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General Anaesthesia is Associated with Adverse Cardiac Outcome after Endovascular Aneurysm Repair

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WHAT THIS PAPER ADDS

- Vascular surgery patients are at increased risk of cardiac complications, due to underlying coronary artery disease. General anaesthesia and epidural or local anaesthesia differ regarding the physical stress response evoked by surgery. It is unclear whether or not this influences the risk of adverse cardiac events. This is the first study evaluating the impact of anaesthesia type on cardiac outcome after endovascular aneurysm repair (EVAR), to adjust for baseline differences between patients receiving different anaesthesia techniques.

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ABSTRACT

Objectives: Endovascular aneurysm repair (EVAR) is associated with reduced cardiac stress compared with open repair and is an attractive therapeutic option, especially in cardiac fragile patients. General and locoregional anaesthesia differ regarding the stress response evoked by surgery. The aim of the study is to compare the incidence of cardiac events after EVAR under general or locoregional anaesthesia.
Methods: A total of 302 consecutive patients undergoing infrarenal EVAR between 2002 and 2011 were analysed in this retrospective cohort study. Selection of anaesthesia type was at the discretion of the treating physicians. Medical history, medication use, anaesthesia technique and follow-up were obtained. The study end point was 30-day cardiac complications, including cardiac death, non-fatal myocardial infarction, heart failure, ventricular arrhythmia and troponin T release. Multivariable analysis, adjusted for the propensity of receiving a locoregional technique and cardiac risk factors according to the Revised Cardiac Risk Index, was used to assess the association between cardiac events and anaesthesia type.
Results: A total of 173 patients underwent general anaesthesia and 129 locoregional anaesthesia. Obesity, aspirin use and therapeutic anticoagulation were more common in patients receiving general anaesthesia. Cardiac events were observed in 13.3% of patients receiving general anaesthesia and in 4.7% of patients receiving locoregional anaesthesia ($P = 0.02$), or 6.4% versus .8% ($P = 0.02$) when asymptomatic troponin release is excluded from the end point. In the general anaesthesia group, two cardiac deaths, six non-fatal myocardial infarctions, two cases of non-fatal heart failure, one non-fatal cardiac arrest and 12 cases of troponin T release were observed, compared with one myocardial infarction and five cases of troponin T release in the locoregional anaesthesia group. In multivariable analysis, general anaesthesia was associated with adverse cardiac events (odds ratio (OR) 3.8; 95%-confidence interval (CI) 1.1–12.9). Non-cardiac complications occurred in 11.6% of patients in both groups ($P = 1.00$).
Conclusion: General anaesthesia was associated with an increased risk of cardiac events in EVAR, compared with locoregional anaesthesia.

Endovascular therapy represents an opportunity to reduce the stress response associated with abdominal aortic aneurysm repair, compared with the conventional open approach.[1] Endovascular aneurysm repair (EVAR), given its inherently minimally invasive

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nature, is associated with less haemodynamic fluctuations, endocrinologic stress reaction, blood loss and postoperative pain. Subsequently, EVAR is associated with a reduced risk of cardiac complications (3.1% vs. 21.8%), pulmonary complications and periprocedural mortality (1.7% vs. 4.7%), as compared with conventional open aneurysm repair.[2–6] EVAR is therefore an attractive treatment strategy, especially in the more frail patients requiring aneurysm repair.

Cardiac complications are a major cause of morbidity and mortality following non-cardiac surgery, most importantly myocardial infarction. The increased risk of myocardial infarction, through either prolonged myocardial oxygen supply-to-demand mismatch or coronary plaque rupture, is thought to arise from the stress response evoked by the surgical procedure.[7] The various types of anaesthesia attenuate the surgical stress response to a different extent. Differences in postoperative cardiac event rates between anaesthesia types have been demonstrated previously.[8]

The performance of EVAR procedures was demonstrated to be feasible under multiple types of anaesthesia, including general, epidural, spinal and local anaesthesia.[9] However, no conclusive data exist on anaesthesia type and cardiac outcome in EVAR. The aim of the current study is to assess the association between anaesthesia type and cardiac events after EVAR procedure.

