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ORIGINAL ARTICLE - ADULT CARDIAC

Superior haemodynamic stability during off-pump coronary surgery with thoracic epidural anaesthesia: results from a prospective randomized controlled trial

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Abstract

OBJECTIVES: Off-pump coronary artery bypass (OPCAB) surgery is a technically more demanding strategy of myocardial revascularization compared with the standard on-pump technique. Thoracic epidural anaesthesia, by reducing sympathetic stress, may ameliorate the haemodynamic changes occurring during OPCAB surgery. The aim of this randomized controlled trial was to evaluate the impact of thoracic epidural anaesthesia on intraoperative haemodynamics in patients undergoing OPCAB surgery.

METHODS: Two hundred and twenty-six patients were randomized to either general anaesthesia plus epidural (GAE) ($n = 109$) or general anaesthesia (GA) only ($n = 117$). Mean arterial blood pressure (MAP), heart rate (HR) and central venous pressure (CVP) were measured before sternotomy and subsequently after positioning the heart for each distal anastomosis.

RESULTS: Both groups were well balanced with respect to baseline characteristics and received a standardized anaesthesia. The MAP decreased in both groups with no significant difference (mean difference (GAE minus GA) −1.11, 95% CI −3.06 to 0.84, $P = 0.26$). The HR increased in both groups after sternotomy but was significantly less in the GAE group (mean difference (GAE minus GA) −4.29, 95% CI −7.10 to −1.48, $P = 0.003$). The CVP also increased in both groups after sternotomy, but the difference between the groups varied over time ($P = 0.05$). A difference was observed at the third anastomosis when the heart was in position for the revascularization of the circumflex artery (mean difference (GAE minus GA) +2.09, 95% CI 0.21–3.96, $P = 0.03$), but not at other time points. The incidence of new arrhythmias was also significantly lower in the GAE compared with the GA group (OR = 0.41, 95% CI 0.22–0.78, $P = 0.01$).

CONCLUSION: Thoracic epidural with general anaesthesia minimizes the intraoperative haemodynamic changes that occur during heart positioning and stabilization for distal coronary anastomosis in OPCAB surgery.

Keywords: Haemodynamics • Epidural anaesthesia and off-pump coronary artery surgery

INTRODUCTION

Coronary artery bypass surgery (CABG) via median sternotomy using opioid anaesthesia leads to sympathetic activation by surgical stress causing tachycardia, hypertension and increased oxygen demand and extraction by the myocardium [1]. This response is stabilized by thoracic epidural anaesthesia [2]. The clinical advantages of thoracic epidural anaesthesia in CABG using cardiopulmonary bypass (CPB) are earlier extubation, reduced postoperative pain and confusion as demonstrated in prospective randomized trials [3, 4]. Off-pump coronary artery bypass grafting (OPCAB) has been shown to lead to a reduction of the stress response and myocardial injury [5, 6]. Combining epidural anaesthesia with OPCAB surgery is expected to have a synergistic effect on reducing sympathetic stress. The variations in haemodynamics during heart positioning for OPCAB anastomosis adds complexity to intraoperative management and could have detrimental clinical sequelae. We hypothesized that thoracic epidural anaesthesia, by reducing sympathetic stress, could help stabilize the heart and facilitate the construction of the distal anastomosis, particularly in the posterior and lateral walls.

The aim of this study was to investigate the effects of thoracic epidural anaesthesia on central intraoperative haemodynamics during OPCAB surgery. The primary analysis of this trial has been reported previously [7].

MATERIALS AND METHODS

Eligible patients were adults (≥16 years) undergoing primary non-emergency OPCAB surgery without the use of CPB and cardioplegic arrest. Four fulltime OPCAB surgeons participated in the trial. Patients on intravenous heparin, warfarin or clopidogrel at the time of surgery or who suffered from bleeding diathesis were excluded. The study was approved by the Central and South Bristol Research Ethics Committee (registration number E5471), and written informed consent was obtained from all patients. Patients were randomized to receive either general anaesthesia plus epidural (GAE) or general anaesthesia (GA) only. Computer generated randomization was performed with allocations stratified by a consultant team in a 1:1 manner, using blocks of varying size. A flow chart of the allocations and numbers subject to analyses is shown in Fig. 1.

