

## NATIONAL REGISTRY

## Editor's Choice – Regional Versus General Anaesthesia in Peripheral Vascular Surgery: a Propensity Score Matched Nationwide Cohort Study of 17 359 Procedures in Denmark

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### WHAT THIS PAPER ADDS

This study draws attention to the importance of considering regional anaesthesia in patients for peripheral vascular surgery to improve clinical results. Results from this nationwide study indicate a better outcome when using neuraxial anaesthesia and/or peripheral nerve blocks, compared with general anaesthesia, in lower limb arterial revascularisation surgery. This observational trial suggests a significant benefit of regional anaesthesia and underlines the importance of performing a future large scale randomised clinical trial to evaluate this observed treatment benefit.

**Objective:** Cardiopulmonary comorbidity is common in vascular surgery. General anaesthesia (GA) may impair perfusion and induce respiratory depression. Regional anaesthesia (RA), including neuraxial or peripheral nerve blocks, may therefore be associated with a better outcome.

**Methods:** This was a nationwide retrospective cohort study. All open inguinal and infra-inguinal arterial surgical reconstructions from 2005 to 2017 were included. Data were extracted from national registries. Multivariable linear and logistic regression models and propensity score matching were used. The propensity score was derived by developing a model that predicted the probability that a given patient would receive GA based on age, comorbidity, anticoagulant medication, procedure type, and the urgency of surgery. Matching was performed in four groups based on American Society of Anesthesiologists' score I – II, score III – V, and gender. Outcome parameters included surgical and general complications (bleeding, thrombosis/embolus, cardiac, pulmonary, renal, cerebral, and >3 days intensive care therapy), length of stay, and 30 day mortality, hypothesising a better outcome after RA.

**Results:** There were 10 509 procedures in the GA group and 6 850 in the RA group. After propensity score matching, 6 267 procedures were included in each group. Surgical and general complications were significantly more common after GA in both matched (3.8 vs. 2.5%,  $p < .001$  and 6.5 vs. 4.2%,  $p < .001$ ) and unmatched analyses (3.8 vs. 2.5%,  $p < .001$  and 6.5 vs. 4.2%,  $p < .001$ ). The 30 day mortality rate was significantly higher after GA, in matched and un matched analyses (3.1 vs. 2.4%,  $p = .019$  and 4.1 vs. 2.4%,  $p < .001$ ). There was no difference in length of stay.

**Conclusion:** RA may be associated with a better outcome, compared with GA, after open inguinal and infra-inguinal peripheral vascular surgery. In the clinical context when RA is not feasible, GA can still be considered safe.

**Keywords:** Chronic limb threatening ischaemia, Danish vascular registry, Outcome, Peripheral vascular surgery, Regional anaesthesia

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## INTRODUCTION

Atherosclerosis is a systemic disease affecting multiple organ systems, including cardiac, cerebral and renal function. Atherosclerosis of the lower limbs may result in critical ischaemia and, in the worst cases, gangrene.<sup>1,2</sup> Surgical arterial revascularisation is considered a high risk procedure because of the comorbidity in this patient group and the nature of the disease, involving ischaemia reperfusion and potential massive blood loss.<sup>3</sup>

Planning anaesthesia and surgery for open vascular procedures of the lower limb requires thorough assessment of the patient's physical reserve and ideally involves cardiac and pulmonary evaluation, and perhaps optimisation.<sup>4</sup> In many cases, however, the indication is critical ischaemia, and surgery is limb saving, leaving only restricted time for pre-optimisation of the patient. General anaesthesia (GA) has potential disadvantages in patients with cardiopulmonary comorbidity and advanced age.<sup>5,6</sup> Positive pressure ventilation affects haemodynamics and pulmonary physiology, which may result in atelectasis and perfusion/ventilation mismatch and GA may affect blood pressure and microcirculation negatively. Decreased tissue perfusion may potentially cause regional ischaemia, which can result in complications, ranging from impaired wound healing to thrombotic events and graft failure and, in the worst cases, organ dysfunction.<sup>7</sup>

Regional anaesthesia (RA) includes neuraxial blockades and peripheral nerve blocks, which include spinal and/or epidural, or peripheral perineural instillation of local anaesthetics, respectively. To date, the evidence for favouring neuraxial anaesthesia over GA is inconclusive.<sup>8,9</sup> In patients using anticoagulants (e.g. because of dysrhythmias, thrombosis or mechanical heart valves), neuraxial blockades are contraindicated.<sup>10</sup> As an alternative, peripheral nerve blocks are increasingly used in vascular surgery.<sup>11–13</sup>

The aim of this retrospective nationwide registry study was to evaluate the effect of GA and RA on outcome after open inguinal and infra-inguinal arterial reconstruction surgery. It was hypothesised that the rates of surgical and general complications (bleeding, thrombosis/embolus, cardiac, pulmonary, renal, cerebral, and >3 days intensive care therapy), length of stay, and 30 day mortality would be lower after RA.

## METHODS

The study was approved by the Danish Data Protection Agency 2008-58-0028, ID 2018–13. In Denmark, registry studies do not need ethical approval.

