Treatment of ruptured abdominal aortic aneurysms in the Amsterdam area

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CHAPTER 5

EFFECT OF REGIONAL COOPERATION ON OUTCOMES FROM RUPTURED ABDOMINAL AORTIC ANEURYSM

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ABSTRACT

Background – Care for patients with a ruptured abdominal aortic aneurysm (rAAA) in the Amsterdam ambulance region (the Netherlands) was concentrated into vascular centres with a 24-hr full emergency vascular service in cooperation with seven referring regional hospitals. Previous population-based survival after rAAA in the Netherlands was 46% (95% confidence interval (CI) 43 – 49%). It was hypothesized that regional cooperation would improve survival.

Methods – This was a prospective observational cohort study carried out simultaneously with the Amsterdam Acute Aneurysm Trial. Consecutive patients with an rAAA between 2004 and 2011 in all ten hospitals in the Amsterdam region were included. The primary outcome was the 30-day survival rate after admission. Multivariable logistic regression, including age, sex, comorbidity, intervention (endovascular or open repair), preoperative systolic blood pressure, cardiopulmonary resuscitation and year of intervention, was used to assess the influence of hospital setting on survival.

Results – Of 453 patients with rAAA from the Amsterdam ambulance region, 61 did not undergo intervention; 352 patients were treated surgically at a vascular centre and 40 at a referring hospital. The regional survival rate was 58.5 (95% CI 53.9 – 62.9%) per cent (265 of 453). After multivariable adjustment, patients treated at a vascular centre had a higher survival rate than patients treated surgically at a referring hospital (adjusted odds ratio 3.18, CI 1.43 – 7.04).

Conclusions – After regional cooperation, overall survival of patients with an rAAA improved. Most patients were treated in a vascular centre and in these patients survival rates were optimal.

INTRODUCTION

The mortality rate of patients with a ruptured abdominal aortic aneurysm (rAAA) is approximately 80 per cent; it is estimated that one-third of these patients do not reach hospital alive.[1] Patients with an RAAA arriving at hospital require emergency intervention. Several studies[2-4] have indicated that a higher caseload decreases surgical death rates and advocated centralization of care for rAAA.

From 2003, care for patients with rAAA in the Amsterdam ambulance region in the Netherlands was concentrated into three central hospitals. These three vascular centres provided a 24-h full emergency vascular service. All patients suspected of having an rAAA by the ambulance staff or by a general practitioner were transported to a vascular centre. The other seven hospitals of the region referred patients with rAAA who were deemed fit for transport. In the present study, it was hypothesized that centralization of care would improve survival after aneurysm rupture. The primary objective was to compare regional survival after rAAA with previous population-based survival from the Netherlands.[4;5] Secondary objectives were to determine the influence of hospital setting (intervention in a vascular centre or in a referring hospital), and of patient transfer (from a referring hospital to a centre, or not) on survival.

METHODS

This was a prospective regional cohort study including consecutive patients with rAAA presenting at one of the ten hospitals in the Amsterdam ambulance region between April 2004 and February 2011. Patients referred from surrounding ambulance regions, and patients with unknown outcome were excluded from the analysis. The primary outcome was 30-day survival after admission, including both patients rejected for intervention and those in whom an intervention was undertaken; this outcome is referred to as 'the admission survival rate'. The secondary outcome was the combined 30-day or in-hospital survival, including only patients in whom an intervention was started (operative survival rate). These two outcomes were reported to allow comparison with previous population- based studies in the Netherlands.

