients included in 141 randomized controlled trials were analysed. However, the majority of fatalities occurred in a fairly small number of the studies involving a minority of the total number of patients. This has raised concerns over the ability to extrapolate these results into clinical practice.

In an attempt to resolve the issue, Rigg and colleagues performed a prospective randomized controlled trial of epidural anaesthesia and analgesia versus general anaesthesia and postoperative systemic opioids in high-risk patients undergoing major surgery (MASTER study). Epidural analgesia was continued for 3 days after operation. The local surgical and anaesthetic teams determined all other postoperative care. Once again, there was no difference in overall mortality between the groups. However, they did show a reduced incidence of pulmonary complications and thromboembolic events and significantly better analgesia in the epidural group.

Given the proven benefits of epidural analgesia, why can't we show an improvement in outcome? There are several possible reasons for this. Firstly, as a result of current surgical, anaesthetic and intensive-care practice, mortality rates from major surgery, even in high-risk patients, are small. Therefore, the use of mortality as an end-point may not be appropriate. Even a study with almost 1,000 patients may not be adequate to demonstrate an effect. Rather than mortality, we should be assessing quality of recovery and return to normal function. These are more difficult to measure but are more likely to demonstrate the benefits of epidural analgesia. A surrogate end-point for these could be length of hospital stay.

Secondly, to provide the beneficial effects, epidurals have to work. In a recent audit of 600 sequential epidurals sited for postoperative analgesia, McLeod and colleagues demonstrated failure to provide good analgesia for the intended duration of the block in one-third of patients. There were a variety of reasons for this:

- Technical problems (*e.g.* leaks, catheters falling out, patchy or unilateral blocks, and catheter occlusions).
- Lack of facilities to care for patients with epidurals. Because of the potential complications of epidural analgesia, many centres undertake postoperative care of these patients in a high-dependency area. At times when there is high demand for these beds, patients may not receive epidurals or may have them discontinued prematurely.
- Lack of acute pain practitioners with sessional time for acute pain management also compounds the technical failures. In particular, it may not be possible to resite epidurals promptly if indicated. McLeod describes successful epidural analgesia in a

few patients who did have epidurals resited. Similarly, if there are delays in topping up epidurals because of lack of personnel, patients may suffer excessive pain.

It is of note that in the epidural cohort of the MASTER study, only 50% of patients achieved satisfactory epidural analgesia for the intended duration of the block; and as the study was analysed on an intention-to-treat basis, those patients for whom epidural analgesia could not be provided were included in the epidural arm of the analysis.

Thirdly, and probably most importantly, the provision of good analgesia alone is not the only factor involved in postoperative recovery. Henrik Kehlet and his group in Copenhagen have pioneered enhanced recovery programmes after major surgery, especially colorectal. The approach is multimodal and involves four main factors, limiting the stress response to surgery, analgesia, mobilization and nutrition. These are achieved by

- limiting surgical injury as far as possible (*e.g.* using laparoscopic techniques where practical);
- maintaining intraoperative normothermia;
- limiting factors likely to contribute to ileus (*e.g.* high-dose systemic opioids, excessive fluid and sodium loading, and prolonged fasting);
- limiting postoperative catabolism by obtunding the stress response with intraoperative epidural analgesia and remifentanyl, limiting preoperative fasting times and allowing early enteral nutrition after operation; and
- early postoperative mobilization (patients are sitting out of bed on the day of surgery and actively mobilizing the following day).

With this postoperative care package, of which effective epidural analgesia is an essential but not the only part, Kehlet's team have demonstrated significant benefits in terms of postoperative recovery. In a study of 60 consecutive patients undergoing colonic resection, they were able to discharge patients home after a median postoperative stay of 2 days. Patients reported an earlier return to normal activities and less fatigue than in patients undergoing equivalent surgery but not participating in such a perioperative care programme.

A similar approach has been used effectively for oesophagectomy with patients managed in an enhanced recovery programme including thoracic epidural analgesia, parenteral nutrition and active mobilization. These patients demonstrated earlier return of gut function, reduced catabolism and earlier extubation and discharge from the intensive-care unit than an equivalent retrospective group undergoing the same procedure, including thoracic epidural analgesia but not included in a multimodal care programme.

## Complications of epidural analgesia

If we are to recommend epidural analgesia to our patients, we need to consider the risks as well as the benefits (Table 1).

**Table 1** Incidence of complications of epidural analgesia

Complication	Reported incidence (%)
Related to catheter insertion	
Dural puncture	0.32–1.23
Neurological damage (usually transient)	0.016–0.56
Related to catheter in situ	
Epidural haematoma	0.0004–0.03
Epidural abscess	0.01–0.05
Catheter migration	0.15–0.18
Related to epidural drugs	
Drug errors	Not known
Respiratory depression	0.13–0.4
Hypotension	3–30
CNS toxicity	0.01–0.12
Motor block	3

In order to reduce the incidence of potentially serious complications, patients must be carefully selected for epidural analgesia. The technique should be avoided if patients have disturbed coagulation. Similarly, protocols must be in place to direct the safe combination of thromboembolic prophylaxis and epidural catheter placement. (The relationship of anticoagulant therapy and epidural complications is discussed specifically in another article in this issue.) Epidurals are contraindicated in overtly septic patients and should be used with care in patients who are immunocompromised. Retaining epidural catheters in situ for longer than 3 days is likely to increase the risk of epidural abscess formation.

In centres where epidural analgesia is in common use and an acute pain service supervises their management, the complication rate has been shown to be the same as that for other forms of analgesia, such as patient-controlled analgesia, in patients after major surgery. In both the MASTER trial and McLeod's study, there were no serious complications in approximately 1,500 epidurals. McLeod also showed that complications such as hypotension and respiratory depression were more common in patients who generally had poor analgesia and require a significant number of top-ups. Perhaps this should lead to early resiting of such epidurals.

For high-risk patients and patients undergoing high-risk surgery, the risk-to-benefit ratio is in favour of epidural anaesthesia, provided there are no specific contraindications. For fit patients undergoing less major surgery, the small risk of serious morbidity is likely to outweigh the benefits.

## Conclusions

Epidural analgesia can be provided safely in appropriate patients undergoing major surgery. It offers a number of proven benefits as a result of pain relief and obtunding the stress response. Epidural analgesia has not been convincingly shown to alter postoperative mortality. However, as part of a multimodal perioperative care programme, it has been shown to improve the quality of patient recovery and reduce the incidence of serious complications. In

addition, an epidural should provide excellent analgesia; this is a major concern of patients and is demonstrated in all the major trials.

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See multiple choice questions 33–35.