This was a retrospective, propensity score matched, cohort study, providing a descriptive analysis of associations between anaesthesia method and outcomes. The cohort comprised all first time open inguinal and infra-inguinal arterial reconstruction procedures in Denmark during the calendar years 2005–2017. All data were registered by the vascular surgeon in charge of the patient and reported to the Danish Vascular Registry. All procedures were included where the question of GA vs. RA was relevant (open arterial revascularisations where RA alone would be sufficient for surgery). Covariates were selected from a clinical

perspective, including variables previously defined as risk factors.<sup>14,15</sup> All residents in Denmark have a unique and permanent civil registration number that enables individual linkage to nationwide administrative registers.<sup>16</sup> Patients were identified from procedure codes in the Danish Vascular Registry. These data were merged with data from the Danish Anaesthesia Database, the Danish National Prescription Database and the National Patient Registry.

### *The danish vascular registry*

This study is based on data from this nationwide database, founded in 1989, now comprising more than 190 000 procedures. Annual reports, evaluating all Danish vascular departments by a set of quality indicators, are accessible online (Karbase.dk).

### *Anaesthesia type*

GA was defined as anaesthesia involving controlled mechanical ventilation. GA in combination with adjunctive RA was defined as GA. RA included solely spinal, epidural and peripheral nerve blocks without airway management. The type of anaesthesia (GA or RA), and the dates of surgery and hospital discharge registered in the Danish Vascular Registry were crosschecked with registrations in the Danish Anaesthesia Database and the National Patient Registry.

### *Comorbidity*

Comorbidity, registered in the Danish Vascular Registry, includes diabetes, previous stroke or transitory cerebral ischaemia, hypertension, cardiac disease (previous myocardial infarction, ischaemic heart disease, valvular disease, and dysrhythmias), pulmonary disease, chronic dialysis, severe liver disease, dementia, and cancer.

The Charlson Comorbidity Index (CCI) was generated from data in the National Patient Registry and includes age, diabetes, liver disease, malignancy, acquired immune deficiency syndrome, moderate to severe chronic kidney disease, chronic heart failure, chronic obstructive pulmonary disease, cerebrovascular accident, dementia, hemiplegia, connective tissue disease, and peptic ulcer disease.<sup>17</sup> The definition of CCI, applied in this study, is reported in the online supplementary material (Supplementary file 1).

The American Society of Anesthesiologists (ASA) score describes patients' pre-operative status and is registered in the Danish Vascular Registry and the Danish Anaesthesia Database by an anaesthetist during the pre-operative anaesthetic consult.

### *Anticoagulant medications*

The Danish National Prescription Database provides information regarding all prescription drugs sold in Danish community pharmacies on an individual level, linked to the national civil registration number.<sup>18</sup> Information was retrieved on the use of new oral anticoagulants, vitamin K antagonists, antiplatelet therapy, and low molecular weight heparin (Supplementary file 2) up to 180 days before surgery.

### Surgical data

The Danish Vascular Registry provides information on procedure code, indication for surgery, urgency of surgery, anaesthesia type, duration of surgery, and estimated blood loss.

### Post-operative complications

The Danish Vascular Registry provides information on wound complications, surgical complications, and general complications, defined in Table 1.

### Mortality

The Danish Vascular Registry provides information on in hospital and 30 day all cause mortality and time to death via a link to the Danish civil registration system, holding information on date of birth, death, sex, and migration.<sup>16</sup>

### Length of stay

The Danish National Patient Registry holds information on all hospitalisations since 1977, including admission and discharge dates, discharge diagnosis, procedure codes, and surgical procedures.<sup>19</sup> Length of stay was defined as the number of days from the date of surgery to the date of discharge from hospital to home or to a nursing facility. Transfers to other specialty wards, in or outside the primary hospital, were included in the length of stay.

### Statistics

Anticipating a 4% mortality rate<sup>1</sup> after GA, a power calculation was performed, estimating a 25% decrease in the RA

group to a mortality rate of 3%. With an  $\alpha$  of 0.05 and 80% power ( $1-\beta$ ), 5 301 procedures were needed in each group. Knowing that only approximately one third of procedures are performed using RA, it was chosen to include all procedures from 1 January 2005 to 31 December 2017.

Categorical variables were presented as percentages and frequencies and continuous variables using medians and first to third quartiles (Q1–Q3). The association between type of anaesthesia and hospital length of stay was examined using linear regression. Hospital length of stay was log transformed, and the assumption of linearity was assessed using QQ plots. Similarly, but using logistic regression, associations between type of anaesthesia and 30 day mortality, surgical, general and wound complications were analysed, and odds ratios presented in Forest plots. Mortality by type of anaesthesia was presented using Kaplan–Meier estimates. Data management was performed with SAS version 9.4 (SAS Institute Inc.) and analyses using R statistical software package version 3.5.0 (R Development Core Team).<sup>20</sup> Propensity score matching was used to identify a set of matched GA/RA pairs so that confounding by indication, associated with the observational study, could be minimised. The propensity score was derived by developing a logistic regression model that predicted the probability that a given patient would receive GA on the basis of age, cardiac and pulmonary disease, previous stroke, cancer, treatment with anticoagulant medication, procedure type (bypass, TEA or other), and urgency of surgery. Stratified matching was performed in four groups based on ASA score I–II, ASA score III–V, female, and male sex. The propensity score was used to match patients on a one to one basis to minimise the overall distance in propensity scores between the groups. The GA and RA patients were matched unless their estimated log odds from the logistic regression model were more than two standard deviations apart.