Patients were identified and registered prospectively by all vascular surgeons in the region. A monthly search of the Amsterdam ambulance registries and the hospital registries was done to check for patients with a discharge diagnosis of rAAA. The diagnosis of rAAA was based on emergency computed tomographic angiography (CTA), evaluated by a vascular surgeon and a radiologist. Rupture was confirmed by contrast extravasion outside the aorta on CTA. In patients evaluated only by duplex ultrasonography, the diagnosis of rAAA was based on findings at operation or autopsy.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Because of its observational design, written informed consent from patients was not necessary. The present report included all items recommended by the STrengthening the Reporting of OBser- vational studies in Epidemiology (STROBE).[6]

Regional and hospital logistics

The Amsterdam ambulance region covers an area of 1025km2 with 1·38 million inhabitants7 and thus has a population density of 1375/km2 . Approximately 280 km2 is urban and 745 km2 is rural. The region is served by ten hospitals. All hospitals in this region agreed to centralize care in three vascular centres. The regional referral system for patients with rAAA was introduced in 2003. Two university hospitals and one teaching hospital, experienced in elective and acute

endovascular aneurysm repair (EVAR) and open repair of abdominal aortic and thoracic aortic pathology, were appointed as vascular centres. These centres rotated a weekly service in which a vascular surgeon, an interventional radiologist and assisting staff were available around the clock. All patients suspected of having an rAAA by the ambulance staff, by a general practitioner or by a surgeon in a referring hospital were transported to the vascular centre on call. Only patients admitted to one of the seven referring hospitals but who were deemed unfit for transfer were treated locally. Fitness for transfer was determined by the local surgeon and was based on clinical judgement of haemodynamic stability. A protocol for permissive hypotension was implemented to optimize conditions during transport and in the emergency room[8]
To confirm the diagnosis and to assess suitability for EVAR, patients were evaluated with CTA on arrival at the hospital. Duplex ultrasonography was used only in patients regarded as too haemodynamically unstable to undergo CTA. The criteria for EVAR were based on the instructions for use of the endograft. Patients with unsuitable aortic anatomy for EVAR underwent open repair. Patients suitable for both EVAR and open repair were consented to be randomized between the interventions in the Amsterdam Acute Aneurysm Trial (AJAX trial)[9]. Between 2004 and 2011, the AJAX trial was conducted in the three vascular centres to compare the death rate following EVAR and open repair in patients suitable for both interventions. The present study expands on the AJAX trial in two ways. First, it included consecutive patients from the region and not only those eligible for both interventions. Second, it did not aim to compare outcomes after EVAR with those after open repair. The vascular centres had specialized cardiovascular anaesthetic care and a closed-format intensive care unit (ICU), with around-the-clock availability of one intensivist for 12 beds, and a minimum of 1500 patient-days of ventilation per year (Dutch level III ICU[10]). Patients from surrounding ambulance regions could also be referred to the vascular centres, but these patients were excluded from the present analysis.

Data collection and statistical analysis
Data were collected on age, sex, co-morbidity (cardiac, pulmonary, renal and cerebrovascular), haemodynamic stability (preoperative lowest in-hospital systolic blood pressure (SBP) measurement and cardiopulmonary resus- citation), hospital setting (vascular centre or referring hospital), patient transfer (transport from a referring hos- pital to a centre, or not) and type of intervention (EVAR or open repair). Double data entry was done and data were checked for inconsistency. Inconsistencies were resolved by consulting the original patient charts. Death rates were checked for errors in the communal registry that registers all death certificates in the Netherlands.
Data collection and statistical analysis were carried out with use of IBM SPSS Statistics 19.0 (SPSS Inc., Armonk, New York, USA). To include all patients in the regression analyses, an imputation procedure was done using logistic and linear regression models, whereby ten data sets were created.[11] The most critically ill patients needed the most urgent decisions and the fewest notes were made. To correct for bias of most missing data in the most critically ill patients, death was included as a predictor in the imputation model. Other predictors were: baseline characteristics, level of consciousness, Glasgow Coma Scale score, and serum haemoglobin and creatinine levels. The statistical analysis was done in the ten separate imputed data sets and the outcomes were pooled.

