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Regional Anesthesia for Major Vascular Surgery

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The relative merits of general *vs* regional anesthesia for patients undergoing major vascular surgery has been the subject of debate over the past decade. Previous studies of regional vs general anesthesia often were deficient in experimental design and, therefore, did not produce definitive answers. Some of these deficiencies related to non-standardized, poorly conducted, and/or described general anesthetic techniques, nonstandardized methods of postoperative analgesia in the general anesthesia groups, and variations in preoperative cardiac status in the study groups. Furthermore, most studies did not conclusively demonstrate a cause and effect relationship between the proposed mechanisms of the beneficial effect of regional anesthesia and outcome.

Recent studies, however, have claimed improvements in outcome following regional anesthesia in patients undergoing peripheral vascular procedures. The reported beneficial effects have included amelioration of the neuroendocrine stress response to surgery, improvement in pulmonary function, cardiovascular stability, enhancement of lower limb blood flow, reduction in the incidence of graft thrombosis, and a reduction in the thrombotic response to surgery.

Skeptics still question whether recent studies have the power to determine whether regional anesthesia decreases the incidence of cardiac and pulmonary complications following major vascular surgery. Furthermore, the issue of whether the beneficial effects of regional anesthesia on the incidence of graft thrombosis and the thrombotic response to surgery relating to intraoperative or postoperative regional anesthesia/analgesia, to regional anesthesia per se, or to the systemic effects of absorbed local anesthetics remains unresolved.

Growing interest in regional anesthesia for major vascular surgery in the past decade has been stimulated by reports claiming physiological benefits and superior pain relief. The reported beneficial effects of regional anesthesia have included the following: amelioration of the neuroendocrine stress response to surgery [1], minimization of protein catabolism [2], improvement in pulmonary function by blunting the reduction in functional residual capacity [3], improvement in myocardial oxygen supply demand ratios, cardiovascular stability, and global left ventricular function [4], enhancement of lower extremity and vascular graft blood flow; and finally [5], a reduction in the thrombotic response to surgery [6] (Table 1).

Major vascular surgical procedures are still associated with significant perioperative morbidity; myocardial infarction, pulmonary complications, and renal or hepatic failure [7]. Whether combined general/epidural anesthesia with epidural analgesia continued into the postoperative period results in significant differences in outcome compared with general anesthesia alone remains controversial.

Regional anesthesia through an indwelling epidural catheter is a well established and widely performed technique for a variety of surgical procedures. However, general acceptance of epidural anesthesia for major vascular surgery was delayed until recently because of concerns for paraspinal hematoma development as a result of intraoperative

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[c]*Abbreviations used:* EAA,epidural anaesthesia analgesia.

Table 1. Regional anesthesia and aortic surgery

Postulated beneficial effects
• Blunting of neuroendocrine stress response
• Diminished protein catabolism
• Preservation pulmonary function
- functional residual capacity
• Cardiovascular stability
• Enhanced graft and lower limb blood flow
• Reduction in thrombotic response

anticoagulation [8]. Although spinal and epidural catheterization are still contraindicated in patients already anticoagulated [9], the safety of epidural anesthesia with subsequent anticoagulation has been clearly documented [10].

Regional anesthesia - intraoperative cardiac function

The first definitive study to examine the isolated effects of primary anesthetic technique *per se* on postoperative outcome was a recent large population study by Baron et al. [11]. A total of 173 patients scheduled for abdominal aortic surgery were randomized to receive either "balanced " general anesthesia or thoracic epidural anesthesia in combination with light general anesthesia. The study, which focused on intraoperative techniques, demonstrated that thoracic epidural anesthesia, combined with light general anesthesia, had no influence on cardiac and respiratory function after abdominal aortic surgery. The authors contended that postoperative epidural analgesia rather than intraoperative epidural anesthesia was responsible for any reduction in postoperative cardiac and respiratory complications.

Left ventricular function during thoracic epidural anesthesia may be impaired by different mechanisms: a decrease in preload related to venodilation [12], impairment in cardiac contractility resulting from cardiac sympathectomy [13], and a decrease in heart rate resulting from either decreased sympathetic tone or increased vagal tone [14], or myocardial ischemia as a consequence of a decrease in arterial perfusion pressure. Although decreases in preload and afterload may reduce myocardial oxygen demand, a substantial reduction in systemic blood pressure may decrease coronary perfusion.