Table 1. Description of complications provided by the Danish Vascular Registry	
Post-operative complications	Definition
<i>General medical complications</i>	
Cardiac	Myocardial infarction, cardiac failure, dysrhythmias
Pulmonary	Pulmonary complication requiring treatment
Cerebrovascular event	Transitory cerebral ischaemia, cerebral infarction, or haemorrhage
Acute renal failure	Need for dialysis
Intensive care unit	Intensive care unit length of stay >3 days
<i>Surgical complications</i>	
Compartment syndrome	Fasciotomy required
Peripheral nerve lesion	Causing motor or sensory deficit
Peripheral embolisation	Symptomatic embolisation distal to the arteriotomy
Bleeding	Requiring surgery
<i>Wound complications</i>	
Wound infection	Deep wound infection, including infection of the prosthesis
Wound necrosis	Requiring revision
Wound lymphocele/-rrhoea	>2 days of lymphorrhoea
Wound haematoma	Requiring revision

### RESULTS

A total of 18 450 first time procedures was identified in the Danish Vascular Registry. Of these procedures, 1 091 were excluded because of one or more of the following: temporary replacement civil registration numbers ( $n = 56$ ), missing data on anaesthesia method ( $n = 376$ ) or registered local infiltration analgesia performed by the surgeon ( $n = 765$ ), leaving 17 359 procedures for analyses. The most frequently performed procedures were bypass surgery from the femoral artery to the popliteal or crural arteries, followed by thrombo-endarterectomy surgery of the femoral artery and its branches (Supplementary file 3).

A total of 6 267 pairs were suitable for propensity score matching.

Unmatched and matched patient characteristics and peri-operative data are presented in Table 2. GA was used in 61% of patients. More octogenarians were represented in the RA group. Also, in the GA group, cardiac and cerebrovascular comorbidity were more prevalent. Previous myocardial infarction was seen in 11.2% of patients in the GA group vs. 8.6% in the RA group ( $p < .001$ ) and previous stroke in 8.5% of GA patients vs. 6.9% of RA patients ( $p < .001$ ). Equivalently,

**Table 2.** Patient characteristics and peri-operative data in the unmatched and matched cohort of patients in the Danish Vascular Registry operated on under general anaesthesia (GA) or regional anaesthesia (RA) for open inguinal and infra-inguinal arterial reconstructions in 2005–2017

	Unmatched GA (n = 10 509)	Unmatched RA (n = 6 850)	p value	Matched GA (n = 6 267)	Matched RA (n = 6 267)	p value
Age – y	70.0 (63.0, 77.0)	72.0 (65.0, 78.0)	<.001	71.0 (64.0, 78.0)	71.0 (64.0, 78.0)	.32
Age > 80 y	1 718 (16.3)	1 265 (18.5)	<.001	1 076 (17.2)	1 082 (17.3)	.91
Female	4 199 (39.9)	2 720 (39.7)	.76	2 505 (40.0)	2 505 (40.0)	1.0
ASA physiology score III–V	4 813 (45.8)	2 511 (36.7)	<.001	2 361 (37.7)	2361 (37.7)	1.0
<i>Charlson Comorbidity Score</i>						
Low	185 (1.8)	29 (0.4)		67 (1.1)	29 (0.5)	
Moderate	4 677 (44.5)	3 249 (47.4)		3 005 (47.9)	3 008 (48.0)	
Severe	5 647 (53.7)	3 572 (52.1)	<.001	3 195 (51.0)	3 230 (51.5)	<.001
<i>Comorbidity</i>						
Cerebrovascular	894 (8.5)	473 (6.9)	<.001	440 (7.0)	448 (7.2)	.81
Cardiac	4 266 (40.6)	2 265 (33.1)	<.001	2 123 (33.9)	2 174 (34.7)	.35
<i>Pulmonary comorbidity</i>						
COPD	1 493 (14.2)	973 (14.2)		873 (13.9)	879 (14.0)	
History of dyspnoea	211 (2.0)	215 (3.1)	<.001	144 (2.3)	150 (2.4)	.98
Anticoagulant medication	2 838 (27.0)	970 (14.2)	<.001	918 (14.6)	952 (15.2)	.41
<i>Surgery</i>						
Emergency*	1 213 (11.5)	203 (3.0)		209 (3.3)	198 (3.2)	
Urgent†	2 286 (21.8)	1 153 (16.8)		1 096 (17.5)	1 106 (17.6)	
Elective	7 007 (66.7)	5 490 (80.1)	<.001	4 960 (79.1)	4 962 (79.2)	.68
Blood loss – mL	250 (100, 450)	200 (100, 400)	<.001	225 (100, 410)	200 (100, 400)	<.001
Duration of surgery – min	129 (90, 180)	125 (92, 175)	.31	131 (95, 180)	125 (93, 180)	<.001
<i>Indication for surgery</i>						
Acute ischaemia	1 625 (15.5)	430 (6.3)		518 (8.3)	414 (7.5)	
Claudication	2 427 (23.1)	2 251 (32.9)		1 716 (27.4)	2 077 (33.2)	
Rest pain	1 957 (18.7)	1 339 (19.6)		1 300 (20.8)	1 202 (19.2)	
Ulceration or gangrene	3 135 (29.9)	2 347 (34.3)		2 082 (33.3)	2 122 (33.9)	
Other indication	1 342 (12.8)	466 (10.4)	<.001	642 (10.3)	436 (7.0)	<.001
<i>Procedure type</i>						
TEA	2 872 (27.3)	1 991 (29.1)		1 832 (29.2)	1 838 (29.3)	
Bypass	4 262 (40.6)	3 160 (46.1)		2 803 (44.7)	2 814 (44.9)	
Other	3 375 (32.1)	1 699 (24.8)	<.001	1 632 (26.0)	1 615 (25.8)	.96