The regional admission survival rate was calculated by dividing the 30-day survival after admission by all admissions. The regional operative survival rate was calculated by dividing the combined 30-day or in-hospital death rate after intervention by all interventions. These rates were compared with the only known and most recent Dutch admission and operative survival

rates of 46 (95 per cent confidence interval (c.i.) 43 to 49) per cent5 and 59 (58 to 60) per cent[4], respectively.
Subsequently, the complete cohort was used to assess the association between hospital setting (vascular centre or referring hospital) and survival. A subgroup analysis was done in patients treated in a vascular centre (centre cohort). The centre cohort was used to assess the association between patient transfer (transfer from a referring hospital to a vascular centre) and survival. Because of the observational design of the present study, the patient risk profiles varied. For example, the regional surgeon's decision to transfer or not meant that relatively more haemodynamically unstable patients were allocated to an intervention in the referring hospitals. A multivariable logistic regression model, a propensity logistic regression model, and a combined multivariable and propensity logistic regression model were developed to adjust for the possible confounders age[12], sex[13], hemodynamic stability[14] (based upon SBP and resuscitation), type of intervention (EVAR or Open repair) and year of intervention. A further detailed description of the propensity score is provided in *Table S1* (supporting information). The $\chi2$ statistic, the Hosmer and Lemeshow test, and the area under the receiver operating characteristic (ROC) curve were reported to represent model performance. The ranges of the performance measures in the ten imputed data sets were reported.

