Aortic centres should represent the standard of care for acute aortic syndrome

Giovanni Mariscalco^{1,*}, Daniele Maselli^{2,*}, Marco Zanobini³, Aamer Ahmed⁴, Vito D Bruno⁵, Umberto Benedetto⁵, Riccardo Gherli⁶, Tiziano Gherli⁷ and Francesco Nicolini⁷

European Journal of Preventive Cardiology 2018, Vol. 25(1S) 3–14 © The European Society of Cardiology 2018 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav DOI: 10.1177/2047487318764963 journals.sagepub.com/home/ejpc

European Society

of Cardiology



Abstract

Background: Existing evidence suggests that patients affected by acute aortic syndromes (AAS) may benefit from treatment at dedicated specialized aortic centres. The purpose of the present study was to perform a meta-analysis to evaluate the impact aortic service configuration has in clinical outcomes in AAS patients.

Methods: The design was a quantitative and qualitative review of observational studies. We searched *PubMed/MEDLINE*, *EMBASE*, and *Cochrane Library* from inception to the end of December 2017 to identify eligible articles. Areas of interest included hospital and surgeon volume activity, presence of a multidisciplinary thoracic aortic surgery program, and a dedicated on-call aortic team. Participants were patients undergoing repair for AAS, and odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were adopted for synthesizing hospital/30-day mortality.

Results: A total of 79,131 adult patients from a total of 30 studies were obtained. No randomized studies were identified. Pooled unadjusted ORs showed that patients treated in high-volume centres or by high-volume surgeons were associated with lower mortality rates (OR 0.51; 95% CI 0.46–0.56, and OR 0.41, 95% CI 0.25–0.66, respectively). Pooled adjusted estimates for both high-volume centres and surgeons confirmed these survival benefits (adjusted OR, 0.56; 95% CI 0.45–0.70, respectively). Patients treated in centres that introduced a specific multidisciplinary aortic program and a dedicated on-call aortic team also showed a significant reduction in mortality (OR 0.31; 95% CI 0.19–0.5, and OR 0.37; 95% CI 0.15–0.87, respectively).

Conclusions: We found that specialist aortic care improves outcomes and decreases mortality in patients affected by AAS.

Keywords

Acute aortic syndrome, aortic dissections, meta-analysis, hospital volume, surgeon volume, quality of health care

Received 15 January 2018; accepted 22 February 2018

Introduction

The prevalence of diseases of the thoracic aorta has steadily increased in the last decade, with an overall global death rate of 2.78 per 100,000 inhabitants.¹ The highest rates have been observed in Australasia and Western Europe (8.38 and 7.68 per 100,000 inhabitants, respectively).¹ Admissions for acute aortic syndrome (AAS) have also increased worldwide, although the epidemiology is difficult to establish since these entities may only be diagnosed after a long period of subclinical development.^{2–5} Their natural history remains poorly understood, and errors in the diagnostic process may account for deaths otherwise attributed to other

¹Department of Cardiovascular Sciences, University of Leicester, Glenfield Hospital, Leicester, UK

²Department of Cardiac Surgery, St. Anna Hospital, Catanzaro, Italy ³Department of Cardiac Surgery, Centro Cardiologico–Fondazione Monzino IRCCS, University of Milan, Italy

⁴Department of Anaesthesia and Critical Care, Glenfield Hospital,

University Hospitals of Leicester NHS Trust, Leicester, UK

⁵Heart Centre, Bristol University, Bristol, UK

⁶Department of Cardiovascular Sciences, Cardiac Surgery Unit, San Camillo Hospital, Rome, Italy

⁷Division of Cardiac Surgery, University of Parma, Parma, Italy

*These authors contributed equally.

Corresponding author:

Giovanni Mariscalco, Department of Cardiovascular Sciences, University of Leicester, Clinical Science Wing, Glenfield Hospital, Leicester, LE39QP, UK.

Email: giovannimariscalco@yahoo.it



pathological conditions.^{2,3} In the face of this increasing problem, however, the optimal service configuration for the management of AAS patients has not been defined.⁶ Across centres and regions, a wide variation in treatment and outcomes has been reported.^{2,3,6-12} In Europe and the wider world, mortality for operated type A dissection ranges from 6% to 47.6%, 3-10,11 whereas high-volume centres in the United States (US) have documented lower mortality rates, ranging from 2.8% to 12.1%^{2,7,8} It is therefore critical that diseases of the thoracic aorta are recognized promptly and surgical care is expedited. International guidelines recommend that affected patients could benefit from high-volume surgical centres with focused multidisciplinary expertise in thoracic aortic surgery.^{2,3} Existing evidence suggests that AAS patients treated in multidisciplinary specialized aortic centres demonstrate significantly improved outcomes and decreased mortality.⁶ The purpose of the present review was to summarize the existing literature that relates to the organization of aortic services and the impact this may have on clinical outcomes in patients affected by AAS.

Methods

Search strategy and outcome measures

Electronic databases (*PubMed/MEDLINE*, *EMBASE*, and *Cochrane Library*) without date or language restriction were searched from inception to the end of December 2017. To supplement the electronic search, the 'first generation' reference lists of pertinent articles were reviewed. Search criteria, adopted keywords and MeSH terms used in relevant combinations are reported in the Supplementary Methods.

