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Risks and benefits of thoracic epidural anaesthesia

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Editor's key points

- Thoracic epidurals are used widely for intraoperative- and postoperative pain control.
- Perceived benefits such as improved outcome, lower mortality and morbidity, and better gastrointestinal function are likely but difficult to prove.
- The major risks of bleeding and infection are now better quantified and understood.
- The authors conclude that the benefits outweigh the risks if guidelines are followed.

Summary. Thoracic epidural anaesthesia (TEA) reduces cardiac and splanchnic sympathetic activity and thereby influences perioperative function of vital organ systems. A recent meta-analysis suggested that TEA decreased postoperative cardiac morbidity and mortality. TEA appears to ameliorate gut injury in major surgery as long as the systemic haemodynamic effects of TEA are adequately controlled. The functional benefit in fast-track and laparoscopic surgery needs to be clarified. Better pain control with TEA is established in a wide range of surgical procedures. In a setting of advanced surgical techniques, fast-track regimens and a low overall event rate, the number needed to treat to prevent one death by TEA is high. The risk of harm by TEA is even lower, and other methods used to control perioperative pain and stress response also carry specific risks. To optimize the risk–benefit balance of TEA, safe time intervals regarding the use of concomitant anticoagulants and consideration of reduced renal function impairing their elimination must be observed. Infection is a rare complication and is associated with better prognosis. Close monitoring and a predefined algorithm for the diagnosis and treatment of spinal compression or infection are crucial to ensure patient safety with TEA. The risk–benefit balance of analgesia by TEA is favourable and should foster clinical use.

Keywords: cardiovascular risk; epidural anaesthesia; infection; intestinal; bleeding

Thoracic epidural anaesthesia (TEA) has been established as a cornerstone in the perioperative care after thoracic and major abdominal surgery providing most effective analgesia.[1 2] Beyond its analgesic properties, TEA's effects on the postoperative neurohumoural stress response, cardiovascular pathophysiology, and intestinal dysfunction have been in the focus of both clinical and experimental investigations for years.[3–7] However, the use of TEA is related to specific complications and contraindications.

This review aims to outline the risks of TEA and its benefits with respect to the perioperative pathophysiology, outcome, and organ protection.

Increased sympathetic activity and the stress response

The increased sympathetic activity associated with injury induces distinct changes in the host's hormonal and immune response and in the coagulation system.[8–11] These highly conserved defence mechanisms can turn against the host in the case of coexisting cardiovascular disease.[12] A number of synergistic mechanisms are involved in cardiac complications during stress. Increased catecholamine levels increase left ventricular afterload and heart rate, while decreasing the time for coronary perfusion.[13] Altered and stenotic coronary arteries do not respond to sympathetic stimulation.[14] Raised corticotropin-releasing hormone levels reduce cardiac NO release and increase endothelin production. This aggravates coronary endothelial dysfunction.[15] After both minimally invasive and major open surgery increased serum levels of stress hormones have been recorded.[7 16 17] Stress induces a pro-coagulatory state in the absence of any trauma.[18] This effect is prolonged with increasing age and may persist for weeks after surgery.[17 19–21] Finally, early after stressful events, a pro-inflammatory response may lead to plaque instability via activation of matrix metalloproteinases.[22 23] This triad triggers acute coronary syndrome and myocardial infarction during and after stressful events. Consequently, cardiovascular causes account for 63% of perioperative mortality in a high-risk patient population and are still responsible for 30% of perioperative mortality in low-risk patients.[24]

TEA and sympathetic block

A segmental temporary sympathetic block during TEA is assumed to be an important mediator of the perioperative effects of TEA.[13 25] However, both clinical and experimental data on sympathetic activity during TEA need careful interpretation. Methodological problems limit objective assessment of sympathetic activity in the perioperative

period.[26] Microneurography allows a direct and quantitative insight into sympathetic activity. It is, however, an invasive technique and limited in spatial resolution.[27–29] Indirect techniques such as skin conductance response and heart rate variability rely on altered effector organ function during a sympathetic block.[26 27 30] Most measurements are based on the assessment of skin perfusion. This, however, may be affected by the microvascular anatomy, emotional and thermoregulatory state, or presence of general anaesthesia.[27 31 32]