Data are presented as n (%) or median (interquartile range). Numbers vary slightly depending on the quantity of missing information, range 0–2.5%. GA = general anaesthesia; RA = regional anaesthesia; ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; TEA, thrombo-endarterectomy.

\* Performed within h.

† Performed within days.

more patients were treated with anticoagulant medication in the GA group (Table 2). More patients were ASA group 3–4 in this group. The difference in CCI was small but statistically significant (Table 2). No difference was found in the prevalence of diabetes, which was present in 24.8% of all patients.

Indication for surgery varied between the groups and more patients in the GA group needed emergency surgery. Accordingly, acute ischaemia was more prevalent in the GA group (Table 2).

Univariable comparison of post-operative complications, using unmatched and matched data are presented in Table 3. Multivariable regression analysis of post-operative outcome, using unmatched and matched data are presented in Table 4 and Figs. 1 and 2.

In unmatched analyses, 30 day mortality and the incidence of general and surgical complications were significantly higher in the GA group. All types of general medical complications were seen more frequently in the GA group. Of the surgical complications, only post-operative bleeding was significantly more frequent in the GA group (Table 3).

After matching, all categories of complications were more frequent, and the 30 day mortality rate was significantly higher in the GA group after multiple regression analysis (Table 4 and Fig. 2).

The overall 30 day mortality was 3.4%, and incidence of general and surgical complications was 5.9% and 3.4%, respectively. Median length of stay was five (3, 10) days. The overall same side one year amputation rate was 9.3%.

Kaplan–Meier curves, demonstrating matched and unmatched 30 day mortality, are presented in Fig. 3. Missing data are reported in the relevant tables. Numbers were small and this study focused on cases with complete data.

## DISCUSSION

In this nationwide cohort of 17 359 open inguinal and infra-inguinal arterial revascularisation procedures, a significantly increased 30 day mortality and complication rate was demonstrated if the surgery was performed using GA compared with RA, in both unmatched and propensity score matched analysis.

**Table 3. Univariable analyses of complications in the unmatched and matched cohort of patients in the Danish Vascular Registry operated under general anaesthesia (GA) or regional anaesthesia (RA) for open inguinal and infra-inguinal arterial reconstructions in 2005–2017**

Post-operative complications	Unmatched GA n = 10 509	Unmatched RA n = 6 850	p value	Matched GA n = 6 267	Matched RA n = 6 267	p value
Cardiac	295 (2.9)	123 (1.8)	<.001	175 (2.8)	113 (1.8)	.002
Pulmonary	172 (1.7)	61 (0.9)	<.001	101 (1.6)	55 (0.9)	.002
Cerebrovascular event	51 (0.5)	17 (0.3)	.028	21 (0.4)	15 (0.3)	.69
Acute renal failure, need for dialysis	37 (0.4)	11 (0.2)	.025	18 (0.3)	10 (0.2)	.18
ICU >3 days	70 (0.7)	11 (0.2)	<.001	33 (0.5)	11 (0.2)	.001
Compartment syndrome	47 (0.5)	10 (0.1)	<.001	15 (0.2)	10 (0.2)	.41
Peripheral nerve lesion	30 (0.3)	19 (0.3)	.85	19 (0.3)	17 (0.3)	.84
Peripheral embolisation	30 (0.3)	13 (0.2)	.26	18 (0.3)	13 (0.2)	.45
Bleeding, requiring surgery	205 (2.0)	94 (1.4)	.003	128 (2.1)	86 (1.4)	.003
Wound infection	200 (1.9)	116 (1.7)	.34	119 (1.9)	106 (1.7)	.50
Wound necrosis	195 (1.9)	128 (1.9)	.97	108 (1.8)	115 (1.9)	.75
Wound lymphocele/-lymphorrhoea	954 (9.3)	626 (9.2)	.83	629 (10.3)	563 (9.1)	.026
Wound haematoma	344 (3.4)	214 (3.2)	.48	205 (3.3)	200 (3.2)	.75

Data are presented as n (%). The description of complications can be found in Table 1. Numbers vary slightly depending on the quantity of missing information, range 0–3.1%. GA = general anaesthesia; RA = regional anaesthesia; ICU = intensive care unit.