Materials and Methods

A total of 302 consecutive patients undergoing infrarenal EVAR between 2002 and 2011 were analysed in this retrospective cohort study. Emergency procedures were excluded, as were hybrid procedures. The study was performed at a single site at the Department of Vascular Surgery of the Erasmus Medical Center, Rotterdam, the Netherlands. The study complies with the declaration of Helsinki and was approved by the Institutional Review Board.

Baseline characteristics

A detailed medical history was obtained from all patients prior to surgery, with the emphasis on cardiovascular history and risk factors. Congestive heart failure was defined as a history of congestive heart failure or the presence of S3 gallop or rales at both bases during physical examination. Ischaemic heart disease was defined as a history of myocardial infarction, evidence of prior myocardial infarction on an electrocardiogram or echocardiogram. Additional clinical data included age, gender, diabetes mellitus, renal dysfunction (creatinine $>$ 2 mg dl^{-1}), hypertension (systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg in non-diabetics, systolic blood pressure $\geq$130 mmHg, diastolic blood pressure $\geq$80 mmHg in diabetics or the use of anti-hypertensive drugs), cerebrovascular disease (history of stroke or transient ischaemic attack), smoking status, body mass index (BMI) and chronic obstructive pulmonary disease (according to the Global Initiative on Obstructive Lung Diseases), and the presence of aortic valve stenosis (flow velocity over the aortic valve $>$2.5 m s^{-1}). In addition, the use of beta-blockers, statins, aspirin, clopidogrel, oral anti-coagulants, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, diuretics and nitrates was recorded.

Antiplatelet, anticoagulant and thromboprophylaxis policy

Chronic aspirin therapy is routinely continued perioperatively. The decision whether or not to interrupt vitamin K antagonist therapy and to initiate bridging therapy with heparin or low-molecular-weight heparin (LMWH) was made on a case-to-case basis. As per hospital protocol, thromboprophylaxis is routinely initiated the night prior to surgery using prophylactic doses of LMWH in patients not receiving therapeutic doses of LMWH or oral anticoagulants. The preoperative dose is administered $>$12 h prior to surgery.

Anaesthesia type

Selection of anaesthesia type was made on a case-to-case basis, reflecting the anaesthesiologists, surgeons and patients considerations. Of all patients, anaesthesia charts were examined for the type of anaesthesia used, including general, epidural and local anaesthesia. Anaesthesia type was categorised as either general or locoregional. Adjuvant sedation in patients undergoing epidural or local techniques without need of mechanical ventilation was not scored as general anaesthesia.

Cardiac outcome

Serial electrocardiograms and troponin T measurements were routinely obtained prior to surgery and on postoperative days 1, 3 and 7, unless discharged earlier, and whenever clinically indicated. Troponin T was measured using the TropT version 2 assay from Roche Diagnostics, Mannheim, Germany. The study end point is 30-day adverse cardiac events, a composite of cardiovascular mortality, non-fatal myocardial infarction, new or worsened congestive heart failure, new arrhythmias (requiring immediate cardioversion, cardiopulmonary resuscitation or pacing) and troponin T release. Also, 30-day 'major' cardiac events are reported, a composite of cardiac death, non-fatal myocardial infarction, new or worsened congestive heart failure and new arrhythmias, but not including troponin T release. Cardiovascular death was defined as any death from cardiovascular cause, including death following myocardial infarction, congestive heart failure, arrhythmia and surgery-related bleeding complications, or sudden unexpected death. Myocardial infarction was defined as postoperative classic rise and fall of troponin T levels above the 99th percentile, with either electrocardiographic or clinical signs of myocardial ischaemia. Troponin T release was defined as at least one troponin T value above the 99th percentile in the absence of electrocardiographic and clinical signs of myocardial ischaemia and in the absence of other cardiac complications. Patients were routinely scheduled for a follow-up visit 30 days after surgery. In patients still admitted or readmitted, follow-up was completed using medical records. Cause of death was ascertained by reviewing medical records or death certificates.