There are limited data on the presence and segmental spread of a thoracic sympathetic block during TEA. Altered skin temperature regulation was shown by thermography in TEA[33] and a cardiac sympathetic block was demonstrated for 6 days during TEA after oesophagectomy.[34] It is unclear whether the sympathetic block is characterized by a limited segmental spread during TEA. This is based on experimental findings in animals demonstrating a segmental sympathetic block with compensatory increase in sympathetic activity in the unblocked area.[29] In humans, a sympathetic block involving splanchnic and lower limb nerves occurred during a limited upper thoracic sensory block with high TEA after injection of 4.2 ml of 0.75% bupivacaine.[35] Midthoracic TEA with 10 ml of 0.25% bupivacaine induced a thoracic sympathetic block that included the legs.[33] In contrast, only segmental sympathetic block was found with a high thoracic TEA using 4 ml bupivacaine 0.5%.[27] The concentration and volume of the local anaesthetic may determine the intensity and the limits of the sympathetic block.[35 36]

Anti-ischaemic effects of TEA in cardiac and non-cardiac surgery

TEA has been shown to decrease adverse perioperative cardiac events.[3 37] Better pain relief with concomitant reduction in the postoperative stress response and systemic sympathetic activity may contribute to this effect.[1 38 39] Regional sympathetic block including the cardiac sympathetic nerves reduces not only ischaemic pain but preserves coronary perfusion during cold pressor testing. This effect was most pronounced in stenotic vessels.[40 41] These data support findings of perioperative anti-ischaemic effects of TEA in both cardiac and non-cardiac surgery. TEA improved diastolic function in patients with coronary artery disease undergoing operative revascularization.[42] Diastolic dysfunction has been reported to be an early sign of cardiac ischaemia. While in this study no effect on systolic function was recorded, an earlier study showed improved systolic function and wall motion in coronary artery disease. Troponin release and long-term survival after coronary artery bypass grafting underline the cardioprotective potential of TEA in that study.[43] In experimental myocardial ischaemia, TEA reduced infarct size.[13] Clinical data on myocardial ischaemia and mortality are inconclusive. In a randomized trial, TEA did not reduce the 30 day complication rate after cardiac surgery.[44] In this study, TEA was only used for <24 h in most patients. In contrast, after off-pump coronary artery bypass grafting, TEA used for 72 h reduced arrhythmia and improved postoperative pain control and recovery.[45] The biggest prospective trial of the outcome effects of TEA did not show a survival benefit.[46] However, the trial is underpowered to show the moderate outcome effect of TEA, and interpretation of the results may be compromised.[47] Some meta-analyses suggest that TEA may decrease cardiac morbidity and mortality after cardiac and major non-cardiac surgery.[37 48 49] However, others do not confirm this and emphasize reduced morbidity such as respiratory complication or cardiac arrhythmias after cardiac surgery.[50]

Intestinal perfusion

Safeguarding intestinal perfusion is a critical issue in the maintenance of intestinal function and the integrity of the mucosal barrier. However, the influence of TEA on intestinal perfusion is not understood, with both improvement and deterioration of tissue perfusion being demonstrated.