In 2016, Kehlet *et al.*<sup>14</sup> evaluated a subpopulation of the present study cohort, comprising 3 202 patients undergoing open arterial revascularisation of the lower limb. One third of patients developed one or more complications. The 30 day mortality rate was 5% and one year mortality rate 15%. After one year, 19% were either amputated or dead. Of independent risk factors, they identified age, female gender, comorbidity, urgent surgery, and GA; anaesthesia type was the only modifiable factor. The present study included 13 years of data from the nationwide cohort and confirms that GA seems to affect outcome negatively.

In a recent retrospective study from the Vascular Quality Initiative, Sgroi *et al.* presented data from 15 997 patients undergoing infra-inguinal bypass surgery from 2011 to 2016.<sup>9</sup> Interestingly, only 3.5% of patients received RA, and this ratio decreased during the study period from 4.6% in 2011 to 2.6% in 2016, with a centre variability ranging from 0% to 30%. Despite the small number of patients in the RA group, they demonstrated a reduced length of stay and a lower frequency of both acute congestive heart failure and acute kidney injury and a trend towards lower mortality (1.1 vs. 2.2%,  $p = .07$ ).

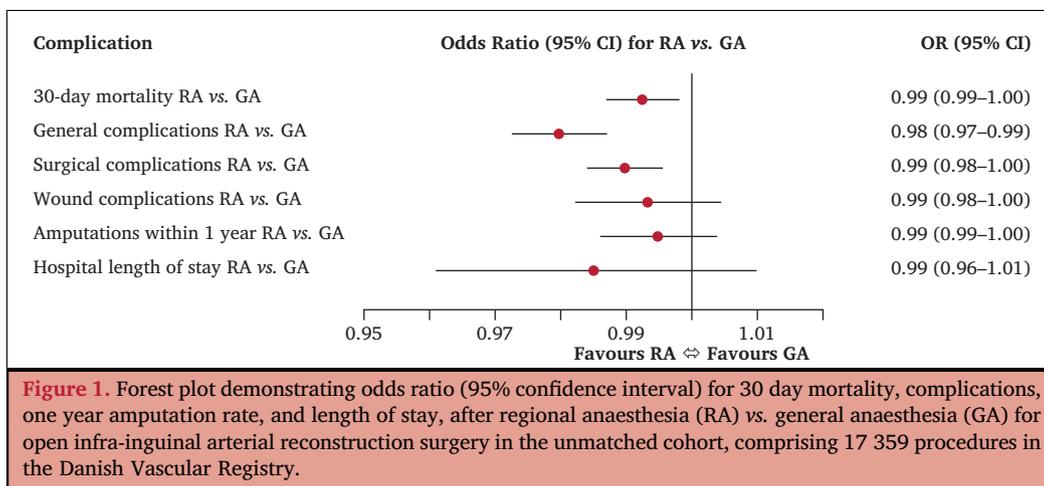
From a clinical perspective, the choice of anaesthesia depends on various factors. In acute surgery, both anaesthetist and surgeon may prefer GA because of presumed difficulty of the procedure, long duration of surgery, and to avoid the potentially more time consuming procedure with RA prior to surgery. The anaesthesia personnel may lack regular experience in vascular surgery and, therefore, prefer GA. In addition, the risk of inadequate peripheral nerve blocks may also have implication for the decision.<sup>21</sup> Thus, acute surgery will often be performed under GA. The present study used multiple regression and propensity score matching to adjust for these differences and confirmed the increased 30 day mortality and complication rate in the GA group.

Ghanami *et al.* studied a cohort of 5 462 patients for elective infra-inguinal bypass procedures and found no difference in outcome after RA vs. GA.<sup>22</sup> Only 13% of procedures were under RA, but the complication rate was as high as 37%. They found increased trainee surgical involvement, transfusion need, and operating time in the GA group, perhaps indicating more complex surgical procedures. However, a fast procedure may also be associated

**Table 4. Outcome data in the unmatched and matched cohort of patients in the Danish Vascular Registry operated on under general anaesthesia (GA) or regional anaesthesia (RA) for open inguinal and infra-inguinal arterial reconstructions from 2005 to 2017**

Outcome	Unmatched GA (n = 10 509)	Unmatched RA (n = 6 850)	p value	Matched GA (n = 6 267)	Matched RA (n = 6 267)	p value
30 day mortality	429 (4.1)	166 (2.4)	<.001	194 (3.1)	150 (2.4)	.019
1 y amputation rate	1 033 (10.0)	550 (8.2)	<.001	546 (8.8)	515 (8.4)	.39
Wound complications	1 533 (15.0)	969 (14.3)	.20	955 (15.6)	879 (14.2)	.030
General complications	723 (7.0)	285 (4.2)	<.001	400 (6.5)	261 (4.2)	<.001
Surgical complications	408 (4.0)	174 (2.6)	<.001	232 (3.8)	157 (2.5)	<.001
Length of stay, days	5 (3, 11)	5 (3, 9)	<.001	5 (3, 9)	5 (3, 8)	.14

Data are presented as n (%) or median (interquartile range). The description of complications can be found in Table 1. Numbers vary slightly depending on the quantity of missing information, range 0–3.1%.



with poor outcomes because of comorbidities and disease severity, that has no revascularisation potential. Also, procedures like femorocrural bypass have a long operating time, but the blood loss is usually low. Procedure type and urgency of surgery were included in the present statistical model to adjust for these variations.