Non-cardiac outcome

We report major pulmonary, renal, cerebrovascular, urological and infectious complications requiring intervention, as well as all surgical procedures for bleeding and device failure complications required within 30 days of the initial EVAR procedure. Length of hospital stay (in days) after EVAR procedure is reported.

Statistical analysis

Dichotomous data are presented as numbers and percentages. Continuous data are presented as means $\pm$ standard deviation. Dichotomous data were compared using Chi-Square tests, continuous data were compared using analysis of variance (ANOVA) or Mann–Whitney *U* tests as appropriate. Univariable and multivariable logistic regression models were used to assess the association between anaesthesia type (general vs. locoregional) and 30-day cardiac events. The following factors were considered as possible

confounding factors: age, gender, congestive heart failure, ischaemic heart disease, preoperative creatinine, preoperative haemoglobin, chronic obstructive pulmonary disease, diabetes mellitus, prior stroke, aortic valve stenosis, obesity (BMI > 30), the use of beta-blockers, statins, aspirin, clopidogrel, oral anti-coagulants, therapeutic anticoagulation at the time of surgery, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, diuretics and nitrates. All possible confounders were included in a multivariable logistic regression model to compute a propensity score for the likelihood of receiving locoregional versus general anaesthesia. To assess the association between anaesthesia type and cardiac outcome, a multivariable logistic regression model was applied. The Revised Cardiac Risk score and propensity score were entered as co-variables. A two-sided *P*-value of <.05 was considered significant for all tests. All analyses were performed using PASW version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Of the 302 patients enrolled, general anaesthesia was applied in 173 (57%) patients, and locoregional anaesthesia in 129 (43%) patients, including 78 (26%) cases of epidural and 51 (17%) cases of local anaesthesia.

Baseline characteristics

General anaesthesia and locoregional anaesthesia groups differed significantly regarding the presence of hypertension (71% vs. 58%, $P = 0.03$) and hypercholesterolaemia (94% vs. 87%, $P = 0.05$). Obesity was more common in patients receiving general anaesthesia (24% vs. 9%, $P < 0.01$). Other co-morbid conditions, age and gender were well balanced between both groups. General anaesthesia patients were more frequently treated with aspirin (73% vs. 49%, $P < 0.01$). Surgery was performed under therapeutic anticoagulation (continuation of oral anticoagulants with an International Normalised Ratio >1.8 or bridging therapy with heparin or LMWH in therapeutic doses) in 7% of general anaesthesia patients and 2% of locoregional anaesthesia patients ($P = 0.11$). No differences regarding clopidogrel use were observed (6% vs. 5%, $P = 0.62$). Baseline characteristics are presented in Table 1.

Table 1
Baseline characteristics according to anaesthesia type.

	General ($n = 173$)	Locoregional ($n = 129$)	*P*-value
Demographics			
Mean age (SD)	72 (8)	72 (8)	.75
Male gender (%)	155 (90)	120 (93)	.42
Medical history (%)			
Congestive heart failure	16 (9)	21 (16)	.08
Cerebrovascular disease	28 (16)	15 (12)	.32
Hypertension	122 (71)	75 (58)	.03
Hypercholesterolaemia	162 (94)	112 (87)	.05
Diabetes mellitus	44 (25)	22 (17)	.09
Current smoking	77 (45)	52 (40)	.48
Serum creatinin >2 mg/dL	25 (15)	26 (20)	.22
Ischaemic heart disease	74 (43)	64 (50)	.25
Aortic valve stenosis	6 (4)	3 (3)	.74
COPD	81 (47)	51 (41)	.29
BMI > 30	41 (24)	12 (9)	<.01
Risk indices (SD)			
Revised cardiac risk index	1.9 (1.0)	2.0 (1.0)	.25
ASA class	2.5 (.6)	2.5 (.5)	.59
Medication use (%)			
Anticoagulants	29 (17)	17 (13)	.42
Continuated perioperatively	12 (7)	3 (2)	.11
Aspirin	125 (73)	63 (49)	<.01
Clopidogrel	11 (6)	6 (5)	.62

Abbreviatons: SD standard deviation; LVEF left ventricular ejection fraction; COPD chronic obstructive pulmonary disease; BMI body mass index.