Anaesthetic technique

Full details of the anaesthetic technique have been described previously [7]. Briefly, premedication with benzodiazepines, and induction with propofol at 0.5–1 mg/kg combined with fentanyl (10–20 μg/kg) was used in all patients. Anaesthesia was maintained with either isoflurane at 0.8–1.0 minimal anaesthetic concentration or IV propofol 3–4 mg/kg/h, at the discretion of the consultant anaesthetist.

In addition, patients in the GAE group had a thoracic epidural catheter sited in the operating theatre immediately before surgery at the T2–3 or T3–4 inter vertebral space. Bilateral neuraxial block was established from T1 to T10 with an initial bolus of 5 ml bupivacaine 0.5% followed by another 5 ml bolus after 10 min. After induction of GA and when central haemodynamic status was stable, a continuous infusion of 0.125% bupivacaine and 0.0003% clonidine (150 μg in 500 ml) was commenced at an initial rate of 10 ml/h in accordance with the protocol described by Scott *et al.* [3]. Vasoplegia related to epidural infusion was treated with norepinephrine infusion. These infusions were commenced prior to heart positioning and haemodynamic measurements where needed. Hypotension related to heart positioning was dealt with by repositioning and limited retraction rather than vasopressor or fluid administration.

Surgical technique

The surgical technique and the method of exposure and stabilization for performing anastomoses in patients undergoing OPCAB surgery have been described previously [8, 9]. Briefly, following median sternotomy, the pericardium is not hitched up to allow free movement of the heart. A half-folded swab (12 cm wide and 70 cm long) is snared to the posterior pericardium (using a single 0-silk suture) placed halfway between the inferior vena cava and the left pulmonary vein. Traction is then applied to the end of the snared suture caudally, which lifts the pericardium and the apex of the heart upwards. The left anterior descending (LAD) coronary artery is grafted first to provide protection against ischaemia and myocardial dysfunction that can result from lifting the heart to revascularize the posterior (second anastomosis onto the posterior descending coronary artery) and lateral walls (third anastomosis onto the circumflex coronary artery). All surgeons used 20° Trendelenburg with addition of right lateral tilt for the circumflex grafting. The two limbs of the swab are used to hold the heart in position by securing it to the drapes. We used the Estech Hercules Universal stabilizer (Estech USA, Canal Winchester, OH, USA) to construct our distal anastomoses, aided by intracoronary shunts and a CO_2 mister blower.

Haemodynamic measurements

Continuous haemodynamic measurements were available from a peripheral pulse wave saturation monitor, central venous monitoring line and radial arterial monitoring line (Hospira, Lake Forest, IL, USA). The baseline measurements of heart rate (HR), mean arterial pressure (MAP) and central venous pressure (CVP) were recorded prior to sternotomy. Subsequent measurements were taken after the heart was positioned for OPCAB anastomosis prior to performing the arteriotomy. This process was repeated for each subsequent anastomosis. In the event of a

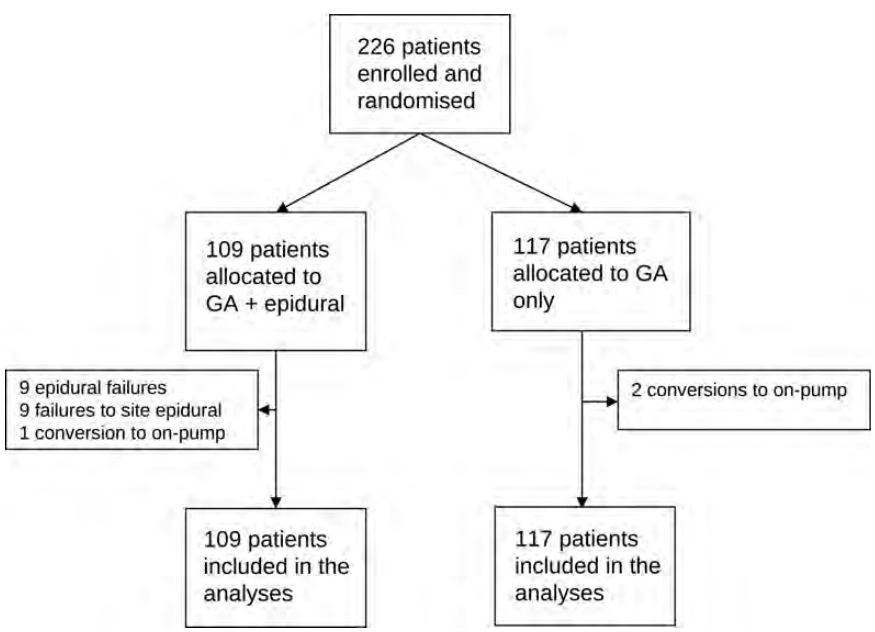

Figure 1: Flow chart for all patients randomized to study.