TEA reversed impaired intraoperative intestinal oxygenation during major surgery and protected intestinal barrier function in experimental hypoxaemia.[51 52] In acute experimental pancreatitis and in sepsis, TEA improved mucosal capillary perfusion.[53 54] In healthy rats, a shift from intermittent to continuous capillary perfusion during mild hypotension was recorded during TEA.[55] Similarly, in patients undergoing oesphagectomy, continuous epidural infusion of bupivacaine without a bolus dose increased anastomotic mucosal blood flow compared with the control group.[56] In these studies, TEA was associated with no or only moderate hypotension. After oesphagectomy, the postoperative increase in cardiac output during the weaning procedure was blunted by TEA, suggesting altered haemodynamic regulation.[56]

However, a number of clinical and experimental studies suggest adverse effects of TEA on measures of intestinal perfusion.[57–60] In 10 patients undergoing oesphagectomy, TEA reduced blood flow in the distal gastric tube mucosa.[61] These studies reported substantial deterioration in systemic haemodynamics. The mean arterial pressure was reduced by 20–50% after induction or during maintenance of TEA.[57 58 60 61] Cardiac output remained stable in one study,[60] but was decreased up to 35% in two.[57 61] Animal studies show that the adverse perfusion effects of TEA are related to an extended or total sympathetic block.[57 58] The clinical study[59] had a sensory block to T4, and as the sympathetic block exceeds the sensory block in epidural anaesthesia, this suggests an almost complete sympathetic block in these patients.[33]

TEA appears to exert beneficial effects on intestinal perfusion as long as its haemodynamic consequences are adequately controlled. The maintenance of systemic perfusion pressure by small doses of norepinephrine has been shown not to compromise intestinal perfusion in experimental abdominal surgery under general anaesthesia.[62] Similarly, systemic hypotension and impaired colonic perfusion after induction of TEA were reversed by vasopressor therapy.[60]

Intestinal motility

After operation, paralytic ileus and abdominal sepsis can be life-threatening and have a major economic impact.[63] Pain, increased sympathetic tone, the use of systemic opioid analgesia, and intestinal neuroinflammatory processes contribute to intestinal hypomotility.[64] The available data on postoperative intestinal function with TEA involve small studies including both thoracic and lumbar epidural anaesthesia, different epidural drug regimens with or without epidural opioids, and covering a wide range of surgical procedures. These studies have been the subject of meta-analyses in the last decade.[65–68] In 2007, a systematic update did not retrieve any major study (group size >100) addressing intestinal function as a primary or secondary outcome.[6] These meta-analyses showed accelerated recovery of intestinal function in all cumulated studies and subsets of studies in major vascular and colorectal surgery.[65 66 68] TEA resulted in a faster resolution of postoperative ileus after major non-intestinal surgery.[69] Epidural infusion of local anaesthetics alone or in combination with opioids was shown to be equally effective in accelerating intestinal recovery and superior to systemic and to epidural opioids alone.[65 70 71] The faster resolution of postoperative ileus after major open surgery has been attributed to superior pain therapy, reduced opioid consumption, and sympathetic block.[6 65]

In the last decade, systemic lidocaine has been studied [72 73] and shown to improve postoperative intestinal motility and hospital stay after surgery.[74 75] Two small studies compared systemic lidocaine with epidural anaesthesia. After colonic surgery, pain control and intestinal recovery were more effective with TEA than with systemic lidocaine.[76] In contrast, a recent study found that both were equally effective.[77] In the latter study, TEA was not used continuously but only started 1 h before the end of the procedure. Furthermore, in many countries the perioperative use of lidocaine for analgesic purposes is unlicensed (off-label-use).

The use of TEA in fast-track and minimally invasive approaches for major procedures has been questioned.[6] Two recent studies of TEA after laparoscopic surgery reported improved bowel motility,[78 79] while another showed no effect.[80] However, differences in the study design, technique of TEA, and the surgical procedures do hinder comparison and interpretation of the data. The faster resolution of ileus was demonstrated on the background of a non-accelerated standard care. Surgery lasted about 3 h and the surgical cases included major resections, such as hemicolectomy, in 12–55%.[78 79] In contrast to this, TEA failed to exert beneficial effects when added to an established fast-track programme after laparoscopic sigmoidal resection with a duration of surgery of 2 h.[80] Pain was significantly lower in the TEA groups in all of the mentioned studies.

