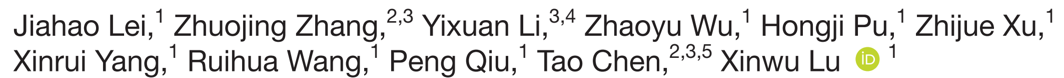
BMJ Open

Fluid balance and clinical outcomes in patients with aortic dissection: a retrospective case-control study based on ICU databases



Jiahao Lei,[1] Zhuojing Zhang,[2,3] Yixuan Li,[3,4] Zhaoyu Wu,[1] Hongji Pu,[1] Zhijue Xu,[1] Xinrui Yang,[1] Ruihua Wang,[1] Peng Qiu,[1] Tao Chen,[2,3,5] Xinwu Lu[1]

To cite: Lei J, Zhang Z, Li Y, *et al*. Fluid balance and clinical outcomes in patients with aortic dissection: a retrospective case-control study based on ICU databases. *BMJ Open* 2025;**15**:e083933. doi:10.1136/bmjopen-2024-083933

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-083933).

JL, ZZ, YL and ZW contributed equally.

Received 03 January 2024
Accepted 30 September 2024

© Author(s) (or their employer(s)) 2025. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Dr Xinwu Lu; luxinwu@shsmu.edu.cn, Dr Tao Chen; t66chen@uwaterloo.ca and Dr Peng Qiu; hiiigh4@163.com

ABSTRACT

Objectives Aortic dissection (AD) is a life-threatening condition that requires intensive care and management. This paper explores the role of fluid management in the clinical care of AD patients, which has been unclear despite the substantial existing research that has been conducted on the treatment of AD.

Design A retrospective case-control study using data for AD patients from public databases.

Setting Two public intensive care unit (ICU) databases with hospital courses from the USA, Medical Information Mart for Intensive Care (MIMIC)-IV critical care dataset and the eICU Collaborative Research Database, with data from 2008 to 2019.

Participants A total of 751 adult AD patients with detailed fluid management records from two databases were included.

Interventions The mean 24-hour intake and output were calculated by dividing the total amount of intake and output by the number of days in the ICU, respectively. The mean 24-hour fluid balance was generated by subtracting the output from the intake.

Outcome measures The relationship between the mean 24-hour fluid management and all-cause in-hospital death was assessed through univariate and multivariable regression analyses.

Results A positive correlation was found between mean 24-hour fluid intake and in-hospital mortality among AD patients (OR 1.029, 95% CI (1.018, 1.041), p<0.001), whereas a negative correlation was revealed between mean 24-hour fluid output and in-hospital mortality (OR 0.941, 95% CI (0.914, 0.968), p<0.001). A similar result was found for mean 24-hour fluid balance (OR 1.030, 95% CI (1.019, 1.042), p<0.001), and the cut-off was selected to be 5.12 dL (AUC=0.778, OR 3.066, 95% CI (1.634, 5.753), p<0.001).

Conclusions This study stresses the importance of fluid balance in the clinical care of AD patients and provides new insights for optimising fluid management and monitoring strategies beyond the conventional focus on blood pressure and heart rate management.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Records in this study were drawn from two recognised intensive care unit databases.
⇒ Detailed monitoring data and fluid management records, which were difficult to collect in general surgical wards, were included in the analyses.
⇒ Variables showing significant differences or demonstrating clear clinical significance were included in multivariable analyses.
⇒ Retrospective observational studies cannot establish causal relationships.
⇒ Patient diagnoses were based solely on discharge diagnoses, leading to protopathic biases.

INTRODUCTION

Aortic dissection (AD) is a severe and potentially life-threatening condition characterised by a tear in the inner lining of the aorta. This cardiovascular emergency requires prompt recognition, diagnosis and management to prevent devastating consequences. The incidence of AD has been estimated to range from 2.53 cases per 100 000 individuals per year, making it a relatively rare but critical medical condition.[1]

In the management of critical illness, fluid balance is undoubtedly a crucial aspect requiring meticulous monitoring, since it significantly impacts patient mortality.[2] This is particularly evident in cardiovascular conditions like shock, heart failure and pulmonary hypertension, where precise fluid management is crucial in clinical practice.[3–5] In the realm of AD, complicated dissection can lead to malperfusion, which is characterised by inadequate blood flow to specific tissue beds, commonly affecting organs such as the kidneys, visceral organs and lower extremities and potentially causing stroke and spinal cord ischaemia.[6] There is, however, a lack of research specifically focused on the precise fluid management in AD patients. In the ESC 2014 guideline, it is recommended to avoid aggressive fluid administration in an aortic emergency (traumatic aortic injury) due to

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Community College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

the potential exacerbation of bleeding, coagulopathy and hypertension.[7] The ACC/AHA 20 guideline suggests that fluid resuscitation should be guided by haemodynamic parameters and the patient's response to therapy.[8]

Despite advancements in the diagnosis and management of AD, it continues to be associated with significant mortality.[9 10] The patients, particularly those in the intensive care unit (ICU) with haemodynamic instability, end-organ malperfusion and complications such as dissection rupture or expansion, require close attention. To ensure that AD patients receive optimal care, it is imperative that fluid management is precise, as it involves striking a delicate balance between addressing malperfusion and preventing the progression of dissection to aortic rupture. In this spirit, the purpose of this study is to determine the relationship between in-hospital mortality and fluid balance, which will be useful for prognostication, resource allocation, and tailored interventions.