When studying the effects of lumbar epidural and anesthesia on cardiac wall motion in ten patients with coronary artery disease undergoing lower abdominal or peripheral surgery, Saada et al. [15] reported decreases in systolic wall motion. The authors attributed the changes, which may indicate transient myocardial ischemia, to decreased coronary perfusion pressure. The use of combined general anesthesia and continuous intraoperative lumbar epidural anesthesia for abdominal aortic surgery has been associated with greater total perioperative fluid volume administration and reduced left ventricular function compared with general anesthesia alone [16].

On the other hand, several mechanisms may contribute to improved left ventricular function during combined general/thoracic epidural anesthesia; these include a decrease in afterload due to the reduction in systemic vascular resistance [12], cardiac effects of local anesthetic agents [17] and the use of direct or indirect sympathomimetic drugs [18]. Alteration of left ventricular function during thoracic epidural anesthesia with general anesthesia results from the effects of these opposing factors and may be either improved or impaired depending on which predominates.

Thoracic epidural anesthetic has been reported to improve myocardial oxygen bal-

ance, increase the diameter of stenotic segments of epicardial coronary artery and reduce the incidence of ventricular dysrhythmias during acute myocardial ischemia [19]. Baron et al. [11], however, stress that although these beneficial effects have been demonstrated when small doses of local anaesthetics are used to induce a selective cardiac sympathetic blockade with a limited hemodynamic effect, these results cannot be extrapolated to patients receiving thoracic epidural anesthesia combined with light general anesthesia. Indeed during abdominal aortic surgery larger doses of anesthetic are necessary to extend caudally the epidural blockade, and light general anesthesia with mechanical ventilation is added to the epidural blockade. Such an anaesthetic technique may induce significant hypotension due to a decrease in venous return [12]. In this context epidural anesthesia could decrease coronary blood flow and promote myocardial ischemia.

Regional anesthesia - respiratory effects

Patients recovering from major vascular surgery are at risk of developing respiratory complications in the immediate postoperative period (Table 4). The postoperative respiratory deficit is primarily restrictive with decreased function residual capacity and pulmonary compliance. Pre-existing obstructive defects may be compounded by altered secretions, impaired cough and mucocillary clearance, atelectasis and postoperative pulmonary infection [7].

Respiratory complications may result from restrictive pulmonary defects as well as ventilation - perfusion abnormality induced by upper abdominal surgery [20]. Diaphragmatic dysfunction is probably the mechanism responsible for these impairments [21]. Thoracic epidural local anaesthetic administration may partially or totally reverse this dysfunction. Conversely, Baron et al. [11] suggested that the intraoperative anesthetic technique probably has no influence on intraoperative pulmonary mechanics and gas exchange since both groups of patients in their study received general anesthesia, mechanical ventilation, an identical surgical procedure and no differences in respiratory complications were observed. The potential benefits of EAA[c] may be related more to postoperative rather than intraoperative influences. Several mechanisms have been suggested to account for the alleged benefits of EAA: better pain control, decreased duration of endotracheal intubation and mechanical ventilation and shorter intensive care unit stay with reduced risk of nosocomial infection [22].

Postoperative morbidity/mortality

Several investigations have been performed comparing combined epidural and light general anesthesia with general anesthesia [23]. The most striking results were those

Table 4. Major vascular surgery/regional anesthesia.

Postulated beneficial respiratory effects.
Hypoxemia
Ventilation/Perfusion
Functional Residual Capacity
Opioid-induced Hypoventilation
Diaphragmatic function
Duration of mechanical ventilation
Infectious Complications
ICU Stay
Nosocomial Infections

described in the study by Yeager et al. [24] of patients undergoing abdominal and major vascular surgery. The authors reported a cardiovascular failure (angina, myocardial infarction, new congestive heart failure, cardiogenic shock, supraventricular tachycardia) rate of 52% in the general anesthesia group and 14% in a combined (regional + light general anesthesia) group. The authors suggested that epidural anesthesia and especially postoperative care, including epidural analgesia with opioids and/or local anesthetics, could be what ultimately determines morbidity and mortality. However no management principles were given as part of the clinical protocol. Intraoperative anaesthetic management and postoperative care was said to be "usual", and no guidelines for invasive monitoring were presented.