Length of stay

The median interquartile (IQR) length of hospital stay after EVAR procedure was 3 (2–4) days in the general anaesthesia group and 2 (2–4) days in the locoregional anaesthesia group ($P < 0.01$).

Thirty-day mortality

In the perioperative period, four (1.3%) deaths were observed, all of which occurred in the general anaesthesia group ($P = 0.14$).

Thirty-day cardiac events

A total of 29 (9.6%) patients suffered a cardiac event within 30 days of surgery, including two cases of cardiac death, seven myocardial infarctions, two cases of new congestive heart failure, one cardiac arrest and 17 cases of asymptomatic Troponin T release. All cases of myocardial infarction and heart failure were managed medically.

All cases of cardiac death, heart failure and cardiac arrest occurred in the general anaesthesia group, as well as six of the seven myocardial infarctions. In total, 6.4% of patients in the general anaesthesia group suffered one of these events, compared with .8% in the locoregional anaesthesia group ($P = 0.02$). Asymptomatic troponin release was observed in 6.9% of general anaesthesia patients and 3.9% of locoregional anaesthesia patients ($P = 0.32$). Significantly, more patients in the general anaesthesia group suffered any cardiac event, compared with the locoregional anaesthesia group (13.3% vs. 4.7%, $P = 0.02$). An overview of all cardiac events is presented in Table 2.

Multivariable propensity-adjusted regression analysis demonstrated that general anaesthesia, compared with locoregional anaesthesia, was associated with a significantly increased risk of any 30-day cardiac event (odds ratio (OR) 3.8; 95%-confidence interval (CI) 1.1–12.9; $P = 0.03$), as well as with an increased risk of 'major' cardiac events, not including asymptomatic troponin release (OR 13.3; 95%-CI 1.2–141.8, $P = 0.03$).

Thirty-day non-cardiac events

In the study population, 39 major non-cardiac complications occurred in 35 patients, of which 20 (11.6%) were in the general anaesthesia group and 15 (11.6%) in the locoregional anaesthesia group ($P = 1.00$). Data are presented in Table 3.

Of the two non-cardiac deaths, one was caused by aspiration and one by pneumonia. Non-fatal pulmonary complications occurred in three patients, including two cases of pneumonia,

Table 2
30-day cardiac complications.

	General ($n = 173$)	Locoregional ($n = 129$)	*P*-value
	n (%)	*n* (%)	
Cardiac events			
Cardiac death	2 (1.2)	0 (0)	.51
Myocardial infarction	6 (3.4)	1 (.8)	.25
Congestive heart failure	2 (1.2)	0 (0)	.51
Arrhythmia	1 (.6)	0 (0)	1.00
Troponin release	12 (6.9)	5 (3.9)	.32
Composite cardiac endpoints			
All cardiac events	23 (13.3)	6 (4.7)	.02
All but troponin release	11 (6.4)	1 (.8)	.02

Table 3
30-day major non-cardiac complications.