METHODS

Data and participants

We retrospectively collected records from public databases, the Medical Information Mart for Intensive Care (MIMIC)-IV critical care data set[11 12] and the eICU Collaborative Research Database.[13 14] MIMIC-IV comprises data from 76540 ICU admissions at Beth Israel Deaconess Medical Center spanning from 2008 to 2019. The eICU database includes information on over 200000 ICU admissions in critical care units across 208 hospitals in the USA, covering the period from 2014 to 2015. To investigate the correlation between fluid management and the short-term outcomes of AD patients, after data acquisition from the PhysioNet[15] by PostgreSQL (version 13.8), we included all ICU admissions from patients with ICD diagnosed as 44100–44103 (ICD9) and I7100-I7103 (ICD10). The ICD codes corresponding to the comorbidities are presented in online supplemental table 1). The study design is illustrated in figure 1. Exclusion criteria were (1) patients under the age of 18; (2) patients over the age of 89, since the shifted anchor age was set at 91 regardless of how old they were; and (3) admissions without records of fluid intake and output.

Patients' age, sex, weight, height, ethnicity at admission, comorbidities, in-hospital death information, length of hospital stay and ICU stay were collected, and the in-hospital death was referred to all-cause mortality. As a single hospitalisation may involve multiple ICU stays, the length of hospital stay was the total time a patient spent in various departments within the hospital. In contrast, the length of ICU stay specifically denoted the duration of each individual ICU stay. We also collected the first results of laboratory examinations including blood gas, blood routine, basic metabolic panel and coagulation panel. To analyse waveform data such as heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), we excluded data during the last 30 min before cardiac arrest and employed functional data analysis (FDA) to reliably estimate the continuous underlying vital sign processes. FDA has been proven as an effective estimation technique capable of recovering the true underlying structure from discretely observed data and has been used in various medical studies for handling vital signs,[16 17] and our data processing procedure was similar to those of previous studies.[18 19] In addition, we calculated the mean and SD of the patient's HR, SBP and DBP on a per-minute basis throughout each ICU stay. The usage and administration times of antihypertensive medications were also included in the analyses (online supplemental table 2). All fluid intake and output events were recorded. The mean 24-hour intake and output were calculated by dividing the total amount of intake and output by the number of days in the ICU, respectively, while the mean 24-hour fluid balance was generated by subtracting the output from the intake.

Statistical analysis

Patients were divided into two groups according to in-hospital survival or death. Those who died in hospital were considered as cases for the case-control study, examining the correlation between different exposures and mortality. Continuous data were presented as mean values±SD, and categorical data were summarised as counts and proportions. The univariate comparisons between the two groups were conducted through the Student's t-test for continuous data and the X^2 test for categorical data. Variables showing significant differences or those with clear clinical significance regarding in-hospital death were included in subsequent multivariable analyses, while variables with a large amount of missing data and those with potential mediation were excluded. Comorbidities that affected less than 10% of the total population in the regression (n=706) were only discussed in the sensitivity analyses due to data imbalance.

Multivariable logistic regressions were built to evaluate the adjusted association between the mean 24-hour intake, output or overall fluid balance and the in-hospital mortality. Results were presented as OR with the corresponding 95% CI. To further provide clinical guidance for fluid management in AD patients, the CatPredi method was applied to the multivariable model to determine a cut-off for the mean 24-hour fluid balance in predicting in-hospital death. In specific, this method converts the continuous variable to a categorical variable based on different cut-off points. The optimal cut-off is subsequently determined as the one with the highest AUC of the logistic regressions based on generalised additive models with P-spline smoothers.