Cardiac complications may be prevented by avoiding the haemodynamic instability that can be induced by GA.<sup>23</sup> In the Danish Vascular Registry, cardiac complications are defined as acute myocardial infarction, congestive heart failure, or dysrhythmias. Cardiac complications were seen in 2.4% of patients in the present study and were significantly more common in the GA group in both unmatched and matched analyses.

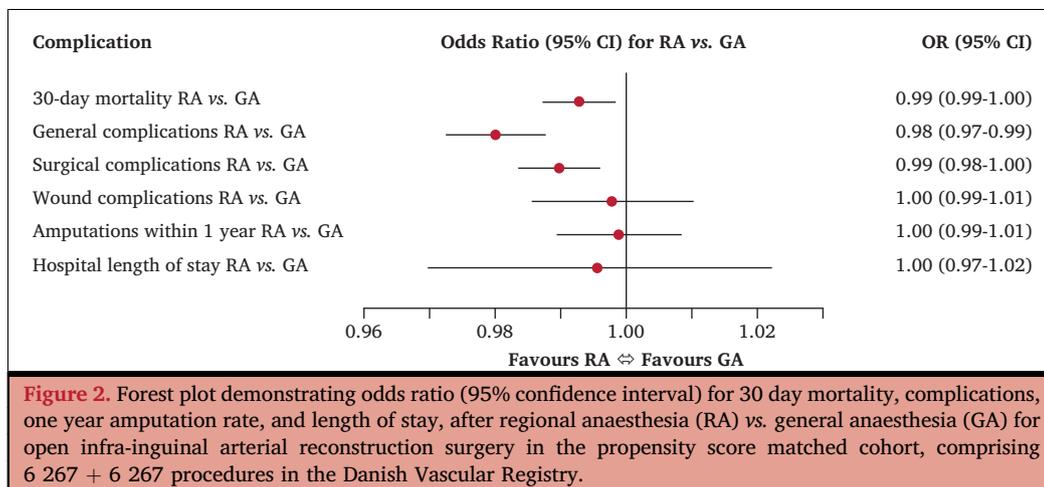
The incidence of a neuraxial haematoma after epidural or spinal blockade ranges from 1:168 000 to 1:190 000.<sup>24</sup> More patients in the GA group received anticoagulant medication, platelet inhibitor, or low weight molecular heparin, which increases this risk significantly. In the present study, use of these medications was included in the propensity score matching model. Unfortunately, there is no available information about the indication for therapy, or whether the medication was discontinued before surgery.

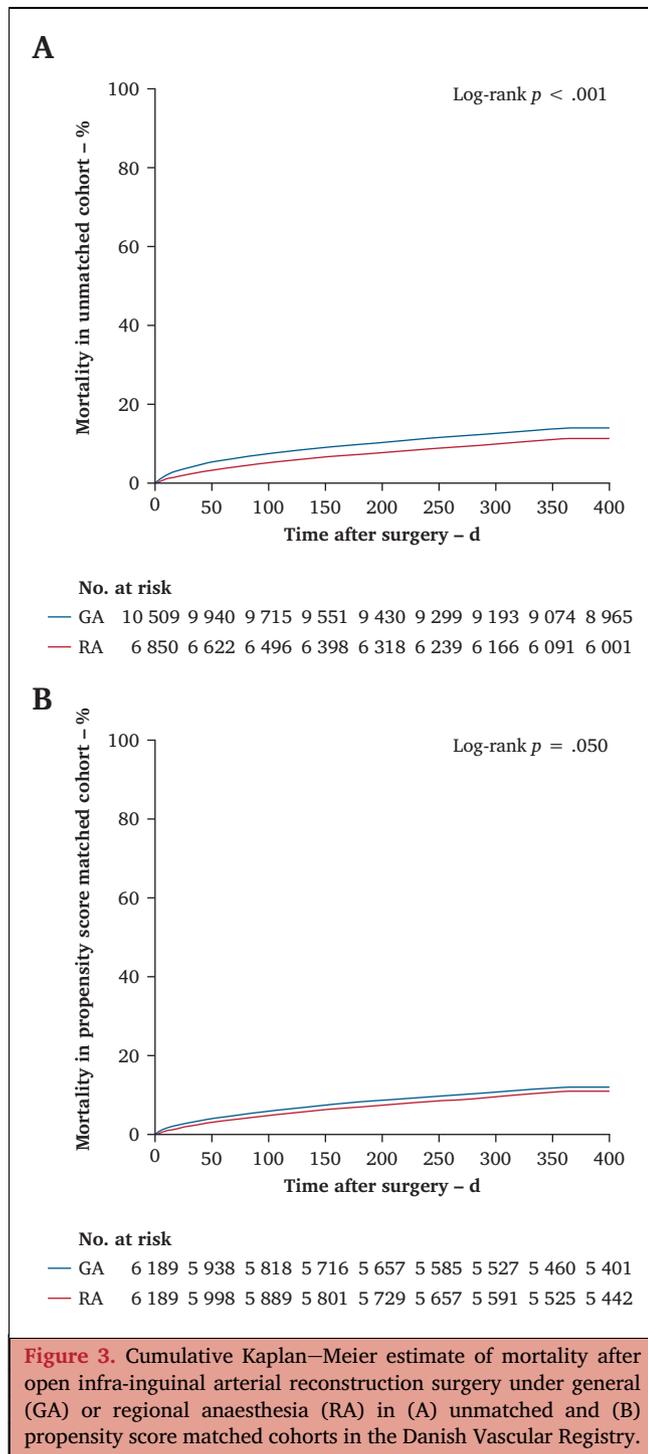
Avoiding mechanical ventilation may contribute to better outcome. Hausman *et al.* demonstrated that the complication rate, risk of pulmonary infection, prolonged length of

