

# No reduction in mortality after centralisation in treatment of patients with ruptured abdominal aneurism

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## ABSTRACT

**INTRODUCTION:** Ruptured abdominal aortic aneurism (rAAA) is a severe condition with all-cause mortality rates reaching 80%. We speculated whether the 2008 centralisation of the treatment of patients with rAAA in Denmark had improved outcome as suggested in other surgical specialties.

Accordingly, our aim was to describe temporal changes in mortality for patients undergoing surgery for rAAA in the Capital Region of Denmark between 2009 and 2015.

**METHODS:** This was a retrospective population-based cohort study of patients in the intensive care unit diagnosed and treated for rAAA at Rigshospitalet from 1 January 2009 to 31 December 2015. Patient characteristics and procedure-related variables were obtained from the medical records. The primary outcome measure was death within 90 days of the primary surgical procedure.

**RESULTS:** A total of 339 patients were diagnosed with rAAA, and 275 patients were included in the final study population; 26.9% of the patients died within 90 days of the primary surgical procedure, whereas the 30-day and one-year mortality was 18.5% and 31.6%, respectively. No consistent reduction in mortality was observed throughout the observation period.

**CONCLUSIONS:** In this population-based cohort study of patients surgically treated for rAAA, we found no consistent reduction in mortality over time following centralisation of treatment.

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Ruptured abdominal aortic aneurism (rAAA) is a severe condition with all-cause mortality rates reaching 80% [1]. Roughly two thirds of patients with rAAA reach the hospital and 40% of these die before surgery [1]. The incidence of rAAA in Denmark is 83/1,000,000, corresponding to 400 to 520 new annual cases [2]. The 30-day mortality rate in Denmark has remained stable around 30-40% in the past two decades [2].

In 2008, the treatment of patients with rAAA in Denmark was centralised and today six, instead of ten, national centres treat patients with rAAA [3]. Centralisation has been demonstrated to improve outcomes in rAAA treated with endovascular repair and in other

acute surgical conditions, such as ruptured suprarenal aneurisms and aortic dissections [4, 5]. We hypothesised that this would also be the case for patients surgically treated for rAAA.

Accordingly, the aim of this population-based observational study was to describe temporal trends in mortality for patients undergoing surgery for rAAA in the Capital Region of Denmark between 2009 and 2015.

## METHODS

### Study design and approvals

This was a population-based retrospective cohort study of patients post-operatively admitted to the intensive care unit (ICU) following surgery for rAAA at Rigshospitalet between 1 January 2009 and 31 December 2015. We have prepared this manuscript according to the Strengthening the Reporting of Observational Studies in Epidemiology statement [6]. The study was approved by the Danish Data Protection Agency (RH-2016-391) and The Danish Health Authority (3-3013-932/I). As the design of the study was observational, ethical approval was waived by the regional research ethics committee.

### Population

We included all consecutive patients with the International Classification of Diseases-10 code DI71.3 (ruptured abdominal aortic aneurism), surgically treated for rAAA at Rigshospitalet. Patients who died before surgery or before reaching the ICU were excluded. Also, patients with non-ruptured AAA, ruptured thoracoabdominal aortic aneurisms or iliacal aneurisms were not included. No other exclusion criteria were applied.

### Organisation of treatment of ruptured abdominal aortic aneurism in Denmark

Since 2008, vascular surgery in Denmark has been centralised at seven hospitals, and six of these provide acute surgery to patients with rAAA. At Rigshospitalet 40-50 patients undergo surgery for rAAA annually, representing approximately a third of the total number of rAAA procedures performed in Denmark [3, 7]. The

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hospital covers an area of 10,000 square kilometres with approximately 2.7 million inhabitants [8]. Post-operatively, all patients are transferred to the ICU for post-operative management, irrespective of risk factors or post-operative physiological state. All patients treated for rAAA in the study period were managed by open surgical repair with insertion of a vascular prosthesis [7].

#### Data extraction and variables

Patients were identified through the Critical Information System, an electronic patient data-managing system used in the ICU. Patients were cross-checked with the surgery-planning programme ORBIT, the Danish Vascular Registry and the medical files.

We extracted the following demographic, baseline and in-hospital data: gender, age, BMI, smoking status, treatment with oral anticoagulants, comorbidities (diabetes mellitus, hypertension, ischaemic heart disease, chronic obstructive pulmonary disease, cerebrovascular disease and renal failure), intraoperative blood loss, blood transfusion during surgery, duration of surgery, the Sequential Organ Failure Assessment score [9], and the Simplified Acute Physiology Score II [10]. From the Danish National Patient Registry [8], we retrieved data on mortality.