Based on the results of the primary outcome, the same regressions were conducted in the sensitive analyses excluding different types of patients. The length of hospital stay and ICU stay were also analysed as secondary outcomes, and multivariable linear regression models were applied, incorporating variables included in the aforementioned logistic regressions. All analyses were conducted by R (version 4.2.0). For both univariate and

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Comm College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

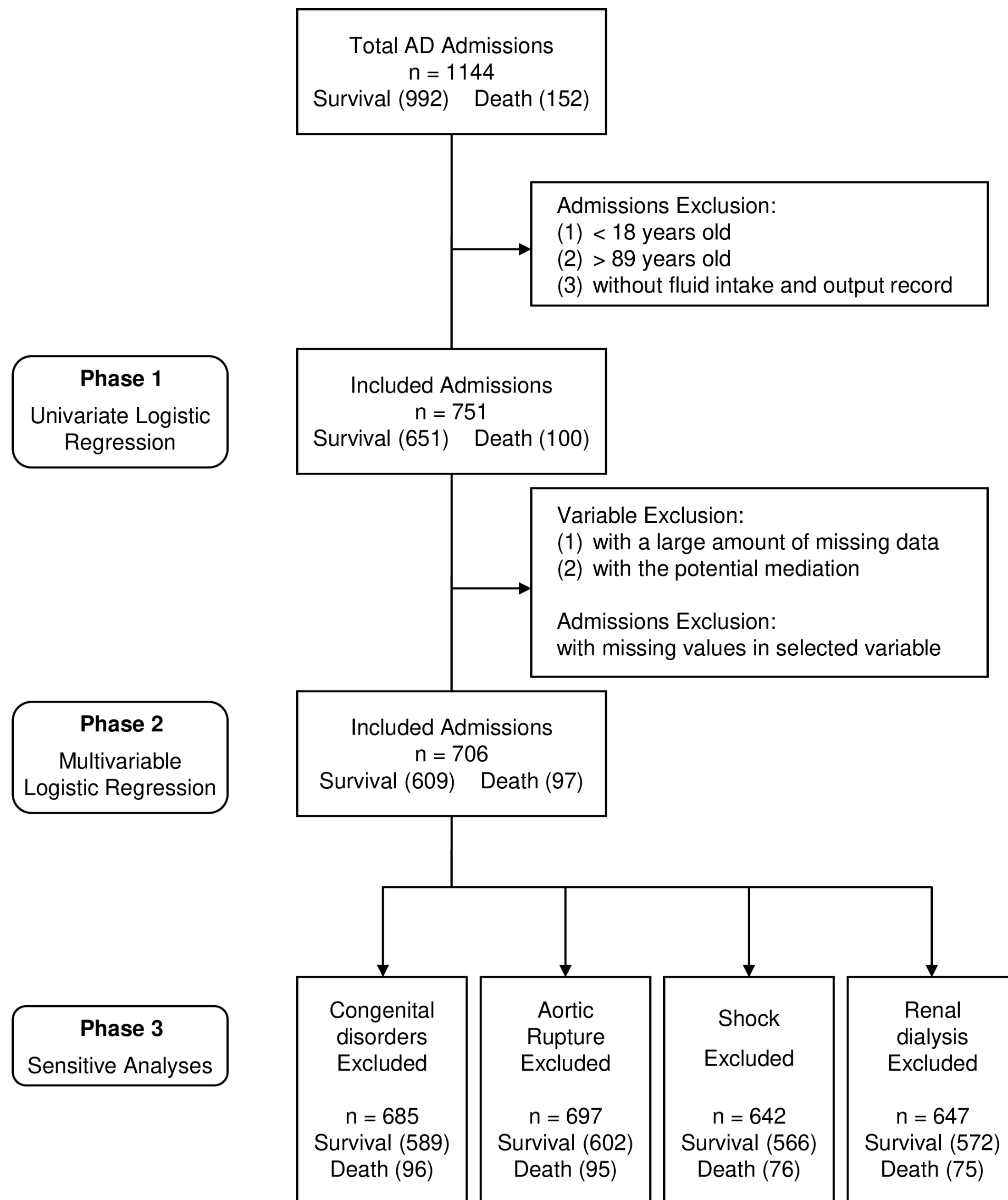


Figure 1 Flowgram of the study population and design.

multivariable comparisons, variables with p values <0.05 were considered to be statistically significant.

Data access and ethics

The Ethics Committee of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine exempted ethics approval for this study because patient data were drawn from two public databases. The author (XL) underwent the necessary credentialing process (Record ID 50038775) and obtained authorised access to the two databases. XL signed the data use agreement, and all authors were responsible for data extraction.

Patient and public involvement

None.