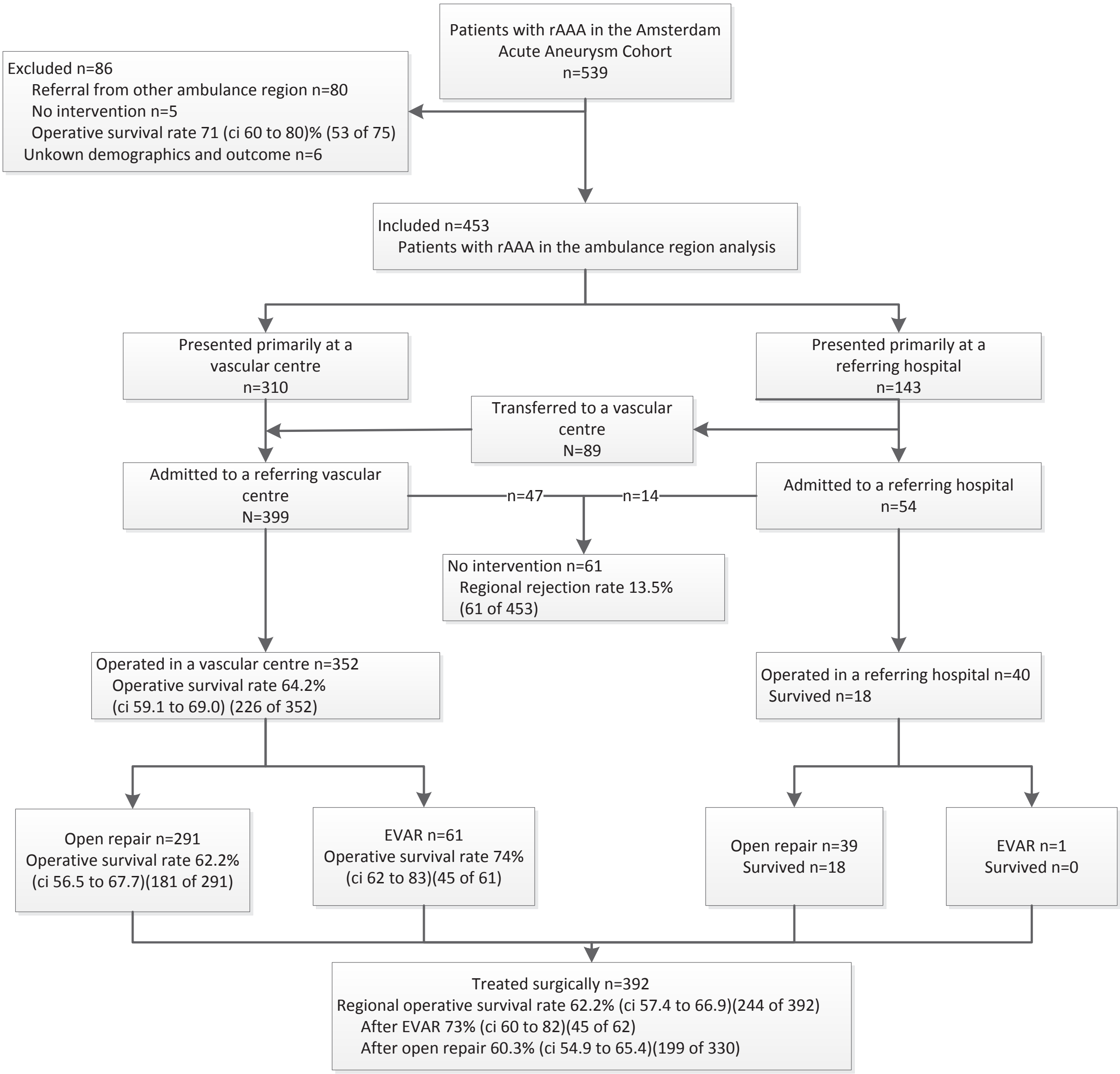
RESULTS

Between April 2004 and February 2011, a total of 539 patients with an rAAA were admitted to ten hospitals in the Amsterdam region. The incidence rate of in-hospital rAAAs was 5.7 per 100 000 person-years. The in-hospital rAAA repair rate was 4.7 per 100 000 inhabitants. A flow chart showing inclusion and treatment allocation is shown in *Fig. 1.*
Of 539 consecutive patients, 80 were excluded from the analysis because they were referred from surrounding ambulance regions, and six were excluded because of unknown demographics and outcome. Only 100 of 453 patients included in the present study were included in the AJAX trial. A total of 399 patients were admitted to the vascular centres, 89 of whom were transferred from a referring hospital. Fifty-four other patients were admitted to the referring hospitals, but not transferred. In total, 61 patients did not undergo intervention, giving a regional rejection rate (non-operative rate) of 13.5 per cent (61 of 453). In the vascular centres the rejection rate was 11.8 per cent (47 of 399). In the referring hospitals the rejection rate was 26 per cent (14 of 54). The baseline characteristics of surgically treated patients are shown in *Table 1. Tables S2* and *S3 (supporting information*) show the data stratified by hospital setting and patient transfer respectively.

Survival rate

The overall regional admission survival rate, including both rejected patients and those operated on, was 58.5 (95 per cent c.i. 53.9 to 62.9) per cent (265 of 453). The admission survival rate in the vascular centres was 61.4 (95 per cent c.i. 56.5 to 66.0) per cent (245 of 399) and that in the referring hospitals was 37 (95 per cent c.i. 25 to 50) per cent (20 of 54).
The overall regional operative survival rate was 62·2 (95 per cent c.i. 57.4 to 66.9) per cent (244 of 392). It was 64.2 (95 per cent c.i. 59.1 to 69.0) per cent (226 of 352) in the vascular centres, and 18 of 40 patients survived the intervention in the referring hospitals (*Fig. 1*).

Figure 1 Flow chart



Flow chart showing operative survival; the combined 30-day or in hospital survival rate included only patients in whom an inervention was started. rAAA, ruptured abdominal aortic aneurysm; EVAR endovascular aneurysm repair; ci 95 per cent confidence interval.

Table 1 Baseline characteristics

	original data set (n=392)		
	available data	missing data	**Imputed datasets^ (n=392)**
Age (years)*	74.4 (8.7)	0	not imputed
Sex ratio (m:f)	319:73	0	not imputed
Cardiac comorbidity$	43.8 (165/377)	3.8 (15/392)	43.9 (172/392)
Pulmonary comorbidity+	18.9 (71/376)	4.1 (16/392)	18.9 (74/392)
Renal comorbidity#	10.9 (41/376)	4.1 (16/392)	11.0 (43/392)
Cerebrovascular comorbidity**	13.8 (52/376)	4.1 (16/392)	13.8 (54/392)
Lowest in-hospital SBP (mmHg)§	90 (70 – 122)	7.7 (30/392)	90 (70 – 120)
Cardiopulmonary resuscitation	43 of 372 (11.6)	5.1 (20/392)	12.5 (49/392)
No CTA	68 (17.4)	0	not imputed
Year of intervention		0	
2004	45 (11.5)		
2005	58 (14.8)		
2006	70 (17.9)		
2007	65 (16.6)		not imputed
2008	54 (13.8)		
2009	51 (13.0)		
2010	44 (11.2)		
2011	5 (1.3)		