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second graft to the same territory, we recorded the measurements for both positions. Postoperative patient management was according to unit protocol as previously reported [9].

STATISTICAL METHODS

Continuous variables are summarized using the mean and standard deviation (SD) (or median and interquartile range if the distribution was skewed), and categorical data are summarized as a number and percentage. Serial haemodynamic measurements were modelled using a mixed regression model, adjusted for baseline value, consultant team and number of grafts. Treatment by time interactions were examined, and if statistically significant at the 5% level, the differences in mean response between the two groups were reported separately for each time point, otherwise an overall treatment difference was given. All effect estimates were reported with 95% confidence intervals (CI).

Analyses were carried out on the basis of intention to treat. All analyses were adjusted for consultant team as the randomization was stratified by teams. Centre by treatment and consultant team by treatment interactions were examined and no evidence of differing treatment effects between centres and teams was found. The validity of the assumptions underpinning the models fitted was checked.

RESULTS

Between August 2003 and November 2007, 226 patients were enrolled in the study, 109 were randomly assigned to GAE and 117 to GA. Relevant summary of baseline characteristics are presented in Table 1. The mean ages were 65.9 and 65.5 years in the GAE and GA groups, respectively. Patient characteristics with respect to cardiovascular symptoms, cardiovascular risk factors, left ventricular function and EuroSCORE were similar between the two groups. The mean number of distal anastomoses performed was 2.7 (SD 0.7).

HAEMODYNAMIC DATA

The central haemodynamic changes from baseline through various heart positions for OPCAB anastomosis is shown in Table 2. MAP decreased from baseline when the heart was positioned to perform the first anastomosis onto the LAD. The reduction in MAP was higher in the GA group compared with the GAE group, which was consistent throughout all the anastomoses (Fig. 2). However, this difference was not statistically significant ($P = 0.26$). The resting HR increased between baseline and first anastomosis in response to sternotomy in both groups. In the GAE group, the rise was significantly less and throughout the procedure the increase in HR was consistently and significantly higher in the GA group ($P = 0.003$, Fig. 3). The right heart-filling pressures as estimated by CVP showed a general increase from baseline with heart positioning in both groups, but the difference in mean CVP between the two groups varied with time ($P = 0.05$, Fig. 4). The mean CVP was similar in the two groups, except at the third anastomosis of the circumflex coronary artery, when the mean CVP was significantly higher in the GAE group.

There was 1 death in the GAE group and no mortality in the GA group. The intubation times were significantly shorter in the GAE group (HR = 1.73, 95% CI 1.31–2.27, $P < 0.001$), as was the in-hospital stay (HR = 1.39, 95% CI 1.06–1.82, $P = 0.017$). There was no difference in blood loss or infective and neurological complications between groups ($P > 0.05$ for all). The incidence of new arrhythmias were significantly lower in the GAE, compared with the GA, group (odds ratio (OR) = 0.41, 95% CI 0.22–0.78, $P = 0.01$), while patients in the GAE group were more likely to require vasoconstrictors intraoperatively than in the GA group (OR = 2.50, 95% CI 1.22–5.12, $P = 0.012$). The incidence of intraoperative myocardial infarction was higher in the GA group

Table 1: Baseline characteristics (reproduced from reference [7])

Variable		Randomized to GAE (*n* = 109)	Randomized to GA (*n* = 117)
Age (years)	Mean (SD)	65.9 (8.8)	65.5 (8.6)
Males	*n* (%)	102 (94)	102 (87)
Body mass index	Mean (SD)	27.4 (3.5)	28.2 (4.1)
Q-wave myocardial infarction	*n* (%)	48 (44)	57 (49)
Diabetes mellitus	*n* (%)	22 (20)	28 (24)
Creatinine value (μmol/l)	Mean (SD)	102 (21.3)	108 (35.5)
Previous CVA/TIA	*n* (%)	14 (13)	12 (10)
Peripheral vascular disease	*n* (%)	13 (12)	15 (13)
Left ventricle function	Good (>50%) *n* (%)	84 (77)	82 (70)
	Moderate (30–50%) *n* (%)	23 (21)	29 (25)
	Poor (<30%) *n* (%)	0 (0)	3 (3)
Triple vessel coronary disease	*n* (%)	78 (72)	80 (68)
Left main stem disease	*n* (%)	28 (26)	36 (31)
EuroSCORE	Median (interquartile range)	3 (2, 4)	3 (1, 4)

CVA: cerebral vascular accident; GA: general anaesthesia only; GAE: general anaesthesia plus epidural; TIA: transient ischaemic attack.