This systematic review was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (Supplementary Material).¹³

Areas of interest included hospital volume activity, generally defined as annual number of major aortic operations performed, subdivided into low- or high-volume, surgeon volume, presence of a multidisciplinary thoracic aortic surgery program and a dedicated aortic team.⁶ The primary outcome of interest was all-cause mortality in hospital or within 30 days from index admission or procedure. Other secondary outcomes were not considered due to heterogeneity definitions.

Study selection, participants and interventions

Only studies considering the impact of aortic service configuration on outcome of patients affected by AAS were included, with no restriction on ethnicity or age. The target disease was an AAS involving the thoracic aorta as per definition of the international guidelines on diagnosis and management of patients with thoracic aortic disease (TAD).^{2,3} Studies with quantitative, qualitative and mixed-method approaches were included in order to obtain a comprehensive overview of the existing literature, while publications without such study design, including conference abstracts, reviews, editorials, and letters were excluded. Inclusion and exclusion criteria for qualitative/quantitative analyses were summarized according to the PICOS approach (Supplementary Table 1).

Titles, abstracts, and full-text articles were independently reviewed by two investigators against the specified inclusion criteria. Discrepancies were resolved through consensus and consultation with a third investigator.

Data collection, extraction and analysis

All included articles were independently appraised by two investigators, and study quality was assessed using the Newcastle–Ottawa Scale.¹⁴ Disagreements about critical appraisal were resolved by discussion. Overall, two reviewers extracted key data from the selected studies using standard dedicated proforma, while a third reviewer checked the collected data for completeness and accuracy. Full details on key study characteristics, including design, year of publication, sample size, aortic centre configuration, baseline patient demographics and outcome results were summarized.

Statistical analysis

Treatment effect on hospital/30-day mortality outcome is reported as an odds ratio (OR) with a 95% confidence interval (CI). Individual ORs and variance were computed using number of events and sample size and pooled by using an inverse-variance method and random-effects model.¹⁵ Finally, to account for inherent patient selection bias related with an observational study design, individual risk-adjusted ORs for hospital/ 30-day mortality were obtained when reported, and pooled adjusted risk estimates were computed by using logarithmic transformation and a generic inverse-variance weighting method.^{6,16} The I^2 statistic was used to estimate the percentage of total variation across studies attributed to heterogeneity rather than chance. Suggested thresholds for heterogeneity were used, with I^2 values of 25% to 49%, 50% to 74%, and \geq 75%, indicative of low, moderate, and high heterogeneity.¹⁷ Publication bias was evaluated using visual inspection of funnel plot asymmetry and by Egger's test.¹⁸ A *p*-value < 0.05 was used as the level of significance and 95% CIs were reported where appropriate. Statistical analysis was conducted using meta package for R (version 4.3-2; R Foundation for Statistical Computing, Vienna, Austria).^{19,20}

Results

Study design, selection and quality assessment

Among the 11,552 identified records, 90 were fully assessed for eligibility. A total of 30 studies that met all the eligibility criteria were finally considered for the qualitative systematic review, and 24 studies were included for the quantitative synthesis (meta-analysis). The PRISMA diagram is shown in Figure 1. All the identified records (14 multi-centre and 16 single-centre) were retrospective observational studies, published between 1994 and 2017, comprising 79,131 patients (sample size range: 30 to 15,641).^{21–50} No randomized nor prospective observational studies were retrieved. The main study characteristics are summarized in Table 1 and in Supplementary Tables 2–4.

Among the studies included in the meta-analysis, seven analysed the impact of hospital volume on mortality, eight the impact of surgeon volume, and one the impact of both. However, the threshold definition for high- and low-volume hospital/surgeon volumes were observed widely heterogeneous, and in six cases no threshold definition was even provided (Table 1). A total of nine papers investigated the role of a specific

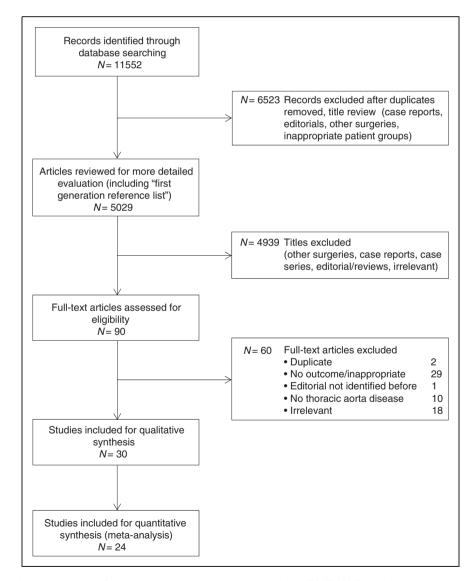


Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram regarding article selection for the systematic review and meta-analysis.