Traditionally, clinical studies using general anesthesia give only the most superficial details of anesthetic management, limiting information to the agents used and perhaps a range of doses administered. No clinical studies comparing regional and general anesthetic techniques have reported a clinical algorithm wherein treatment methodology was specified (eg. definitions of blood pressure and heart rate limits, treatment of extremes, management of emergence, preparation for postoperative pain relief, plans for extubation and intraoperative pulmonary toilet). Also, preoperative guidelines for the use of invasive monitoring are not presented, nor is the use of parameters obtained from such devices described. Because all these aspects of clinical care are highly individualized, it is difficult to determine whether differences found in comparative studies are universally applicable or only relate to the investigator's institution.

Postoperative analgesia

Several studies have compared epidural and parenteral analgesia in patients undergoing intraabdominal and major vascular surgery [25–32]. Although epidural opioids are frequently used to manage postoperative pain, there are only few controlled studies comparing this method with other adequate means of pain control that would indicate epidural administration has advantages over effective pain control achieved by other means. Two recent studies could not demonstrate any clinical advantage to epidural infusion versus intravenous infusion of fentanyl for postoperative analgesia [33–34]. However, Salomaki et al. [35] demonstrated a clinical advantage of epidural infusion over intravenous infusion with fentanyl for analgesia after thoracotomy in a study where each therapy was titrated to achieve similar median pain scores. The authors noted that fentanyl produced effective analgesia of comparable quality when infused either intravenously or epidurally, but that epidurally administered fentanyl required a lower dose and serum concentration compared to that with intravenous administration. Respiratory function was better preserved and the incidence of nausea and sedation was less in the epidural group than in the intravenous group. These, however, are the only data to support the conclusion that medications administered epidurally have a more beneficial effect than similar medications given by simpler routes.

The role of epidural anesthesia and postoperative analgesia relating to patient outcome after major vascular surgery is controversial [36]. Studies comparing epidural and parenteral analgesia have been limited by methodology deficiencies, and small patient numbers. Among these studies, only two include a large number of patients [25–26] and only a few demonstrate superiority of EAA compared with parenteral morphine [24, 32].

To examine the interactions of epidural anesthesia, coagulation status and outcome after lower extremity revascularisation, Tuman et al. [37] prospectively randomized 80 patients with atherosclerotic heart disease to receive general anesthesia combined with postoperative epidural analgesia or general anesthesia with on demand narcotic analgesia. The authors claimed that EAA was associated with beneficial effects on coagulation sta-

tus and postoperative outcome compared with intermittent on demand opioid anesthesia after isoflurane, fentanyl - nitrous oxide anesthesia. Although the mechanisms of these beneficial effects of epidural analgesia compared with other forms of analgesia are not yet known, data are accumulating that indicate differences in pain control may not be the primary means by which EAA can positively effect outcome. EAA may have beneficial effects that can occur independent of their superior analgesia potential compared with other pain relief methods. The impact of alternative analgesia techniques such as patient controlled analgesia on outcome following major vascular surgery must be carefully evaluated.

Neurohumoral stress responses

Considerable interest has been expressed in recent years concerning the possible anaesthetic modification of the hormonal and associated metabolic responses to surgical trauma. The so-called surgical stress response consists of increases in plasma concentration of the catecholamines, cortisol, anti-diuretic hormone (ADH), human growth hormone, glucose, lactate, pyruvate, and other hormones and metabolites (Table 2). Increases in plasma concentration of the stress hormone occurred during general anesthesia with most inhalational and intravenous agents and are increased further with surgery [38]. Increases in the majority of these stress hormones are related to the severity of the operative trauma [39], being greater during intra-abdominal surgery than peripheral procedures [40]. These stress responses are considered undesirable because they promote hemodynamic instability and perioperative metabolic catabolism.