*Values in parenthesis are percentages unless indicated otherwise; values are * means(sd) and §median (iqr). ^ The baseline charecteristics of the ten separate imputed data sets were pooled and these pooled data are reported. History of $arhytmia, cardiac surgery or myocardial infarction, +chronic obstructive pulmonary disease, #chronic kidney failure or dialysis, or ** transient ischemic attack or stroke.*

Logistic regression

Multivariable adjustment for possible confounders showed that patients treated surgically in a vascular centre had a higher survival rate than patients treated in a referring hospital (adjusted odds ratio 3·18, 95 per cent c.i. 1·43 to 7·04) *(Table 2).* Propensity adjustment (odds ratio 2·29, 1·16 to 4·52), and combined propensity and multivariable adjustment (odds ratio 2·41, 1·19 to 4·87) also showed that patients treated surgically in a vascular centre had a higher survival rate (*Tables S1 and S4*, *supporting information).*

Multivariable adjustment for possible confounders showed that, among patients treated surgically in the vascular centres, patient transfer was not associated with survival (adjusted odds ratio 1·07, 0·57 to 2·02) *(Table 2)*. Propensity adjustment (odds ratio 0·89, 0·50 to 1·60), and combined propensity and multivariable adjustment (odds ratio 1·07, 0·58 to 1·98) also showed that patient transfer was not associated with survival (*Tables S1 and S4, supporting information*).

Table 2. Multivariable adjusted logistic regression models.

Variable	Odds ratio Complete cohort	Centre cohort
Age (per year)	0.94 (0.91 – 0.97)*	0.95 (0.92 – 0.98)*
Men	1.32 (0.72 – 2.43)	1.38 (0.72 – 2.63)
Cardiac comorbidity	0.66 (0.39 – 1.09)	0.68 (0.40 – 1.15)
Pulmonary comorbidity	0.47 (0.25 – 0.88)*	0.41 (0.21 – 0.78)*
Renal comorbidity	0.58 (0.28 – 1.24)	0.58 (0.27 – 1.29)
Cerebrovascular comorbidity	0.71 (0.35 – 1.43)	0.87 (0.41 – 1.85)
Lowest in-hospital SBP[a] (per 10 mmHg)	1.20 (1.12 – 1.29)*	1.21 (1.12 – 1.30)*
Cardiopulmonary resuscitation	0.28 (0.11 – 0.70)*	0.28 (0.11 – 0.70)*
Type of intervention (open repair[b])	0.73 (0.37 – 1.46)	0.69 (0.34 – 1.40)
Year of intervention (2007 or 2008)	1.43 (0.80 – 2.56)	1.45 (0.79 – 2.65)
Year of intervention (2009 or 2010 or 2011)	2.11 (1.14 – 3.93)*	1.94 (1.01 – 3.74)*
Vascular centre	3.18 (1.43 – 7.04)*	-
Patient transfer	-	1.07 (0.57 – 2.02)

Values in parentheses are 95 per cent confidence intervals. SBP, systolic blood pressure. The complete cohort model included all patients to assess the influence of hospital setting (vascular centre or referring hospital) on survival: 392 patients and 244 survivors (performance: χ2 statistic 110·0 – 119·8 (12 d.f.), P < 0·001; Hosmer and Lemeshow test:
P = 0·169 – 0·954; area under the receiver operating characteristic (ROC) curve (AUC) 0·80–0·81). The centre cohort included only patients treated in a vascular centre to assess the influence of patient transfer (transport from a referring hospital to a centre, or not) on survival: 352 patients and 226 survivors (performance: χ2statistic 92·3–102·1 (12 d.f.), P < 0·001; Hosmer and Lemeshow test: P = 0·289 – 0·842; AUC 0·79 – 0·80).