	Thoracic program or aortic team	Yes	°Z	Ŷ	°Z	Ŷ	Yes	Tes	2	Yes	2
guration	Surgeon volume T threshold p (cases/yr) a										
confi	Sur vol thr (ca	AA	~ 두	A	AN	AN	ΔN	ΔA	AN	₹Z	AN
Aortic centre configuration	Hospital volume threshold (cases/yr)	AN	AN	Lowest:1–4 Low: 5–9 MV: 10–14 High: 15–19 Highest: ≥ 20	LV: <i MV: 1–2.5 HV: >2.5</i 	LV: 5–20 ⁶ MV: 20–40 HV: > 40	AN	AN	НV	AN	Lowest:1–4 Low: 5–9 MV: 10–14 High: 15–19 Highest: ≥ 20
	AAS (%)	100%	47%	8001	%001	33.4%	42%	%001	8001	%001	%000I
	Exclusion criteria	1	I	1	I	Hospitals < 5 procedures/yr, centre with incomplete submission data	IMH, aortic ulcers, chronic aneurysms and dissections	latrogenic dissection	Vasculitis, connective tissue disorders, aortic dissection, concomitant aneurysm, patients treated with both open surgery and TEVAR	latrogenic dissection, chronic dissection, recurrent dissection	1
	Inclusion criteria	Blunt thoracic aortic transection	Ascending and aortic arch (+ concomitant cardiac surgeries)	Acute type A aortic dissection	Acute type A aortic dissection	Thoracic aortic surgery including combined CABG, valve surgery or other surgical operations	Acute aortic dissection, symptomatic TAA and TAAA, AAA	Acute aortic dissection	TAA-descending (ruptured)	Acute type A aortic dissection	Acute type A aortic dissection
	Sample size	30	296	10,097	3013	2875	621	101	923	380	14095
	Country	USA 1986–1990	UK 1992–2003	Japan 2000–2004	USA 1995–2003	Japan 2003–2005	USA 2007–2008	USA 2003–2009	USA 2006–2008	France 1990–2009	Japan 2005–2009
	Design	Retrospective case con- trolled, Monocentre	Retrospective cohort study, Monocentre	Retrospective cohort study, Multicentre	Retrospective cohort study, Multicentre	Retrospective cohort study, Multicentre	Retrospective case con- trolled, Monocentre	Retrospective case con- trolled, Monocentre	Retrospective cohort study, Multicentre	Retrospective cohort study, Monocentre	Retrospective cohort study, Multicentre
	Study (author, year)	Albrink et al. ²¹ 1994	Narayan et al. ²² 2004	Kazui et al. ²³ 2007	Knipp et al. ²⁴ 2007	Miyata et al. ²⁵ 2009	Davies et al. ²⁶ 2010	Harris et al. ²⁷ 2010	Gopaldas et al. ²⁸ 2010	Chavanon et al. ²⁹ 2011	Sakata et al. ³⁰ 2012

Table 1. Characteristics of the studies included in the qualitative systematic review.

6

							Aortic centre configuration	configuration	
Study (author, year)	Design	Country	Sample size	Inclusion criteria	Exclusion criteria	AAS (%)	Hospital volume threshold (cases/yr)	Surgeon volume threshold (cases/yr)	Thoracic program or aortic team
Chikwe et al. ³¹ 2013	Retrospective cohort study, Multicentre	USA 2003–2008	5184	Acute aortic dissection	Lack of surgeon identification	100%	Lowest: < 3 Low: 3 < 8 High: 8 < 13 Highest: > 13	Lowest: < I Low: 1 < 2 High: 2 < 5 Highest: > 5	Ŷ
Tsagakis et al. ³² 2013	Retrospective cohort study, Monocentre	Germany 2004–2011	124	Acute type A aortic dissection	Patients died preoperatively	%00 I	NA N	NA N	Yes
Andersen et al. ³³ 2014	Retrospective case con- trolled, Monocentre	USA 1999–2011	128	Acute type A aortic dissection	latrogenic dissection	%00 I	٩Z	٩Z	Yes
Murzi et al. ³⁴ 2014	Retrospective cohort study, Monocentre	ltaly 2003–2013	867	Aortic root, ascending and aortic arch surgery	Descending and thoraco-abdominal aortic surgery	13.2%	AN	Н Н С	°Z
Sales et al. ³⁵ 2014	Retrospective case con- trolled, Monocentre	Brazil 2003–2010	332	Thoracic aortic surgery, TAAA surgery	1	46.1%	AN	۸A	Yes
Beller et al. ³⁶ 2015	Retrospective case con- trolled, Monocentre	USA 2005–2014	101	Acute type A aortic dissection	1	%00 I	NA	AN	Yes
Grau et al. ³⁷ 2015	Retrospective case con- trolled, Monocentre	USA 2002–2013	54	Acute type A aortic dissection	I	%00 I	٩Z	۸A	Yes
lribarne et al. ³⁸ 2015	Retrospective cohort study, Multicentre	USA 2005–2008	1230	Acute aortic dissection	Non-emergent patients, patients < 18 years, TEVAR	%00 I	LV:≤5 MV: 6–10 HV:>10	AN	°Z
Lenos et al. ³⁹ 2015	Retrospective cohort study, Monocentre	Germany 2002–2013	162	Acute type A aortic dissection	I	%001	٩Z	н Ч	Yes
Shaffer et al. ⁴⁰ 2015	Retrospective cohort study, Multicentre	USA 2005–2010	11,996	TEVAR	I	21.6%	LV: < 20 ^c MV: 20−99 HV: ≥ 100	AN	°Z
Shaffer et al. ⁴¹ 2015	Retrospective cohort study, Multicentre	USA 1999–2010	5578	Open descending thoracic aorta and thoracoabdom- inal repair	I	46%	LV: < 50° MV: 50–200 HV: <u>></u> 200	LV: < 25 MV: 25–49 HV: <u>></u> 50	°Z
Andersen et al. ⁴² 2016	Retrospective cohort study, Monocentre	USA 2005–2013	212	Acute type A aortic dissection	I	%00 I	٩N	AN	Yes
Bashir et al. ⁴³ 2016	Retrospective cohort study, Monocentre	UK 1998–2015	200	Acute type A aortic dissection	1	%001	۲Z	٩N	Yes
Buonocore et al. ⁴⁴ 2016	Retrospective cohort study, Monocentre	Italy 2007–2014	Ξ	Acute type A aortic dissection	Penn class Ab, Ac, and Abc	%001	۲Z	Н Ч	٥N
Merlo et al. ⁴⁵ 2016	Retrospective cohort study, Multicentre	USA 2004–2008	1507	Acute type A aortic dissection	Patient < 18 years	%001	LV:≤5 MV: 5–10 HV:≥11	AN	٥
Shin et al. ⁴⁶ 2016	Retrospective cohort	South Korea 2010–2014	198	Acute aortic disease	I	%001	AN	AN	Yes