	General ($n = 173$)	Locoregional ($n = 129$)	*P*-value
	n (%)	*n* (%)	
Non-cardiac complication			
Non-cardiac complications	22	17	
Patients with ≥1 complication	20 (11.6)	15 (11.6)	1.00
Mortality			
All-cause	4 (2.3)	0 (0)	.14
Non-cardiac	2 (1.2)	0 (0)	
Pulmonary			
Any pulmonary complication	5 (2.9)	0 (0)	.07
Pneumonia	3 (1.7)	0 (0)	
Aspiration	1 (.6)	0 (0)	
Pneumothorax	1 (.6)	0 (0)	
Renal			
Renal failure requiring intervention	4 (2.3)	0 (0)	.14
Surgical			
Additional surgical procedure required	5 (2.9)	9 (7.0)	.11
Intervention for endoleak	0 (0)	4 (3.1)	
Access site bleeding	2 (1.2)	4 (3.1)	
Arterial embolism	3 (1.7)	1 (.8)	
Other			
Urinary tract infection	2 (1.2)	2 (1.6)	
Access site infection	1 (.6)	2 (1.6)	
Urine retention	4 (2.3)	2 (1.6)	
Sepsis	1 (.6)	1 (.8)	
GI bleeding	0 (0)	1 (.8)	
Stroke / TIA	0 (0)	0 (0)	
Venous thrombo-embolism	0 (0)	0 (0)	

Abbreviatons: GI gastro-intestinal; TIA transient ischaemic attack.

managed with antibiotics, and one case of pneumothorax, treated with a chest tube. All pulmonary complications occurred in the general anaesthesia group (2.9% vs. 0%, $P = 0.07$).

Additional procedures for endoleak within 30 days of the baseline procedure were required in four patients, all of whom received locoregional anaesthesia for the index procedure. Additional surgery for access site bleeding was required by two patients in the general anaesthesia group and four in the locoregional anaesthesia group. Peripheral macroembolisation required embolectomy or thrombolysis in three patients in the general anaesthesia group and one in the locoregional anaesthesia groups. In total, five additional procedures were required in the general anaesthesia group and nine in the locoregional anaesthesia group (2.9% vs. 7.0%, $P = 0.11$).

Major renal complications occurred in four patients, all of whom were in the general anaesthesia group (2.3% vs. 0%, $P = 0.14$). Of these, two required permanent dialysis, one required a kidney transplant and one required a percutaneous transluminal angioplasty (PTA) procedure of a renal artery due to trash nephropathy.

Discussion

Our data show a high risk of adverse cardiac events after EVAR procedure, probably related to the presence of extensive co-morbidity in the study population. This study demonstrates an increased risk of cardiac complications after EVAR with general anaesthesia, compared with locoregional anaesthesia, after adjusting for cardiovascular co-morbidity, obesity and medication use.

The severity of the physiological stress response to surgery depends on the invasiveness and length of the surgical procedure, and its effects on haemodynamic stability, fluid shifts, blood loss and body temperature changes.[10] The surgical stress response causes tachycardia, increased myocardial contractility, systemic inflammation, reduced fibrinolytic activity, platelet activation and consequent hypercoagulability.[11] In the presence of coronary artery disease, these changes may result in perioperative myocardial infarction through either rupture of unstable coronary plaque and subsequent coronary thrombosis, or prolonged myocardial oxygen supply to demand mismatch.[7]

A coronary tree unaffected by atherosclerosis is present in only 8% of vascular surgery patients. These patients are at high risk of perioperative cardiac events, with a peak incidence on the first postoperative days.[12,13]

The surgical stress response is more effectively attenuated by locoregional anaesthesia, compared with general anaesthesia.[14] It was hypothesised that locoregional anaesthesia might improve cardiac outcomes in major surgery patients. In a case-control study of 88,188 patients, Wijeysundra demonstrates that epidural anaesthesia is associated with a small but significant reduction of all-cause mortality after major surgery.[15] In a meta-analysis of 30 trials which randomised for locoregional anaesthesia, Rodgers also found a reduced risk of perioperative myocardial infarction (OR .67; 95%-CI .45–1.00).[8]

Previous studies indicate that the performance of EVAR is feasible under multiple types of anaesthesia including general, neuraxial and local anaesthesia.[16,17] Analysis of the EUROpean collaborators on Stent-graft Techniques for abdominal aortic Aneurysm Repair (EUROSTAR) cohort of EVAR procedures indicates that surgical outcomes (incidence of endoleaks) are similar for all types of anaesthesia.[18]

No conclusive data exist regarding the relation between anaesthesia type and cardiac outcome in EVAR. In the current study, we observed a significantly increased incidence of cardiac events in the general anaesthesia group (OR 3.8). The CI is compatible with both a very minor increase and a more than 10-fold increase (95%-CI 1.1–12.9).