Table 2: Haemodynamic data

Baseline (prior to sternotomy)	Randomized to GAE (n = 109)		Randomized to GA (n = 117)		Treatment difference	P-value
	Mean	SD	Mean	SD		
Mean arterial pressure (mmHg)	92.2	16.9	93.0	16.7		
Heart rate (beats/min)	59.8	11.6	63.2	11.3		
Central venous pressure (mmHg)	9.20	2.96	8.57	3.31		
Intraoperative (after application of stabilizer)	Mean	SE	Mean	SE		
Mean arterial pressure (mmHg)						
First anastomosis (LAD)	72.9	1.05	74.6	1.03	−1.68	
Second anastomosis (PDA)	75.0	0.99	75.8	1.10	−0.77	
Third anastomosis (Cx)	72.8	0.98	74.2	1.50	−1.44	
Postoperative	75.4	0.90	75.9	1.01	−0.54	
Test for treatment × time interaction						0.91
Overall estimate of treatment effect					−1.11 (−3.06, 0.84)	0.26
Heart rate (beats/min)						
First anastomosis (LAD)	62.5	1.05	67.7	1.30	−5.15	
Second anastomosis (PDA)	63.7	1.19	68.2	1.42	−4.48	
Third anastomosis (Cx)	63.9	1.12	69.1	1.63	−5.21	
Postoperative	66.5	1.13	68.8	1.05	−2.32	
Test for treatment × time interaction						0.29
Overall estimate of treatment effect					−4.29 (−7.10, −1.48)	0.003
Central venous pressure (mmHg)						
First anastomosis (LAD)	11.8	0.49	11.0	0.48	0.77 (−0.56, 2.10)	0.25
Second anastomosis (PDA)	14.0	0.64	13.4	0.62	0.57 (−1.18, 2.32)	0.52
Third anastomosis (Cx)	13.5	0.68	11.5	0.68	2.09 (0.21, 3.96)	0.03
Postoperative	9.1	0.30	9.0	0.30	0.12 (−0.69, 0.94)	0.76
Test for treatment × time interaction						0.05

LAD: left anterior descending artery; PDA: posterior descending artery; Cx: circumflex coronary artery.

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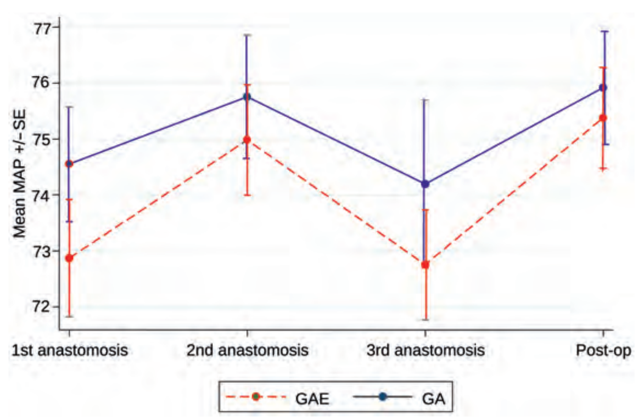

Figure 2: Mean arterial pressure.

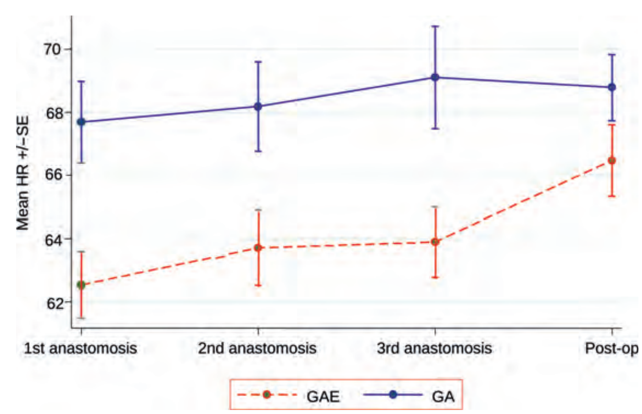

Figure 3: Heart rate.

compared with the GAE group, but the difference was not statistically significant (OR = 0.49, 95% CI 0.14–1.73, P = 0.27).