The postoperative period may be stressful, due to the onset of pain during emergence from anesthesia, fluid shifts, temperature changes, and alterations of respiratory function. Marked changes occur in plasma catecholamine concentrations, hemodynamics, ventricular function and coagulation following abdominal aortic surgery [41]. Decreases in cortisol, renin, aldorsterone and catecholamine levels have been associated with EAA, especially when used for procedures involving the abdomen and lower extremities. Reduction of this stress response associated with major vascular surgery by EAA may influence patient outcome by reducing the incidence of myocardial ischemia and attenuating the hypercoagulable state observed in the postoperative period.

Coagulation and graft patency

Why might EAA improve graft patency (Table 3)? Based on previous studies of clinical outcome, EAA appears to modify the postoperative thrombotic response. Measurement of coagulation activity in the postoperative period consistently demon-

Table 2. Regional anesthesia - neurohumoral stress response.

- Increased catecholamines
- Increased cortisol
- Increased antidiuretic hormone (ADH)
- Increased human growth hormone
- Increased metabolites
  - glucose
  - lactate
  - pyruvate
- Related to
  - surgical site
  - severity of operative trauma

Table 3. Regional anesthesia - coagulation and graft patency.

Postoperative thrombotic response
• Increased fibrinogen
• Increased Factor VIII
• Increased von Willebrand factor
• Increased platelet reactivity
• Decreased antithrombin III
Epidural Anesthesia Analgesia
• Increased lower limb and graft blood flow
• Decreased stress hormone response
- catecholamine
- cortisol
- ADH
- growth hormone
• Decreased thrombotic response
- Decreased fibrinogen
- Decreased Factor VIII
- Decreased platelet reactivity
• Increased fibrinolysis
- Increased antithrombin III

strates elevations of platelet reactivity, factor VIII, and von Willebrand factor. Antithrombin III, the principal inhibitor of thrombin activity, progressively decreases during the early postoperative period [42].

Hypercoagulability manifested by increased fibrinogen and platelet activity has been implicated in the genesis of unstable angina, intracoronary thrombosis, and myocardial infarction. Patients undergoing peripheral vascular surgery have postoperative increases in platelet reactivity and in factor VIII related antigen and have decreases in antithrombin III levels indicative of hypercoagulable state that may be associated with early arterial graft failure. These disease-related changes in coagulation may be exacerbated by surgical and postoperative stress [37].

As most cardiovascular mortality occurs in the hours and days after completion of vascular surgery, postoperative stress-induced hypercoagulability could play a causal role. Epidural anesthesia and analgesia continuing into the postoperative period may attenuate the postoperative stress response in specific patient populations. Mechanisms may include epidurally-mediated alterations in lower limb blood flow, as well as stress hormone and von Willebrand factor concentrations. Epidural anesthesia increases blood flow to both calf and femoral veins [43]. Blood flow in the legs of patients with occlusive atherosclerotic disease is increased after epidural anesthesia [44]. This effect may be enhanced when postoperative epidural analgesia includes a dilute solution of local anaesthetic to maintain some degree of sympathetic block after arterial reconstruction. The stress-mediated release of cortisol, catecholamines, corticotropin, antidiuretic hormone and other metabolic precursors are blunted by high levels of epidural anesthesia [45].

Tuman et al. [37] reported that patients about to undergo peripheral vascular surgical procedures were hypercoagulable before operation compared with control patients without atherosclerotic heart disease; the use of EAA attenuated this hypercoagulability postoperatively. The authors suggested that decreases in cortisol, renin, aldorsterone, and catecholamine levels associated with EAA might translate to higher antithrombin III and

lower fibrinogen levels with attenuated platelet activity postoperatively, consistent with the thromboelastographic findings in their study.

Myocardial ischemia /perioperative cardiac morbidity

The ever expanding interest in perioperative myocardial morbidity and mortality may be attributable, in part, to an increased prevalence of abdominal aortic procedures in patients with known or suspected coronary artery disease [7].

Until the early 1980's, investigators attempted to identify perioperative clinical factors for cardiac complications, such as recent myocardial infarction and congestive cardiac failure [41]. From the mid 1980's, laboratory based investigations became available to assess ventricular function and identify potentially ischemic myocardium. These techniques included resting and exercise radionuclide angiography dipyridamole-thallium scanning and ambulatory electrocardiographic monitoring.