mechanical ventilation, and unplanned post-operative intubation were reduced when using RA compared with GA in 2 644 patients with severe chronic obstructive pulmonary disease (COPD) undergoing a variety of surgical procedures.<sup>25</sup> In the present study, in the unmatched cohort, a higher prevalence of patients with dyspnoea and patients with COPD was found in the RA group, suggesting that RA was preferred in this patient category. As expected, significantly more post-operative pulmonary complications were found after GA in the unmatched cohort, although the overall pulmonary complication rate was only 1.4%.

Peripheral nerve blocks may be more favourable than neuraxial anaesthesia. A post hoc analysis from a large, randomised trial demonstrated that epidural analgesia was associated with increased cardiovascular morbidity.<sup>26</sup> Peripheral nerve blocks have the advantage that they can be used despite anti-coagulation therapy and severe cardiac comorbidity, such as aortic stenosis. Yazigi *et al.* randomised 50 patients for peripheral vascular surgery to GA or peripheral nerve blocks (combined sciatic and femoral nerve block) and found reduced frequency of intra-operative myocardial ischaemia in the RA group.<sup>11</sup> Furthermore, peripheral nerve blocks may have the potential to reduce post-operative chronic pain.<sup>27</sup>

The risk of peripheral nerve damage and masking of severe ischaemia, however, must be acknowledged when using RA in peripheral artery disease. No difference was found





in the incidence of peripheral nerve damage. More cases of compartment syndrome and amputation were seen in the GA group; however, this was not reflected in the propensity score matched analysis and may be more related to the severity of limb ischaemia than to the type of anaesthesia.

It would have been informative to investigate the development and frequency of peripheral nerve blocks during the 13 year study period. Anticoagulant medication is increasingly used, resulting in fewer procedures with neuraxial blockade. Peripheral nerve block procedures, however, have been an increasing part of standard anaesthesia practice in many

hospitals during this period. Unfortunately, the distribution of peripheral and neuraxial nerve blocks is not provided by the Danish Vascular Registry. From the present study, it can be concluded only that avoiding GA may be beneficial.

One strength of this study was the nationwide character of the Danish Vascular Registry, including 17 359 procedures. Validating data using the Danish Anaesthesia Database and the National Patient Registry further strengthens the results in terms of data purity. Propensity score matching with a matched sample size of 72% is acceptable and the risk of potential influence of incomplete matching can be considered small.<sup>28</sup>

The validity of the Danish Vascular Registry has been evaluated repeatedly and more than 95% internal and external validity has been demonstrated.<sup>29–31</sup> Data are, however, confined to the Danish population and healthcare system, which may impair generalisability.<sup>32</sup>

Limitations of this study include that this is a retrospective cohort study. Confounding with selection and information bias may represent a potential problem. All data were registered by the vascular surgeon in charge of the operation, including registration of surgical complications, and some degree of under reporting may be expected. It was not possible to identify patients with unsuccessful or complicated procedures. Unfortunately, this information can be extrapolated only from registered complications and length of hospital stay, an endpoint that is somewhat insecure and debatable.<sup>33</sup>

Additionally, the Danish Vascular Database does not provide detailed information about the timing of complications. It would be of interest to distinguish between intra-operative and post-operative complications, especially in terms of cardiac incidents, which were more common in the GA group. Whether this reflects intra-operative hypotension and hypoperfusion or insufficient post-operative pain control remains unanswered in the present study. Post-operative pain is affected by adding RA to GA. The frequency of combined GA and RA was registered by the surgeon, who may not have been aware of the importance of this specific information. As a result of poor validation and risk of severe registration bias, these data were not reported in the present study.