DISCUSSION

The main finding reported here is that thoracic epidural anaesthesia seems to better stabilize the intraoperative haemodynamic during OPCAB surgery performed via a median sternotomy. OPCAB surgery demands more collaboration between the surgical and anaesthetic teams to maintain consistent haemodynamics by a combination of alterations in right heart-filling pressures (Trendelenberg/intravenous filling) and vasoconstrictor use to facilitate the construction of the distal anastomosis. Haemodynamic variability during heart positioning and stabilization may result in inaccuracy of the construction of the coronary anastomosis.

It has been suggested that the technical difficulties in performing the distal anastomosis may be associated with the less optimal mid-term outcomes after OPCAB surgery [10]. Data from our institution and others have shown an increase in HR, decrease in stroke volume and cardiac output and decrease in MAP with the biggest difference occurring during lateral wall revascularization [11, 12]. Improvements in techniques and stabilization devices along with experience has no doubt had significant impact on reducing technical error during construction of anastomosis with excellent long-term results [13]. However, better intraoperative

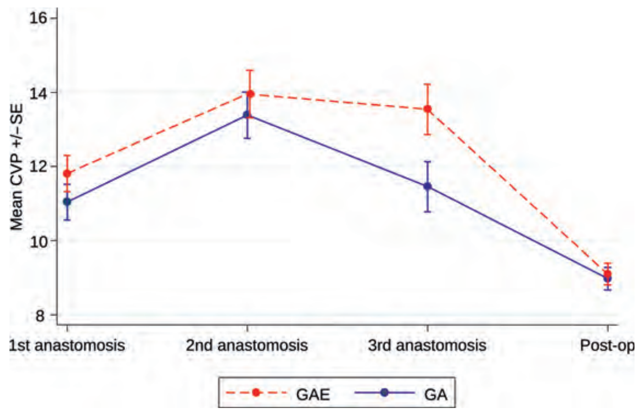

Figure 4: Central venous pressure.

haemodynamic stability with thoracic epidural should offer a further technical advantage, particularly in the early stage of a surgeon's learning curve or when teaching trainees.

Thoracic epidural anaesthesia reduces the sympathetic drive associated with intense surgical stimulation of CABG surgery via median sternotomy [14]. The result is stabilization of the HR throughout the intraoperative course, thus prolonging diastolic filling time and consequently improving coronary perfusion. Large epicardial arteries and coronary arterioles are densely innervated by adrenergic sympathetic nerve fibres, which cause vasoconstriction [15, 16]. Accordingly, improvements in coronary blood flow and increases in myocardial oxygen supply/demand ratio have been demonstrated in clinical studies with thoracic epidural [17, 18].

Another finding of this study previously reported [7] is the reduced incidence of postoperative new arrhythmias with the use of thoracic epidural, which has also been reported by other investigators [19, 20]. Atrial fibrillation (AF) after CABG has been observed in 30–40% of patients and has a significant clinical impact [21, 22]. Atrial ectopics seem to precede postoperative AF in the majority of cases [22]. One of the mechanistic predispositions is a heightened sympathetic tone and vagal rebound [23]. High regional anaesthesia of the first five thoracic segments resulting in blocks in cardiac afferent and efferent fibres and lower catecholamine release has been demonstrated in CABG patients [19, 20, 24, 25]. A consistent effect of thoracic epidural anaesthesia on the cardiovascular system is vasodilatation [14]. This resulted in larger vasoconstrictor requirement in the GAE group. Theoretically, this may jeopardize organ perfusion, but no such deleterious end-organ effects were observed between our study groups.

The main limitation of our study is the use of standard haemodynamic monitoring rather than more invasive cardiac output monitoring, which is not used routinely in our service.

CONCLUSION

The addition of a thoracic epidural to GA helps to stabilize the intraoperative haemodynamic changes that occur during heart positioning for distal coronary anastomosis in OPCAB surgery.

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Conflict of interest: none declared.

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