DISCUSSION

The implementation of a regional referral network with centralized care in hospitals with a 24-h full emergency vascular service improved survival in patients with rAAA. The regional admission survival rate of 58·5 (95 per cent c.i. 53·9 to 62·9) per cent was higher than the previous Dutch admission survival rate of 46 (95 per cent c.i. 43 to 49) per cent.[5] The regional operative survival rate of 62·2 (95 per cent c.i. 57·4 to 66·9) per cent was comparable to the previous Dutch operative survival rate of 59 (95 per cent c.i. 58 to 60) per cent.[4] However, compared with this second study[4], the age of the patients and the proportion of women were higher in the Amsterdam region. Both of these factors are likely to influence operative survival rates negatively [4;5;12;13]. An exploratory analysis adjusting the survival rates for age and sex differences confirmed that the outcomes compared favourably with those of the two Dutch studies (data not shown).

The present findings are in agreement with the conclusions of previous studies[2-4;15] that reported an association between an increased annual caseload and improved survival. The present study design and methods differed in three ways from those in these previous studies. First, in the present study all consecutive patients from the region were identified prospectively by the vascular surgeons, resulting in a precise estimate of the survival rates. In the previous studies, patient identification was with use of procedure codes in large administrative databases, which are subject to inaccuracies. Second, detailed preoperative patient data were collected for this study, allowing mul- tivariable adjustment for haemodynamic stability in the statistical analysis. Third, the present study also included data on patients who did not undergo intervention.

From an international perspective, the regional operative survival rate was higher than regional results from the UK between 2005 and 2007 (42 (95 per cent c.i. 31 to 54) per cent) [16] and comparable to nationwide results from the USA in 2008 (64 per cent; c.i. not available)[17]. The regional 30-day survival rate of 67·6 (95 per cent c.i. 62·8 to 72·0) per cent (265 of 392) reported here was lower than nationwide results from Sweden between 2006 and 2010: 72 (95 per cent c.i. 68 to 75) per cent[18]. Finally, the regional rejection rate was lower than the reported pooled rejection rate of 26 (95 per cent c.i. 7 to 51) per cent in four high-quality studies from different countries since 1990[1]. However, the validity of the comparison with these international results can be questioned because of different age and racial distributions between these countries.
Several studies[17-19] reported an improvement in survival over the years in patients surgically treated for rAAA. The present results are in line with this global trend. The authors of these studies hypothesized that the improvement was attributable to the introduction of EVAR. The results of two trials[9;20] randomizing between EVAR and open repair indicate that the improved survival is probably not attributable to the type of intervention. Logistical aspects of care in treatment protocols have been subject to change alongside the introduction of EVAR[21-23] and this seems a more plausible explanation.

The exact logistical aspects of care that improve survival are difficult to determine. A protocol of permissive hypotension during transport and the availability of a 24-h full emergency vascular service with specialized staff are probably important. CTA was carried out in 324 (82·7 per cent) of 392 patients. Despite some loss of time, the operative survival rate in patients evaluated with CTA was 67·0 (95 per cent c.i. 61·7 to 71·9) per cent (217 of 324). This shows that immediate preoperative CTA is possible in the majority of patients. It can provide important anatomical information before starting open repair. Finally, specialized anaesthetic care[24] and level III intensive care were available at the vascular centres.
The majority of patients (352 of 392, 89·8 per cent) were treated in the vascular centres. The agreement to refer patients to a centre only if deemed fit with regard to haemodynamic stability meant that relatively more unstable patients were allocated to an intervention in the referring hospitals. Although these unstable patients were not expected to survive transfer, almost half of them did survive intervention in a referring hospital (18 of 40). In the comparison of survival rates between the vascular centres and referring hospitals, the potential problem of confounding was addressed by multivariable and propensity adjustment. After adjustment, the patients treated surgically in the vascular centres had better survival than those treated surgically in the referring hospitals.