Downloaded from https://academic.oup.com/eurjpc/article/25/1_suppl/3/5925556 by guest on 25 April 2023

Ŧ	
ntinued	
Con	
<u> </u>	
Table	

							VOLUC CEILUL	Aoruc centre configuration	
Study (author, year)	Design	Country	Sample size	Inclusion criteria	Exclusion criteria	AAS (%)	Hospital volume threshold AAS (%) (cases/yr)	Surgeon volume threshold (cases/yr)	Thoracic program or aortic team
Zimmerman et al. ⁴⁷ 2016	Retrospective cohort study, Multicentre	USA 2003–2012	15,641	15,641 Acute type A & B aortic dissection	Patient < 18 years, aortic aneurysms	8001	HV H	AN	Ž
Arsalan et al. ⁴⁸ 2017	Retrospective cohort study, Multicentre	USA 2008–2014	672	Acute type A aortic dissection	I	%00I	LV: < 100 HV: > 100	AN	٥N
Bashir et al. ⁴⁹ 2017	Retrospective cohort study, Multicentre	UK 2007–2013	1550	Acute type A aortic dissection	I	%001	NA	LV: < 4 HV: ≥ 4	٥N
Duceau et al. ⁵⁰ 2017	Retrospective cohort study, Multicentre	France 2010–2016	853	Acute aortic disease	I	69.5%	AN	AN	Yes

AA: abdominal aortic aneurysm; AAS, acute aortic syndrome; CABG: coronary artery bypass grafting; HV: high-volume hospital; IMH: intramural hematoma; LV: low-volume hospital; MV: medium volume nospital; NA: not analysed; TAA: thoracic aorta aneurysm; TAAA: thoracoabdominal aneurysm; TEVAR: thoracic endovascular aortic repair general definition of LV (versus MV) versus HV hospital only.

(n = 2 hospitals)^aNot specified the threshold (cases/year);

excluded ^bLow volume thoracic aortic centre performing < 5 case/yr

period. study Volume activity defined over the entire volume and low-volume surgeons, respectively. Pooled unadjusted ORs showed that patients treated by high-volume surgeons had a 59% relative risk reduction in mortality with a moderate heterogeneity among studies $(I^2 = 74\%)$, and no publication bias (p = 0.30); Figure 2 lower panel and Supplementary Figure 1). Overall, eight studies reported on adjusted effect size of hospital and surgeon volume on mortality, and pooled adjusted estimates of individual logarithmic ORs confirmed that both high-volume centres and high-volume surgeons were independently associated with a significantly reduced incidence of mortality (adjusted OR 0.66; 95% CI 0.45–0.96; p = 0.031, and OR 0.32; 95% CI 0.11–0.93; p = 0.037, respectively; Figure 3).

Centres that introduced a specific multidisciplinary aortic program also reported a significant reduction in mortality in comparison with the prior patient management (OR 0.31; 95% CI 0.19-0.51). A moderated heterogeneity was observed $(I^2 = 50\%)$, but no publication bias (p = 0.67; Figure 4 upper panel). Finally, better survival after AAS surgery was also observed in centres that introduced a dedicated oncall aortic team (OR 0.37; 95% CI 0.15-0.87). A significant heterogeneity was noted, but no publication bias $(I^2 = 83\%$ and p = 0.18, respectively) (Figure 4 lower panel).

Discussion

Our results suggest that designated specific aortic centres reduce the mortality of patients undergoing surgical repair for AAS, and should represent the standard of care in this population setting. Our data also demonstrated that mortality varies widely across hospitals and surgeons, and centres with and without a dedicated specialized aortic program.

aortic multidisciplinary program in improving the outcome following the AAS diagnosis, and three the role

Quality assessment indicated that 80% studies were at significant risk of bias (Newcastle-Ottawa scale

A total of 6864 and 9893 patients affected by AAS underwent surgery in high- and low-volume centres, respectively. Pooled unadjusted ORs showed that

high-volume centres were associated with a 49% relative risk reduction in mortality when compared with low-volume centres with no heterogeneity among studies $(I^2 = 0\%)$, and publication bias (p = 0.10; Figure 2 upper panel and Supplementary Figure 1). Similarly,

1707 and 2961 patients were operated on by high-

of a dedicated on-call aortic team.