In a cohort study of 424 EVAR procedures by Parra (279 general, 95 regional and 50 local anaesthetics), cardiac event rates were 7%, 14% and 0% in the general, regional and local anaesthetic group, respectively, with a statistically significant difference between the epidural and local anaesthetic group.[9] No multivariable analysis, adjusting for differences in baseline characteristics, was performed. De Virgilio found no difference in cardiac events after EVAR between general and local anaesthesia in a cohort of 229 patients.[19] Analysis of data from EUROSTAR suggests a reduced risk of cardiac events in local (1%) and regional (2.9%), as compared with general anaesthesia (3.7%). However, neither the definition of cardiac complications nor the method used to score these complications was provided.[18]

Possible explanations of our results include differences in surgical stress response attenuation, and in arterial perfusion due to vasodilation induced by locoregional anaesthesia, although the latter is unlikely due to the limited area of effect of both local anaesthesia and lumbar epidural anaesthesia. In addition, differences in fluid requirements between general and locoregional anaesthesia might have influenced tissue perfusion due to haemodilution. Another factor of possible influence is the occurrence of per- and postoperative hypoxaemia. Due to the retrospective study design, we are unfortunately not able to provide adequate data on this parameter.

We observed no difference in the non-cardiac complication rate between general (11.6%) and locoregional (11.6%) anaesthesia groups ($P = 1.00$). However, general anaesthesia was associated with a trend towards an increased risk of pulmonary complications (2.9% vs. 0%, $P = 0.07$) and increased length of stay. This is in accordance with previous reports.[20] A trend towards an increased risk of the requirement for additional surgical procedures for endoleak, access site bleeding or macro-embolisation was observed in the locoregional anaesthesia group (7.0% vs. 2.9%, $P = 0.11$).

Study limitations include the retrospective cohort design, because of which no causal relationship between anaesthesia type

and outcome can be established. This type of study is likely to be subject to selection bias. To reduce selection bias, we excluded patients undergoing hybrid procedures, as well as patients undergoing emergency procedures, as both are likely to influence both the choice of anaesthesia type and the risk of cardiac complications. In addition, we used propensity-adjusted multivariable regression analysis to adjust for co-morbidity, obesity and antiplatelet and anticoagulant drug use, as these are also known to influence the choice of anaesthesia technique. Possible factors influencing our results are differences in surgical and anaesthetic management over time, and a relatively small sample size. We decided to pool local and regional anaesthesia, as both have been demonstrated to effectively attenuate the surgical stress response, compared with general anaesthesia. The study end point is a composite end point including asymptomatic troponin release, as postoperative asymptomatic troponin release is known to be highly predictive of both short and long-term mortality.[21] As many patients who suffer postoperative troponin release do not experience any symptoms, the cardiac event rate in this study is higher than in previous studies of EVAR that did not include asymptomatic troponin release in the study end points.

In conclusion, general anaesthesia, compared with locoregional anaesthesia, is associated with an increased risk of cardiac events after EVAR. Patient preferences, expected patient compliance, procedure length and anatomical factors should be considered in selection of anaesthesia type. However, when no contra-indications are present, a locoregional anaesthesia technique might be favourable for EVAR. In our opinion, despite possible difficulties involved, including the need for a very large sample size, as well as reluctance from both surgeons and patients, a randomised trial of general and locoregional anaesthesia techniques in elective EVAR is warranted.

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None.

Conflicts of Interest

None.

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