Patients with rAAA require emergency intervention. From the perspective of the referring surgeon, it is counterintuitive to postpone intervention by transporting a patient to a vascular centre. However, the majority of patients were referred to a vascular centre (89 of 143, 62·2 per cent), and all patients survived transport. Some adverse events occurred among the referred patients; 4 per cent (4 of 89) died after the decision to refrain from intervention, 4 per cent (3 of 82, 3 unknown) required preoperative resuscitation, 5 per cent (4 of 85) died during the intervention, and 27 per cent (22 of 81) died after the intervention. The rejection rate of transferred patients was low (4 per cent, 4 of 89) compared with that of patients presenting primarily to a vascular centre (13·9 per cent, 43 of 310). Despite postponement of intervention

and these adverse outcomes for individual patients, from a regional perspective the survival of referred patients was comparable to that of patients who presented to the centres.
The most important limitation of the present study is that regional survival was compared with that of two historical control groups. No results were available from a more recent interval in the Netherlands, from a control group in the Amsterdam ambulance region or from a randomized control group. The previous Dutch population-based studies included patients from more than a decade ago. Nowadays there is a trend towards specialization among surgeons and radiologists. In the Amsterdam region, open repair was carried out by a team including a vascular surgeon, and an interventional radiologist was also present in case of endovascular repair. This is associated with improved survival[19] Between 1990 and 2000, some rAAAs were treated by general surgeons, which confounds the comparison. However, the fact that a specialized team improved survival underlines the importance of regional cooperation and a 24-h full emergency vascular service. Another potential confounder is the use of massive transfusion protocols, which are discussed in the literature from 2004[25], and may have attenuated the negative effects of massive bleeding. The incidence rate of hospital admission for rAAA in the Amsterdam region was 5·7 per 100 000 person-years. Based on the estimate that one-third of patients did not reach hospital1, the total population-based incidence rate was 8·6 per 100 000 person-years. This is a little lower than the most recently published incidence rates of 14·0 per 100 000 person-years from the UK16 and 10·6 per 100 000 person- years from Sweden26. The in-hospital rAAA repair rate of 4·7 per 100 000 was also lower in Amsterdam than the rate of 8·4 per 100 000 in Sweden during the same interval[18]. These differences might be explained by different age and racial distributions or detection by chance of AAAs between countries. Another explanation might be a failure to identify all patients with rAAA, despite the prospective registration by all vascular surgeons, and checks on the ambulance and hospital registries. The impact of these missing patients on the present conclusions is difficult to determine.

Despite the regional agreement that patients were to be referred to a vascular centre if deemed fit, lowest in-hospital SBP and resuscitation were not associated with ‘intervention in a referring hospital’ in the propensity score (*Table S5, supporting information*). Possibly, the variables ‘lowest in-hospital SBP’ and ‘resuscitation’ failed to represent haemodynamic stability sufficiently accurately. However, there was a clear association between lowest in-hospital SBP and resuscitation and survival *(Table2)*. This suggests that these parameters accurately represent haemodynamic stability. Moreover, an analysis including other markers of haemodynamic stability, such as a subjective judgement by a vascular surgeon (unstable, controlled hypotension, or stable), or the first SBP measurement in the emergency room, did not alter the conclusions.
Although statistical methods were used to eliminate differences in observed confounders, another limitation of the present study was that it was not possible to adjust for differences in unobserved confounders such as hypothermia[27] , income quintile of the patient[28] , after-hours intervention[28] and annual volume of rAAA interventions of the surgeon[28]. Finally, there is an important geographical limitation to the external validity of the conclusions. The Amsterdam region is urban and densely populated, and the conclusions might not be valid for more rural areas.
Although the results presented here should be interpreted within the context of a global trend towards improved outcome of patients with rAAA, regional survival was improved by regional cooperation compared with that reported in two Dutch population-based studies[4,5]. It was possible to treat the majority of patients in a vascular centre where survival was optimal. Furthermore, despite delaying intervention, patient referral was not associated with impaired survival.

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