(NOS) < 8; Supplementary Table 5).

Outcome measures

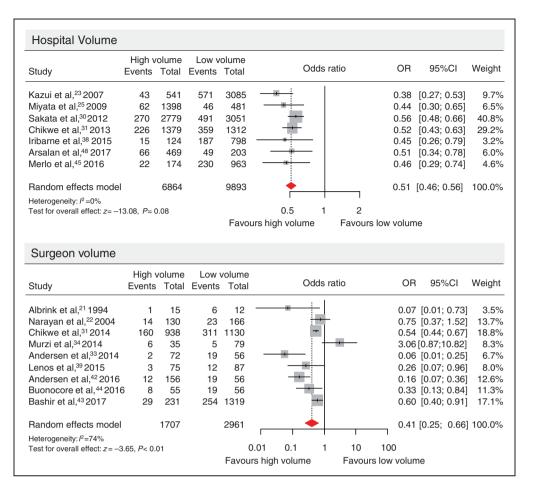


Figure 2. Forest plot with unadjusted risk estimates for in-hospital/30-day mortality in high-volume versus low-volume hospitals (upper panel) and in high-volume versus low-volume surgeons (lower panel). Cl: confidence intervals; OR: odds ratio.

However, despite this large body of evidence, patients affected by complex aortic diseases are still predominantly treated at hospitals where few complex aortic procedures are performed and where a low level of expertise is present. An analysis of data from the UK national cardiac surgery database clearly demonstrates higher mortality rates in centres where the volume of cases is low, even for elective aortic surgery.⁶ Currently, there is no accepted minimum service specification for the delivery or commissioning of care for patients with aortic disease, especially those affected by AAS.^{3,4}

In 1984, Albrink et al.²¹ firstly demonstrated the importance of designated thoracic programs in reducing mortality after traumatic aortic transection. Operations performed by designated high-volume thoracic surgeons produced a dramatic reduction in mortality (7% versus 50%) when compared with low-volume general surgeons. More recently, Andersen et al.³³ analysed the outcomes following acute type A aortic dissection repair after the implementation of a multi-disciplinary thoracic aortic surgery program,

confirming even more significantly the above survival benefits. Operative mortality after this implementation fell from 33.9% to 2.8%, thereby approximating the results observed after conventional elective cardiac surgery.³³

Operations on the thoracic aorta (mainly on the aortic arch and descending thoracic aorta) are certainly challenging surgical procedures, with prolonged learning curves, for individuals and surgical teams.^{22,33,34} Previous data on patients with abdominal aortic aneurysm, a complex pathology with subsequent morbidity and mortality similar to aortic disease, have confirmed that volume and centre experience are of crucial importance to subsequent outcomes, with a 13% estimated reduction in the odds of mortality for each additional 20 cases performed.⁵¹ However, if hospital volume and surgeon experience are intuitive factors influencing postoperative outcomes, other important factors should not be neglected. Our systematic review showed that availability and coordination of critical care, imaging and other treatment modalities

			Hospit	al volum	ie		
	volume	Low-	volume		Weight	SE [95%CI]	
Miyata et al, ²⁵ 2009 Chikwe et al, ³¹ 2013 Iribarne et al, ³⁸ 2015 Zimmerman et al, ⁴⁷ 2016 Merlo et al, ⁴⁵ 2016 RE Model <i>Test for overall effect:</i> $P = 0.031$	62 226 15 - 22	1398 1379 124 - 174	46 359 187 - 230	481 1312 798 - 963	• • • • • • • • • • • • • • • • • • •	20.17% 15.95% 22.18% 17.15% 100.00% 0	1.00 [0.99, 1.00] 0.45 [0.32, 0.64] 0.47 [0.27, 0.82] 0.97 [0.76, 1.24] 0.48 [0.29, 0.79]
			Surge	on volun	ne		
I	High-vo	lume	Low-v	olume		Weight	SE [95%CI]
Chikwe et al, ³¹ 2014 Lenos et al. ³⁹ 2015	160 3	938 75	311 12	1130 87	+ = ∔ ■ -1		0.56 [0.42, 0.75]
Buonocuore et al, ⁴⁴ 2016	8	55	19	56	∎	22.03%	0.16 [0.05, 0.50]
Bashir et al, ⁴⁹ 2017	29	231	254	1319	ŀ∎ł	29.30%	0.85 [0.73, 0.99]
RE Model Test for overall effect: P = 0.037				-0	0.5 0.25 1 Observed o		0.32 [0.11, 0.93]

Figure 3. Forest plots with adjusted risk estimates for in-hospital/30-day mortality in high-volume versus low-volume hospitals (upper panel) and low-volume surgeons (lower panel).