However, several studies in the early 1990's have shown that cardiac morbidity in patients undergoing major vascular surgery is best predicted by postoperative myocardial ischemia, rather than traditional perioperative clinical predictors [45, 46]. Long duration postoperative ischemia, rather than the mere presence of postoperative ischemia, may be the factor most significantly associated with cardiac outcome [47].

The intense procoagulant activity and sympathetic stimulation in the postoperative period has been implicated in the development of coronary vasospasm, thrombosis, and rupture of atheromatous plaque and, thus, leading to myocardial ischemia and infarction. Alternatively, postoperative pain, and physiological and emotional stress may all combine to cause tachycardia, hypertension, increase in cardiac output, and fluid shifts which, in high risk patients, might result in subendocardial ischemia and eventual myocardial infarction. Intermittent brief periods of myocardial ischemia have been reported to have a cumulative effect and may cause myocardial necrosis [48]. Mean heart rates are generally higher in the postoperative period than before or during surgery. Thus, it seems that the cascade of events leading to postoperative cardiac complications begins with long duration subendocardial ischemia rather than acute coronary occlusion.

If postoperative myocardial ischemia is the cause of late postoperative myocardial infarctions in patients undergoing non-cardiac surgery, then treatment of postoperative myocardial ischemia should reduce morbidity. Additionally reducing pain and stress in the perioperative period might prevent postoperative myocardial ischemia and minimize the need for extensive preoperative cardiac evaluation. The latter approach seems to be the current focus of clinical investigation.

Postoperative myocardial ischemia is virtually always silent and has been documented up to 7 days postoperatively [41]. The postoperative period is associated with significantly higher heart rates than either the pre- or intra-operative period. The generalized tachycardia may be the result of surgical pain and stress. In addition, weaning from mechanical ventilation in the intensive care unit has been associated with both myocardial ischemia and infarction. Circadian variation in postoperative myocardial ischemia has been reported, with the majority of ischemic episodes occurring during the morning hours [49].

The incidence of hypertension approaches 50% after abdominal aortic surgery [7]. Postoperative hypertension increases myocardial oxygen consumption and may precipitate myocardial ischemia in patients with occlusive coronary artery disease. Surgery is associated with increased sympathetic nervous system activity and perioperative changes in arterial pressure have been correlated with plasma catecholamine levels [50]. While interruption of afferent pain impulses by epidural installation of either local anesthetic or opioid prevents an increased level of plasma catecholamines following surgery [51], there

are scant data regarding the effects of these agents on the incidence of postoperative hypertension. In a double-blind, placebo-controlled study of twenty-four patients undergoing abdominl aortic surgery in which 6 mg of epidural morphine sulphate was administered, Breslow et al. [52] reported that although epidural morphine had no effect on plasma adrenaline and ADH levels, fewer patients required treatment for hypertension and blood pressures were lower following surgery than in the control group. These data suggest that sympathetic nervous system activity and not adrenal adrenaline or pituitary ADH secretion is responsible for the development of hypertension following abdominal aortic surgery.

SUMMARY

Proponents of EAA claim numerous beneficial effects resulting in improved outcome in patients following abdominal aortic surgery. However, the debate about whether general/EAA results in significantly improved outcomes compared with general anesthesia alone remains controversial.

Unfortunately, studies reporting beneficial effects of EAA used different surgical populations and combined patients who received epidural analgesia with opioids and local anesthetics. Indeed, the effects of epidural analgesia with local anesthetic on cardiac and respiratory functions are different from those of epidural analgesia with opioids. Diaphragmatic dysfunction after upper abdominal surgery is reversed by epidural analgesia with local anaesthetic [21] and is not influenced by epidural analgesia with opioids [53]. Beneficial effects of epidural analgesia on myocardial oxygen balance seem to be directly related to the cardiac sympathetic blockade induced by local anaesthetic agents [54]. Most authors would now hold that postoperative epidural analgesia rather than intraoperative epidural anesthesia is the most important determinant in preventing postoperative cardiac and respiratory complications.

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