Further studies of laparoscopic fast-track regimens are needed to define the role of TEA in comparison with techniques such as transversus abdominis plane (TAP) block or wound catheters and systemic lidocaine infusion.[68] In open upper abdominal surgery, TEA resulted in significantly less opioid consumption compared with a TAP block three times daily.[81] In thoracic and breast surgery, a paravertebral block might be a valuable addition to the portfolio of regional anaesthesia.[82 83] However, similar precautions as in neuraxial anaesthesia must be taken into account.

Anastomotic perfusion and patency

The impact of TEA on anastomotic perfusion and healing of the anastomosis is unclear.

In colorectal surgery, TEA has been found to decrease anastomotic blood flow and to improve gastric and transverse colonic blood flow.[59] After oesphagectomy, reduction in the already compromised mucosal circulation of the proximal end of the gastric tube was more pronounced compared with the distal end.[61] In both studies, however, significant systemic haemodynamic alterations were present. In contrast to this, 1 h (sedated patients) and 18 h (awake and extubated patients) anastomotic mucosal blood flow was increased in TEA after oesophageal resection.[56]

Data on anastomotic patency are also equivocal until today. In 2001, a meta-analysis of 12 clinical trials comparing epidural and systemic analgesia with respect to anastomotic breakdown was unable to show either improved or impaired anastomotic healing due to considerable heterogeneity in the studies.[84] Only two of these studies included more than 30 patients in each group. The drugs used differed between the studies and both lumbar and thoracic epidurals were tested in different surgical procedures. In two larger retrospective case–control studies including 259 mixed gastrointestinal (GI) anastomoses and 400 rectal cancer resections, TEA did not influence anastomotic healing.[85 86]

Recently, TEA was shown to reduce the rate of anastomotic insufficiency after emergency laparotomy.[87] A retrospective analysis of oesophageal anastomosis demonstrated a 70% risk reduction for anastomotic leak in the TEA group.[88] A retrospective analysis of GI surgery found a significantly reduced rate of anastomotic leak.[89] These protective effects might be of great importance in the light of the fivefold increase in mortality in patients with anastomotic leak. However, large randomized controlled trials are needed.

TEA and outcome

TEA provides better pain relief in a wide range of thoracic and abdominal surgery.[1] However, irrespective of better pain control, improvement in the clinical postoperative course by TEA seems to be procedure-specific. While the efficacy of TEA in open colonic resection is well documented, little benefit is reported after hysterectomy.[90] However, in both procedures, TEA significantly improved pain control for up to 2 weeks after surgery.[78–80] Superior pain control and reduced metabolic response are related to an improved quality of life after colonic resection.[91 92] TEA improves the short-term quality of recovery and may affect long-term psychic well being.[45 93] A recent meta-analysis of the pulmonary effects of TEA showed a reduced rate of pneumonia

after TEA, probably due to earlier mobilization, reduced opioid consumption, and improved cough.[94]

A 30% relative risk reduction in fatal outcome was shown after surgery in unselected patients with neuraxial anaesthesia.[3] These findings are in agreement with a retrospective analysis which demonstrated reduced mortality in a TEA group after colectomy or lung resection.[95 96] In cardiac surgery, a meta-analysis showed reduced myocardial ischaemia and mortality and a reduced need for ventilation with TEA for cardiac surgery.[48] While a recent study demonstrated reduced early morbidity after off-pump cardiac surgery, a study including >600 patients with or without epidural anaesthesia during cardiopulmonary bypass did not demonstrate differences in the long-term outcome.[44 45] However, in the latter study, TEA was used only for 24 h. In a very large retrospective analysis in intermediate- and high-risk procedures, TEA resulted in a mild but significant reduction in perioperative mortality.[49]