CI: confidence intervals; OR: odds ratio.

are additional crucial elements in the care of AAS patients. Specifically, the availability of a designated 'aortic team' for the treatment of AAS patients has been proved to influence clinical postoperative results.⁴⁸⁻⁵⁰ Bashir et al.⁴⁹ revising their experience after the introduction of dedicated on-call rota for acute type A aortic dissection observed that this surgical reorganization resulted in lower early and late mortality. Patients who underwent surgical repair in the post-dissection rota era were less likely to suffer in-hospital mortality (30% versus 13.3%), and similar benefits were observed in the 5-year survival rate.49 Implementation of diagnostic aortic protocols, regionalization of services, and inter-hospital coordination are other important factors in the care of AAS patients.^{26,27,29,50} Davies et al.²⁶ firstly observed a significant increase in volume (referrals) and reduction in time to definitive treatment for AAS patients after initiation of an acute aortic treatment centre, and a prompt diagnosis and proper treatment is crucial since patients with acute type A dissection who do not receive treatment die at a rate of 1-2% per hour during the first day and almost half die by one week.⁵² Similarly, Harris et al., after the introduction of a standardized protocol within a regional hospital network, observed a drastic reduction in the length of time to both diagnosis and surgical repair (median time reduction of 30% and 50%, respectively) with improved survival postoperative outcomes.²⁷ The rate of follow-up care in the outpatient setting also improved, from 75% before the protocol to 85% after the protocol.²⁷

Similar data have been observed in other cardiovascular procedures, where hospital and surgical expertise has been increasingly recognized as an important contributor to operative outcomes.⁵³

As a matter of fact, an evidence-based hospital referral as a key part of safety standards to reduce nationwide mortality for several procedures, including coronary artery bypass grafting and aortic valve replacement has been adopted by the Leapfrog Group (Washington, DC, USA).^{54,55} Improved surgical results and outcomes have been also observed in specialized

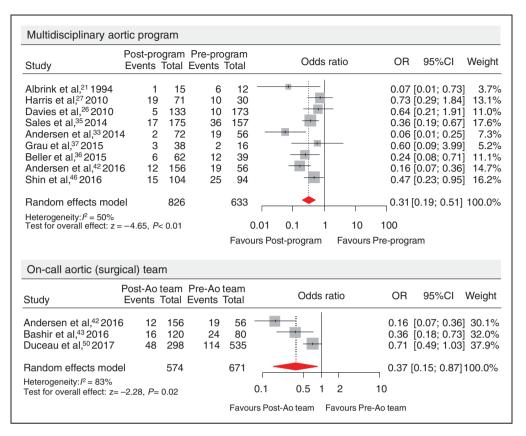


Figure 4. Forest plots with unadjusted risk estimates for in-hospital/30-day mortality in hospitals with dedicated multidisciplinary standardized care for acute aortic syndromes (before and after implementation, upper panel) and hospitals with dedicated on-call aortic team (lower panel).

Ao: aortic; CI: confidence intervals; OR: odds ratio.

centres for mitral valve diseases, leading international guidelines to recommend having mitral valve repairs at heart valve centres of excellence where the likelihood of successful repair is high and comorbidity low.^{56–59}

Limitations

The present study has limitations. First, owing the emergent nature of AAS, no randomized trials of abdominal aortic aneurysm interventions were retrieved, therefore limiting our qualitative and quantitative analysis to retrospective observational studies size.²¹⁻⁵⁰ often with a limited sample only. Retrospective studies are subject to confounders and bias, possibly resulting in a decline in the power of our meta-analysis. The majority of collected data were derived from a simple univariate comparison analysis, therefore limiting the opportunity to perform subgroup analysis, especially with reference to the different entities included in the wide definition of AAS. It is well known that management, and treatment approaches with related outcomes largely vary among acute type A and B dissections, intramural hematoma, and penetrating ulcers.¹² Second, due to the nature of these lifethreatening diseases, several patients who died before the diagnosis or those felt inappropriate for high-risk surgical approaches were not considered in the included studies, therefore limiting the recommendation of the present study for this sub-group of individuals, which is not negligible. Bottle et al.⁶ in their nationwide analysis of patients affected by thoracic diseases showed that 30% of aortic patients are refused surgery. Third, definitions of high- and low-volume centres and/or surgeons are heterogeneously defined across the included studies, and the great majority of these reports originate from small centre experiences. Unfortunately, international guidelines are lacking in terms of agreed service specification for TAD, and of recognized recommendations for aortic service organizations, hindering the establishment of clear and well accepted definitions of high- and low-volume thresholds.^{3,4} The present systematic review with meta-analysis is an attempt to overcome this knowledge gap.

Conclusion

Specialist aortic care improves outcomes and decrease mortality in patient affected by AAS. Aortic centres

with multidisciplinary expertise should constitute the standard of care for this population of patients.

Author contribution

GM and DM contributed equally to this work. GM and BVD had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Other contributions were as follows: Study concept and design: GM, AM, DM and BVD; Acquisition of data: GM and BVD; Analysis and interpretation of data: GM and BVD; Drafting of the manuscript: GM and AM; Critical revision of the manuscript for important intellectual content: GM, RG, FN, UB; Paper supervision: GM, FN; Language revision: AA.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

- 1. Sampson UK, Norman PE, Fowkes FG, et al. Global and regional burden of aortic dissection and aneurysms: mortality trends in 21 world regions, 1990 to 2010. *Glob Heart* 2014; 9: 171–180.
- 2. Hiratzka LF, Bakris GL, Beckman JA, et al. ACCF/AHA/ AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. J Am Coll Cardiol 2010; 55: e27–e129.
- 3. Erbel R, Aboyans V, Boileau C, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J 2014; 35: 2873–2926.
- 4. Olsson C, Thelin S, Ståhle E, Ekbom A and Granath F. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. *Circulation* 2006; 114: 2611–2618.
- von Allmen RS, Anjum A and Powell JT. Incidence of descending aortic pathology and evaluation of the impact of thoracic endovascular aortic repair: a population-based study in England and Wales from 1999 to 2010. *Eur J Vasc Endovasc Surg* 2013; 45: 154–159.