Residual confounding should also be considered. It is difficult to compare patients affected by different pathologies (i.e. diabetic arteriopathy, aneurysmal disease, acute limb ischaemia), which may present with different severity of the disease, despite treatment probably being surgical in most cases. Neither the anaesthetist's nor the surgeon's reason for choosing RA or GA are available in these data. Also, the seniority of both anaesthetist and surgeon may have added important information to the study.

The study period was 13 years, which may represent an additional limitation. During this period, endovascular treatment options have improved<sup>34</sup> and thus the most fragile patients may no longer need open surgery.

The perspective of this hypothesis generating study is to bring attention to the importance of considering RA in patients scheduled for inguinal and infra-inguinal vascular surgery. Regular use of peripheral nerve block procedures

and sedation may make RA more attractive. Large scale randomised clinical trials, evaluating the effect of GA vs. RA on outcome are needed, and can, according to these results, be considered safe and ethically justifiable.

Neither the 2018 ESC/ESVS Guidelines on peripheral artery disease,<sup>35</sup> nor the 2019 Global Vascular Guidelines on the Management of Chronic Limb Threatening Ischaemia, discuss the topic of GA vs. RA.<sup>36</sup> According to the present results, this modifiable element of treating patients with chronic limb threatening ischaemia may deserve consideration in future guidelines and recommendations.

In summary, in this nationwide cohort study, including 17 359 open inguinal and infra-inguinal arterial revascularisation procedures, GA was associated with a significantly higher 30 day mortality and more surgical and general complications than RA. The rate of wound complications, one year amputation rate, and length of stay were not affected.

After propensity score matching of 6 267 pairs, 30 day mortality and rates of all types of complications were significantly higher in the GA group. Length of stay and one year amputation rate were not affected. In conclusion, RA may be associated with a better outcome, compared with GA, after open inguinal and infra-inguinal vascular surgery. In a clinical context when RA is not feasible, GA can still be considered as safe.

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#### CONFLICT OF INTEREST

None.

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None.

#### APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejvs.2020.11.025>.

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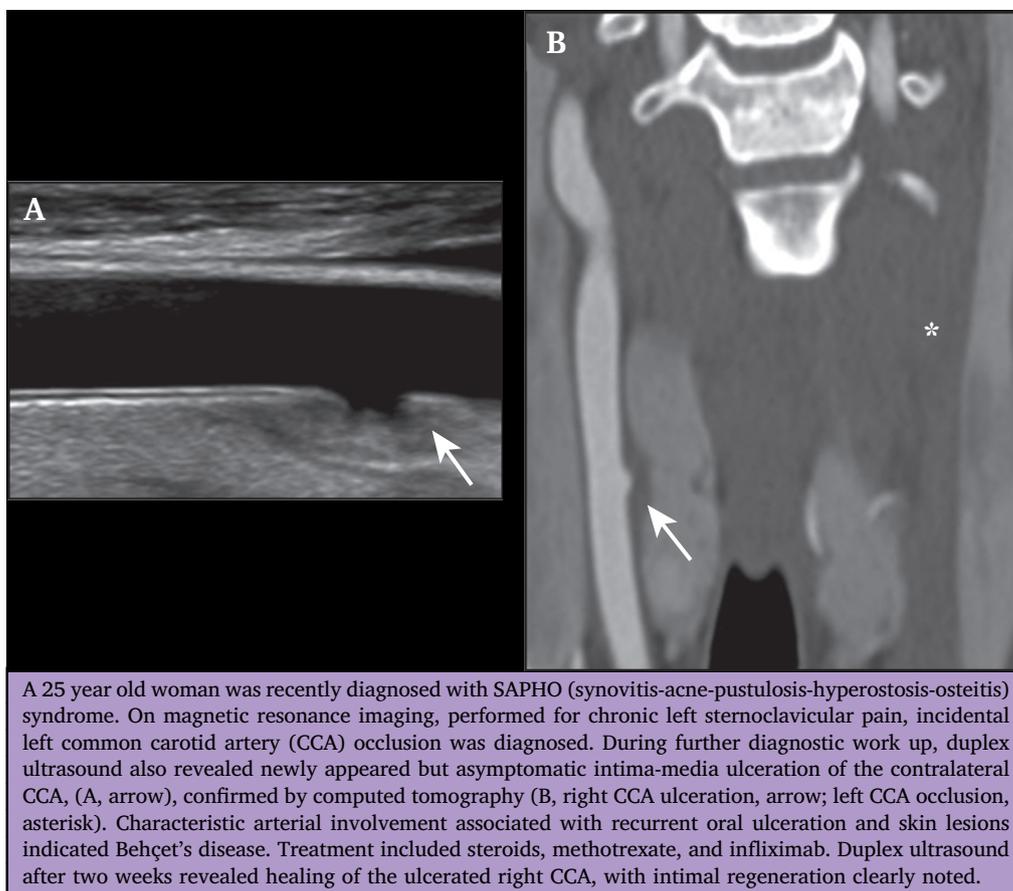
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## COUP D'OEIL

### Carotid Ulceration in a Young Woman with SAPHO Syndrome

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