TEA and tumour spread

Tumour resection is important in the treatment of cancer, but the procedure has significant risks as surgical manipulation promotes systemic spread of tumour cells, which predicts a poor outcome [97 98] Surgical stress impairs the host's immune function and ability to eliminate circulating tumour cells. This includes suppression of natural killer cell function, increased Th2 T-cell activity, and reduced innate immune reactivity.[99] These studies attracted attention to techniques of regional anaesthesia such as TEA or paravertebral block as a potential tool to influence the long-term outcome by perioperative measures.[100]

Four retrospective studies recently demonstrated reduced tumour recurrence rate and improved survival after TEA or paravertebral block.[101–104] Additional retrospective data from colonic surgery suggest that age might influence the effects of TEA on cancer recurrence.[105] The most recent data describe a reduced cancer recurrence only when TEA is used intraoperatively.[106] Prolonged TEA was not better than general anaesthesia alone in this patient population. A disputed *post hoc* analysis of a subpopulation of the MASTER trial patients revealed no difference in oncological outcome.[107] However, there is an urgent need for further scientific effort to clarify this important issue. Morphine has been repeatedly shown to reduce natural killer cell activity and to promote growth in experimental colonic cancer metastasis and experimental breast cancer.[108–111] However, animal experimental data demonstrate that the immunological effects of opioids are only partially understood.[112–115]

Adrenergic response also promotes experimental tumour growth.[116] Social stress increases metastatic growth partially by sympathetic activity.[117] Tumour growth can be prevented by an effective sympathetic block and analgesia in mice.[118] β-Adrenergic inhibition reduces experimental tumour growth, whereas β-adrenergic stimulation increased metastatic growth.[119 120] The observed protective effects of regional anaesthesia might be therefore based on both an opioid-sparing effect and reduced neurohumoral stress response.

Risks of TEA

The benefits of TEA can be demonstrated in large patient populations only. An uneventful perioperative course in a high-risk patient can never be attributed solely to the use of TEA. The procedural complications, however, are highly specific to TEA. Complications can result in severe impairment from spinal cord injury. Consequently, patient safety issues are a dominant aspect in the clinical use and patient perception of TEA. However, the risk of harm as a result of TEA is lower than that of other perioperative treatment strategies. For example, the POISE study of perioperative β-blocker therapy resulted in death or persistent neurological deficit in one of 98 treated patients.[121] This risk greatly exceeds that of TEA, but its manifestations are far more unspecific and usually not clearly related to the therapeutic intervention, which leads to caution in the use of TEA in critically ill patients, despite potential benfits.[122]

Epidural bleeding after TEA

Until today, the risk of bleeding complications both after epidural anaesthesia in general and specifically after TEA is not known. However, there is increasing evidence that the overall number of vertebral canal haematomas after epidural block might be misleading in clinical decision-making. The overall incidence of bleeding within the vertebral canal in the 1990s was 1:18 000 in Sweden.[123] This number, however, includes obstetric epidural patients who have a low risk of vertebral column bleeding after epidural puncture both in the retrospective analysis and in the most recent prospective National Audit Project 3 (NAP3) in the UK.[123 124] The risk of epidural bleeding in the perioperative patient population in the retrospective study was higher, reaching a risk of 1:10 200 for surgical patients,[123] which matches the prospective NAP3 data. In that study, the estimated risk of vertebral canal haematoma ranged between 1:5747 (pessimistic estimation) and 1:12 195 (optimistic estimation) in the perioperative population.[124] In a recent single-centre database analysis, the incidence ranged between 1:2700 and 1:4761.[1 123 125]