#### Outcome measures

The primary outcome measure was death within 90 days of the primary surgical procedure. Secondary outcomes measures were: 1) death within 30 days of the primary surgical procedure, 2) death within one year of the primary surgical procedure, 3) secondary surgery associated with the primary surgical procedure before discharge from hospital, 4) intestinal ischaemia irrespective of whether this was surgically verified or a tentative diagnosis, 5) renal replacement therapy during the ICU stay, 6) sepsis [11] and 7) length of stay in the ICU.

#### Statistical analyses

Baseline and clinical characteristics are presented as medians with interquartile ranges (IQR) for continuous variables, and frequencies and percentages for categorical variables, stratified for 90-day mortality. We compared survivors and non-survivors using the chi-squared test or Fisher's exact test for categorical variables, and Student's t-test or the Wilcoxon rank-sum test for continuous variables, as appropriate. The prevalence of missing data is presented in **Table 1**. All statistical tests were two-tailed, and a  $p < 0.05$  was considered statistically significant. The survival probabilities were estimated using the Kaplan-Meier method. We used SAS software 9.4 for the analyses.

*Trial registration:* not relevant.

## RESULTS

A total of 339 patients were diagnosed with rAAA and scheduled for surgery at Rigshospitalet from January 2009 to December 2015. Nine patients were cancelled before reaching the operating theatre because additional treatment was considered futile, and 55 patients (16.7%) died in the theatre due to excessive bleeding or other complications. In total, 275 patients were included in the final study population (**Figure 1**).

The number of patients surgically treated annually for rAAA fell in the 35-45 range (**Figure 2A**). The majority of patients were males (86.6%), the median (IQR) age was 73 years (68-77), and most of the patients had one or more comorbidities (Table 1). In general, survivors were younger, had a lower disease severity, fewer co-existing diseases and experienced fewer complications (Table 1 and **Table 2**).

A total of 26.9% (74/275) of the patients died within 90 days of the primary surgical procedure, whereas the 30-day and one-year mortality was 18.5% and 31.6%, respectively (Figure 2A). No consistent reduction in mortality was observed throughout the observation period, although the 90-day mortality rate varied between 20% and 38% (Figure 2A). The long-term survival is presented in Figure 2B. The figure illustrates a high mortality rate in the first six months following surgery, after which the curve flattens out. Around 50% of the patients remained alive seven years after their rAAA.

A total of 88 patients (32%) underwent re-surgery, 36 patients (13.1%) developed intestinal ischaemia and 59 patients (21.5%) required renal replacement therapy due to acute kidney injury. In total, 150 patients (54.6%) suffered one or more post-operative complications (Table 2), and the median (IQR) length of stay in the ICU was 4.3 days (1.7-7.7 days).

## DISCUSSION

In this retrospective population-based cohort study of 275 patients admitted to the ICU following open surgical repair for rAAA at Rigshospitalet from 2009 to 2015, we found a high morbidity and mortality with no consistent reduction in mortality following centralisation. In contrast to the findings in studies of other surgical conditions [4, 5, 12, 13], we observed no consistent reduction in mortality following centralisation of the treatment in 2008. This is somewhat surprising as open surgical repair of rAAA is a complicated surgical procedure in which the anaesthetic and surgical team needs routine, which they are assumed to achieve with centralisation. Perhaps there are too few cases per year to gain significant experience in handling these critically ill patients. In ovarian cancer and oesophago-gastric cancer, centralisation resulted in improved outcomes [12, 13]. The reason for this is likely the higher volume

**TABLE 1**

Baseline and demographic characteristics of patients undergoing open repair for ruptured abdominal aortic aneurism at Rigshospitalet in 2009-2015. Stratified by 90-day mortality.