- 6. Bottle A, Mariscalco G, Shaw MA, et al. Unwarranted variation in the quality of care for patients with diseases of the thoracic aorta. *J Am Heart Assoc* 2017; 6.
- Raghupathy A, Nienaber CA, Harris KM, et al. Geographic differences in clinical presentation, treatment, and outcomes in type A acute aortic dissection (from the International Registry of Acute Aortic Dissection). *Am J Cardiol* 2008; 102: 1562–1566.
- Hughes GC, Zhao Y, Rankin JS, et al. Effects of institutional volumes on operative outcomes for aortic root replacement in North America. *J Thorac Cardiovasc Surg.* 2013; 145: 166–170.
- Wang W, Duan W, Xue Y, et al. Clinical features of acute aortic dissection from the Registry of Aortic Dissection in China. *J Thorac Cardiovasc Surg* 2014; 148: 2995–3000.
- Russo CF, Mariscalco G, Colli A, et al. Italian multicentre study on type A acute aortic dissection: a 33-year follow-up. *Eur J Cardiothorac Surg.* 2016; 49: 125–31.
- Pompilio G, Spirito R, Alamanni F, et al. Determinants of early and late outcome after surgery for type A aortic dissection. *World J Surg* 2001; 25: 1500–1506.
- Mussa FF, Horton JD, Nicholson J, et al. Acute aortic dissection and intramural hematoma. A systematic review. JAMA 2016; 316: 754–763.
- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; 339: b2535.
- The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed 31 December 2017).
- Borenstein M, Hedges LV, Higgins JPT, et al. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods* 2010; 1: 97–111.
- Benedetto U, Mohamed H, Vitulli P, et al. Axillary versus femoral arterial cannulation in type A acute aortic dissection: evidence from a meta-analysis of comparative studies and adjusted risk estimates. *Eur J Cardiothorac Surg* 2015; 48: 953–959.
- 17. Higgins JP and Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; 21: 1539–1558.
- Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315: 629–634.
- R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available at: http://www. R-project.org (accessed 31 December 2017).
- 20. Available at: https://cran.r-project.org/web/packages/ meta/meta.pdf (accessed 31 December 2017).
- Albrink MH, Rodriguez E, England GJ, et al. Importance of designated thoracic trauma surgeons in the management of traumatic aortic transection. South Med J 1994; 87: 497–501.
- Narayan P, Caputo M, Rogers CA, et al. Early and midterm outcomes of surgery of the ascending aorta/arch: is there a relationship with caseload? *Eur J Cardiothorac Surg* 2004; 25: 676–682.

- 23. Committee for Scientific Affairs, Kazui T, Osada H, et al. An attempt to analyze the relation between hospital surgical volume and clinical outcome. *Gen Thorac Cardiovasc Surg* 2007; 55: 483–492.
- 24. Knipp BS, Deeb GM, Prager RL, et al. A contemporary analysis of outcomes for operative repair of type A aortic dissection in the United States. *Surgery* 2007; 142: 524–528.
- 25. Miyata H, Motomura N, Ueda Y, et al. Toward quality improvement of thoracic aortic surgery: estimating volume-outcome effect from nationwide survey. *Eur J Cardiothorac Surg* 2009; 36: 517–521.
- Davies MG, Younes HK, Harris PW, et al. Outcomes before and after initiation of an acute aortic treatment center. J Vasc Surg 2010; 52: 1478–1485.
- Harris KM, Strauss CE, Duval S, et al. Multidisciplinary standardized care for acute aortic dissection: design and initial outcomes of a regional care model. *Circ Cardiovasc Qual Outcomes* 2010; 3: 424–430.
- Gopaldas RR, Dao TK, LeMaire SA, et al. Endovascular versus open repair of ruptured descending thoracic aortic aneurysms: a nationwide risk-adjusted study of 923 patients. J Thorac Cardiovasc Surg 2011; 142: 1010–1018.
- Chavanon O, Baguet JP, Albaladéjo P, et al. Direct admission to the operating room: an efficient strategy for patients with diagnosed or highly suspected acute type A aortic dissection. *Can J Cardiol* 2011; 27: 685–691.
- Sakata R, Kuwano H and Yokomise H. Hospital volume and outcomes of cardiothoracic surgery in Japan: 2005– 2009 national survey. *Gen Thorac Cardiovasc Surg* 2012; 60: 625–638.
- Chikwe J, Cavallaro P, Itagaki S, et al. National outcomes in acute aortic dissection: influence of surgeon and institutional volume on operative mortality. *Ann Thorac Surg* 2013; 95: 1563–1569.
- Tsagakis K, Konorza T, Dohle DS, et al. Hybrid operating room concept for combined diagnostics, intervention and surgery in acute type A dissection. *Eur J Cardiothorac Surg* 2013; 43: 397–404.
- 33. Andersen ND, Ganapathi AM, Hanna JM, et al. Outcomes of acute type a dissection repair before and after implementation of a multidisciplinary thoracic aortic surgery program. J Am Coll Cardiol 2014; 63: 1796–1803.
- Murzi M, Miceli A, Di Stefano G, et al. Enhancing quality control and performance monitoring in thoracic aortic surgery: a 10-year single institutional experience. *Eur J Cardiothorac Surg* 2015; 47: 608–615.
- Sales Mda C, Frota Filho JD, Aguzzoli C, et al. Aortic center: specialized care improves outcomes and decreases mortality. *Rev Bras Cir Cardiovasc* 2014; 29: 494–504.
- Beller JP, Scheinerman JA, Balsam LB, et al. Operative strategies and outcomes in type A aortic dissection after the enactment of a multidisciplinary aortic surgery team. *Innovations (Phila)* 2015; 10: 410–415.
- Grau JB, Kuschner CE, Ferrari G, et al. Effects of a protocol-based management of type A aortic dissections. *J Surg Res* 2015; 197: 265–269.
- 38. Iribarne A, Milner R, Merlo AE, et al. Outcomes following emergent open repair for thoracic aortic dissection are