These numbers, however, include both lumbar epidurals and TEA. In the Swedish study, haematoma occurred after eight TEAs and 17 lumbar epidural punctures.[123] However, it is not clear how often the respective procedures were performed, and estimation of the risk of TEA is not possible. In NAP3, five of eight bleeding complications occurred after TEA, but again the underlying numbers of TEA and lumbar epidurals are not available. Assuming a less frequent use of TEA, the authors suggest a higher risk of bleeding complications with TEA compared with lumbar epidural block.[124] This is supported by a retrospective analysis of 8100 patients, in which three vertebral column haematomas occurred after TEA but none after lumbar epidural puncture. The total

numbers of the respective procedures, however, are not provided.[125] In contrast, no epidural bleeding was reported in 10 000 cases of TEA, but three occurred after lumbar epidural anaesthesia resulting in a risk of 1:832.[1] Patient age and sex seem to be a major influence in vertebral column haematoma after TEA.[1 123–127] In a case series of 3736 orthopaedic patients, predominantly older women, no bleeding complications were reported.[128] The higher risk for older patients may be related to different causative factors such as reduced epidural space or degeneration of the spine, resulting in more frequent traumatic puncture. However, the higher rate of concomitant use of anticoagulant or antiplatelet drugs in combination with (unrecognized) impairment of renal function may be important. Consequently, the available data allow a reasonable estimation of the overall risk of epidural anaesthesia but do not allow conclusions on the specific incidence of bleeding complications with TEA.

TEA in patients receiving an anticoagulant, antiplatelet, or fibrinolytic drug needs to be performed with caution. The sudden increase in bleeding complications in the presence of twice-daily low-molecular-weight heparin (LMWH) led to the first national guidelines on the use of neuraxial blockade in anticoagulated patients. In 2010, the European guidelines were updated and now cover most recently introduced antiplatelet and anticoagulant drugs.[129] All recommendations refer to patients with normal drug elimination. In patients with (unrecognized) organ dysfunction, for example, renal insufficiency, adapted risk evaluation and careful patient selection are warranted. Glomerular filtration can be assessed from serum creatinine by the simplified equation validated in the Modification of Diet in Renal Disease (MDRD) trial.[130] The higher risk of bleeding after epidural anaesthesia in older women in major studies underlines this necessity.[1 123–126] For example, even mild impairment of renal function increases the time of effective anticoagulation by LMWH from 6.6 to 9.9 h. In severe chronic renal disease, LMWH lasts >15 h.[131] In these patients, a 50% dose reduction in LMWH is required. Most elective surgical cases are not in hospital for more than 1 day before surgery; therefore, prophylactic anticoagulation can be started the evening after surgery.[129 132] This ensures the maximal safety of TEA even in older patients with impaired renal function.

The withdrawal of antiplatelet drugs leads to rebound effects with an increased rate of thromboembolic events.[133–135] This rebound effect is aggravated by the prothrombotic and pro-inflammatory state induced by surgery. Stopping antiplatelet drugs within 3 weeks after stenting results in a mortality of 30–86%.[136] Late stent thrombosis after stopping antiplatelet drugs can occur more than 1 yr after stenting.[137 138] Consequently, a consensus has been reached to continue antiplatelet medication in almost all surgical cases other than in emergency intracranial, spinal, and intraocular surgery, where bleeding is potentially catastrophic and bridging with tirofiban and heparin is recommended.[136] In patients taking acetylsalicylic acid, the European and US guidelines allow neuraxial blockade without restrictions on the timing and dosage.[129 139] In all guidelines, the additional risk of the concomitant use of acetylsalicylic acid and other anticoagulant drug is emphasized.

While acetylsalicylic acid is regarded as safe antiplatelet therapy, thienopyridine derivates such as clopidogrel are not recommended 5–7 days before TEA. This warning is based on the increased incidence of surgical bleeding under thienopyridines and two cases of vertebral column haematoma after a neuraxial block under clopidogrel medication.[129 139 140] Recently, however, a case series of 309 vascular surgery patients treated with lumbar epidural anaesthesia was published.[141] Of them, 217 were on dual platelet aggregation inhibition with additional acetylsalicylic acid. None of these patients showed any sign of epidural or spinal bleeding. There are two cases of epidural catheter removal after commencement of a dual antiplatelet therapy due to postoperative myocardial infarction.[142 143] An uneventful course after spinal anaesthesia during dual antiplatelet therapy has been described.[144] In contrast, a number of case reports of spontaneous spinal haematomas during dual antiplatelet therapy without any anaesthetic manipulation raise serious concerns.[145–147] Additionally, spontaneous spinal haematomas have been described both with clopidogrel and acetylsalicylic acid alone.[140 148] Thus, the case series must not lead to an assumption of safety.