	Non-survivors (n <sub>n</sub> = 201)	Survivors (n <sub>s</sub> = 74)	Total (N = 275)	p-value	Patients with missing values n (%)
Age, median (IQR), yrs	71 (67-76)	76 (71-80)	73 (68-77)	< 0.01	0 (0.0)
BMI, median (IQR), kg/m <sup>2</sup>	26.1 (23.8-29.4)	26.1 (24.3-28.1)	26.1 (23.8-29.3)	0.40	3 (1.1)
Male gender, n (%)	174 (86.6)	64 (86.5)	238 (86.6)	0.99	0 (0.0)
SAPSII, median (IQR)	40 (35-48)	51 (42-63)	43 (36-52)	< 0.1	27 (9.8)
<i>Co-existing diseases, n (%)</i>					
COPD	30 (15.9)	22 (32.8)	52 (20.3)	0.01	19 (6.9)
Ischaemic heart disease	55 (27.6)	21 (29.2)	76 (26.6)	0.80	4 (1.5)
Hypertension	129 (64.8)	44 (62.0)	173 (64.1)	0.67	5 (1.8)
Cerebrovascular disease	32 (16.2)	20 (27.8)	52 (19.3)	0.03	5 (1.8)
Renal failure	11 (5.5)	6 (8.3)	17 (6.3)	0.40 <sup>a</sup>	4 (1.5)
Current smoker	87 (53.1)	20 (39.2)	107 (49.8)	0.20	60 (21.8)
Diabetes	29 (14.5)	9 (12.5)	38 (14.0)	0.67	3 (1.1)
<i>Pre-operative medications, n (%)</i>					
Betablocker	45 (24.5)	12 (19.4)	57 (23.2)	0.41	29 (10.5)
Clopidogrel, n (%)	10 (5.3)	4 (6.2)	14 (5.5)	0.76 <sup>a</sup>	20 (7.3)
Acetylsalicylic acid, n (%)	79 (41.6)	20 (32.3)	99 (39.3)	0.19	23 (8.4)
Warfarin, n (%)	14 (7.3)	11 (16.9)	25 (9.7)	0.02	18 (6.5)
<i>Intra-operative variables</i>					
Duration of surgery, median (IQR), min.	179 (144-228)	187 (142-262)	180 (144-237)	0.21 <sup>b</sup>	0 (0.0)
Estimated blood loss, median (IQR), l	5.1 (3.3-7.3)	6.6 (3.8-10.9)	5.5 (3.4-8.1)	0.02 <sup>b</sup>	7 (2.5)
Red cell transfusion, median (IQR), l	3.2 (2.2-4.2)	4.4 (2.5-5.9)	3.4 (2.2-5.0)	< 0.01 <sup>b</sup>	11 (4.0)

COPD = chronically obstructive lung disease; IQR = interquartile range; SAPS = Simplified Acute Physiology Score.

a) Fisher's exact test.

b) Wilcoxon rank-sum test.

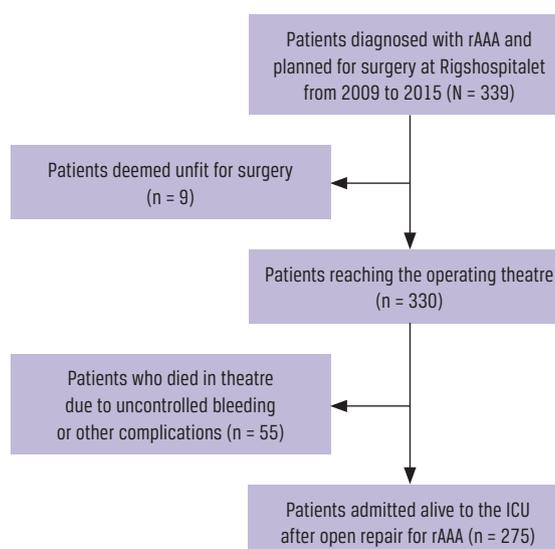
of patients at each centre, yielding more experience in the multidisciplinary handling of these patients and a higher quality of care. Although nearly one third of patients with rAAA in Denmark are treated at Rigshospitalet the surgical volume may be too low – as compared to other surgical conditions – to improve the quality of care and outcome. It may be also possible that the number is high enough to make further centralisation irrelevant.

In the process of centralisation of the treatment of patients with rAAA, the surgeons might have been re-allocated to a new department along with the procedure, so that the number of procedures performed by each surgeon remained unchanged. This was the case in a British study from 2018 [14], and might, at least partly, explain the observed lack of an improved outcome following the centralisation of surgery for rAAA in Denmark as well. This is supported by the fact that the number of procedures performed at Rigshospitalet annually, has not increased significantly after the centralisation (Figure 2A).