improved at higher volume centers. *J Card Surg* 2015; 30: 74–79.

- Lenos A, Bougioukakis P, Irimie V, et al. Impact of surgical experience on outcome in surgery of acute type A aortic dissection. *Eur J Cardiothorac Surg* 2015; 48: 491–496.
- Schaffer JM, Lingala B, Miller DC, et al. Midterm survival after thoracic endovascular aortic repair in more than 10,000 Medicare patients. *J Thorac Cardiovasc Surg* 2015; 149: 808–820.
- Schaffer JM, Lingala B, Fischbein MP, et al. Midterm outcomes of open descending thoracic aortic repair in more than 5,000 Medicare patients. *Ann Thorac Surg* 2015; 100: 2087–2094.
- 42. Andersen ND, Benrashid E, Ross AK, et al. The utility of the aortic dissection team: outcomes and insights after a decade of experience. *Ann Cardiothorac Surg* 2016; 5: 194–201.
- Bashir M, Shaw M, Field M, et al. Repair of type A dissection-benefits of dissection rota. *Ann Cardiothorac* Surg 2016; 5: 209–215.
- 44. Buonocore M, Amarelli C, Scardone M, et al. Cerebral perfusion issues in acute type A aortic dissection without preoperative malperfusion: how do surgical factors affect outcomes? *Eur J Cardiothorac Surg* 2016; 50: 652–659.
- 45. Merlo AE, Chauhan D, Pettit C, et al. Outcomes following emergent open repair for thoracic aortic dissection are improved at higher volume centers in direct admissions and transfers. *J Cardiothorac Surg* 2016; 11: 118.
- 46. Shin KC, Lee HS, Park JM, et al. Outcomes before and after the implementation of a critical pathway for patients with acute aortic disease. *Yonsei Med J* 2016; 57: 626–634.
- Zimmerman KP, Oderich G, Pochettino A, et al. Improving mortality trends for hospitalization of aortic dissection in the National Inpatient Sample. *J Vasc Surg* 2016; 64: 606–615.
- Arsalan M, Squiers JJ, Herbert MA, et al. Comparison of outcomes of operative therapy for acute type A aortic dissections provided at high-volume versus low-volume medical centers in North Texas. *Am J Cardiol* 2017; 119: 323–327.
- Bashir M, Harky A, Fok M, et al. Acute type A aortic dissection in the United Kingdom: Surgeon volume-outcome relation. *J Thorac Cardiovasc Surg* 2017; 154: 398–406.
- Duceau B, Alsac JM, Bellenfant F, et al. Improved survival after implementation of a large-scale regional dedicated aortic network. *J Am Coll Cardiol* 2017; 70: 3068–3069.
- Landon BE, O'Malley AJ, Giles K, et al. Volume outcome relationships and abdominal aortic aneurysm repair. *Circulation* 2010; 122: 1290–1297.
- 52. Booher AM, Isselbacher EM, Nienaber CA, et al. The IRAD classification system for characterizing survival after aortic dissection. *Am J Med* 2013; 126: 730.
- Birkmeyer JD and Dimick JB. Understanding and reducing variation in surgical mortality. *Annu Rev Med* 2009; 60: 405–415.

- Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med* 2002; 346: 1128–1137.
- Birkmeyer JD1, Stukel TA, Siewers AE, et al. Surgeon volume and operative mortality in the United States. *N Engl J Med* 2003; 349: 2117–2127.
- Kilic A, Shah AS, Conte JV, et al. Operative outcomes in mitral valve surgery: combined effect of surgeon and hospital volume in a population-based analysis. *J Thorac Cardiovasc Surg* 2013; 146: 638–646.
- 57. Vassileva CM, McNeely C, Spertus J, et al. Hospital volume, mitral repair rates, and mortality in mitral valve surgery in the elderly: an analysis of US hospitals

treating Medicare fee-for-service patients. J Thorac Cardiovasc Surg 2015; 149: 762–768.

- Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017; 135: e1159–e1195.
- Falk V, Baumgartner H, Bax JJ, et al. ESC/EACTS Guidelines for the management of valvular heart disease. *Eur J Cardiothorac Surg* 2017; 52: 616–664.