Complications due to infection

TEA is an invasive analgesic technique and as such is inevitably associated with the risk of complications due to infection. Iatrogenic pathogen inoculation and haematogenous infection of the insertion site or the epidural catheter are the potential causes of infection within the vertebral canal.[149] Estimates of incidence vary widely.[149] Recent data from Germany report an incidence of one abscess in 10 000 patients with TEA.[1] In the UK, an incidence of 1:24 000 epidural abscesses was found after perioperative neuraxial blockade with 10 of 13 cases in the study period related to epidural anaesthesia.[124] In paediatric postoperative pain therapy, epidural infections and abscesses are also rare.[150] Epidural abscess with spinal cord and radicular compression is the predominant complication after TEA and usually caused by *Staphylococcus aureus*. Meningitis has also been reported with a lower incidence. It is usually caused by *Streptococcus*.[149 151] Infectious complications may occur as early as day 2 but more commonly from day 4. They may be accompanied by signs of infection at the insertion site but usually present with non-specific symptoms. This frequently results in delayed diagnosis and underlines the necessity of close clinical observation and a high level of suspicion.[124] The prognosis of complications due to infection is better than that for epidural bleeding. All patients with meningitis had full recovery and ~50% of the patients with epidural abscesses recover without permanent disability.[124]

Practical patient safety measures

Recent data from the UK reported delayed diagnosis in four of five cases of epidural haematoma with persistent harm. Only one patient was treated in time and reached full recovery.[124] Renal function must be checked in patients receiving TEA to detect any impairment. As catheter removal is a critical phase which may trigger epidural bleeding, neurological monitoring must be continued until 24 h after catheter removal. Regular neurological assessment must be an integral part of postoperative care for TEA. Patients and medical and nursing personnel in the surgical wards must be aware of the early signs of neurological complications during or early after TEA. Thoracic catheter insertion and the consequent use of low concentrations of local anaesthetic further foster timely suspicion of epidural complications as there will be a low incidence of dense motor blocks. Any new or unexpectedly dense motor block must trigger an algorithm including discontinuation of epidural drug administration, frequent clinical reassessment, and low threshold for urgent magnetic resonance imaging of the epidural space in the case of persistent signs. Preparation of epidural drug solutions should only be provided by a pharmacy without the further need of manipulation.[152]

In conclusion, TEA provides optimal pain therapy in a wide range of surgical procedures and may reduce perioperative morbidity and mortality after major abdominal and thoracic surgery. TEA may influence tumour progression after oncological surgery. However, the low event rate and changes in the surgical technique and perioperative management mean that a large number of patients would be required to prove the effects of TEA in a randomized controlled trial.[49] The available studies vary with respect to surgical procedures, insertion level of epidural anaesthesia, choice of epidural drugs and infusion regimen, measurement parameters, and methodological quality. Therefore, with respect to perioperative outcome and pathophysiology, large retrospective analyses or meta-analyses are often still the best available evidence. Large prospective studies and retrospective analyses of TEA have allowed accurate estimation of the risk of neuraxial damage and persistent neurological deficits. Rigid adherence to good operating procedures and a high level of awareness can largely improve the safety of TEA in patients receiving antiplatelet and anticoagulant drugs. The available data suggest a high level of safety when TEA is used as established in guidelines. The additional beneficial effects on intestinal, cardiovascular, and immune function and on better pain control must be considered along with the background of safety.

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