Another explanation for the lack of an improved outcome following centralisation may be that the bene-

**FIGURE 1**

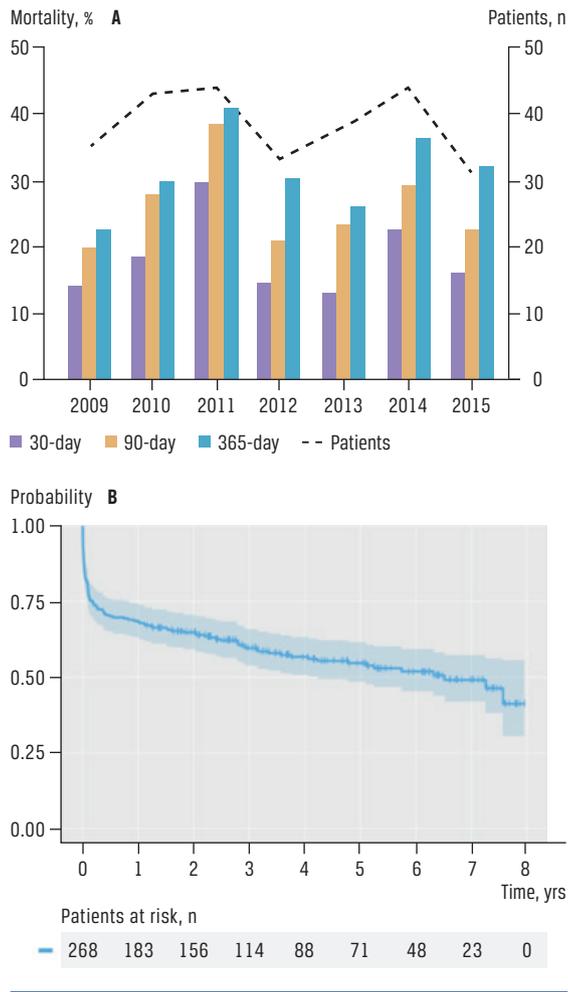
Patient flow diagram of patients diagnosed and planned for surgery at Rigshospitalet between 2009 and 2015.



ICU = intensive care unit; rAAA = ruptured abdominal aortic aneurism.

**FIGURE 2**

**A.** Number of patients admitted to the intensive care unit after surgery for ruptured abdominal aortic aneurism at Rigshospitalet per year and the post-operative mortality in the 2009-2015 period. **B.** Overall survival of patients treated for ruptured abdominal aortic aneurism at Rigshospitalet in the period 2009-2015 period. The shaded area shows the 95% confidence interval.



fits from centralisation need more time to take effect [15]. Also, patients with rAAA are severely ill with a high risk of an adverse outcome, why the impact of centralisation on the outcome may be difficult to detect (low absolute effect). Finally, it may be that we did not detect a reduction in mortality because we did not register data before the centralisation; only after the centralisation. Compared with an earlier cohort from the same centre [16], mortality was lower. In general, the outcome at Rigshospitalet is at the same level as in other European centres [17, 18]. The strengths of our study include its population-based design with a low risk of selection bias, a high data completeness and a high data validity [19].

A number of limitations also apply. First, the single-centre design may limit generalisability to other centres with a different case mix. Second, our cohort did not include patients treated with endovascular aortic repair. Third, patients who died before and during surgery were not accounted for; this will tend to underestimate the reported mortality. Most other cohorts include these cases, which need to be considered when comparing outcomes. Fourth, the number of patients treated outside the Capital Region of Denmark before and after the centralisation remains unknown; this may have affected the temporal trends observed. Fifth, the observational design with retrospective data collection is prone to selection bias and confounding, including residual confounding and confounding by indication. Sixth, the statistical power is low due to the limited number of included patients. Finally, we did not use statistical process control to assess the temporal time trends, as recently recommended [20].

**CONCLUSIONS**

In this retrospective population-based cohort study of 275 patients admitted to the ICU following open surgical repair for rAAA at Rigshospitalet between 2009 and 2015, we found an overall high morbidity and mortality with no consistent reduction in mortality over time following centralisation.

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**LITERATURE**

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**TABLE 2**

Secondary outcomes stratified by survival 90 days after repair for ruptured abdominal aortic aneurism at Rigshospitalet in 2009-2015. Stratified by 90-day mortality.

	Survivors (n <sub>s</sub> = 201)	Non-survivors (n <sub>n</sub> = 74)	Total (N = 275)	p-value
Post-operative renal replacement therapy, n (%)	32 (15.9)	27 (36.5)	59 (21.4)	< 0.01
Re-operative surgery, n (%)	52 (25.9)	36 (48.7)	88 (32.0)	< 0.01
Bowel ischaemia, n (%)	16 (8.0)	20 (27.0)	36 (13.1)	< 0.01
Septic shock, n (%)	17 (8.5)	26 (35.1)	43 (15.6)	< 0.01
Length of stay in ICU, median (IQR), days	4.1 (1.7-7.9)	5.2 (1.7-11.0)	4.3 (1.7-9.4)	0.28 <sup>a</sup>

ICU = intensive care unit; IQR = interquartile range.

a) Wilcoxon rank-sum test.

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