RESULTS

Patient characteristics and univariate comparisons

Among the 751 AD admissions identified in the MIMIC-IV and eICU datasets, 100 (13.3%) died in the hospital. A total of 62 variables were used to assess their association with in-hospital mortality, and no significant difference was found in demographics (table 1). A number of laboratory tests, including blood pH, lymphocytes, red blood cell (RBC) counts, haemoglobin, red cell distribution width (RDW), platelets, activated partial thromboplastin time (APTT), creatinine, albumin, bicarbonate, chloride, sodium and phosphate, showed significant differences between the patients who survived in hospital and those who did not. The comorbidities such as hypertension and

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Comm College City Centre Campus .
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 1 Demographic and clinical characteristics from admissions in MIMIC-IV and eICU

Variable	Survival (n=651) excluding missing data	Missing (%)	Death (n=100) excluding missing data	Missing (%)	*p* value*
Demographics					
Age (years)	66.56±14.03	0 (0.00%)	66.85±13.48	0 (0.00%)	0.845
Sex (%)					0.410
Female	273 (41.94%)	0 (0.00%)	37 (37.00%)	0 (0.00%)	
Male	378 (58.06%)	0 (0.00%)	63 (63.00%)	0 (0.00%)	
Weight (kg)	83.07±22.04	15 (2.30%)	88.49±27.07	1 (1.00%)	0.060
Height (cm)	171.11±11.11	125 (19.20%)	171.03±11.24	15 (15.00%)	0.952
Location of dissection					0.648
Thoracic	383 (58.83%)	0 (0.00%)	62 (62.00%)	0 (0.00%)	
Abdominal	76 (11.67%)	0 (0.00%)	9 (9.00%)	0 (0.00%)	
Both	112 (17.20%)	0 (0.00%)	14 (14.00%)	0 (0.00%)	
Unspecified	80 (12.29%)	0 (0.00%)	15 (15.00%)	0 (0.00%)	
First laboratory examinations					
pH	7.37±0.09	219 (33.64%)	7.30±0.13	8 (8.00%)	<0.001
Basophils (%)	0.28±0.26	213 (32.72%)	0.24±0.28	30 (30.00%)	0.295
Eosinophils (%)	1.13±1.68	211 (32.41%)	0.85±1.29	32 (32.00%)	0.115
Lymphocytes (%)	12.97±8.02	210 (32.26%)	10.59±7.76	29 (29.00%)	0.019
Monocytes (%)	6.03±3.39	210 (32.26%)	6.29±3.26	29 (29.00%)	0.533
Neutrophils (%)	78.59±10.68	224 (34.41%)	80.28±10.48	33 (33.00%)	0.225
WBC counts (K/μL)	11.33±10.16	4 (0.61%)	11.79±5.34	0 (0.00%)	0.492
RBC counts (M/μL)	3.75±0.82	4 (0.61%)	3.48±0.84	0 (0.00%)	0.004
Haemoglobin (g/dL)	11.22±2.40	2 (0.31%)	10.53±2.47	0 (0.00%)	0.010
MCH (pg)	30.03±2.50	23 (3.53%)	30.15±2.16	0 (0.00%)	0.618
MCHC (g/μL)	33.13±1.54	11 (1.69%)	32.88±1.67	0 (0.00%)	0.173
MCV (fL)	90.63±6.64	11 (1.69%)	91.80±6.35	0 (0.00%)	0.093
RDW (%)	14.51±1.80	24 (3.69%)	15.29±1.94	2 (2.00%)	<0.001
Platelets (K/μL)	203.47±99.75	5 (0.77%)	174.92±78.93	1 (1.00%)	0.002
Fibrinogen (mg/dL)	231.83±136.87	384 (58.99%)	242.81±187.76	43 (43.00%)	0.677
PT (s)	15.31±6.25	72 (11.06%)	18.02±14.95	5 (5.00%)	0.084
APTT (s)	37.08±21.50	83 (12.75%)	44.23±30.34	5 (5.00%)	0.029
Creatinine (mg/dL)	1.31±1.25	2 (0.31%)	1.78±1.95	0 (0.00%)	0.020
ALT (IU/L)	65.22±198.80	242 (37.17%)	246.45±839.55	14 (14.00%)	0.050
AST (IU/L)	141.29±1 1060.83	235 (36.10%)	443.44±1 4030.49	13 (13.00%)	0.062
Albumin (g/dL)	3.19±0.66	285 (43.78%)	2.79±0.72	17 (17.00%)	<0.001
Bicarbonate (mmol/L)	23.96±3.43	8 (1.23%)	22.41±4.76	2 (2.00%)	0.002
Calcium (mg/dL)	8.59±0.77	16 (2.46%)	8.78±1.36	0 (0.00%)	0.181
Chloride (mmol/L)	104.33±5.25	2 (0.31%)	106.25±6.25	0 (0.00%)	0.004
Sodium (mmol/L)	139.02±4.55	2 (0.31%)	141.09±6.78	0 (0.00%)	0.004
Potassium (mmol/L)	4.21±0.73	2 (0.31%)	4.28±0.94	0 (0.00%)	0.430
Phosphate (mg/dL)	3.69±1.10	79 (12.14%)	4.44±1.98	10 (10.00%)	<0.001
Magnesium (mg/dL)	2.09±0.45	50 (7.68%)	2.19±0.55	2 (2.00%)	0.111
Cardiac output (L/min)	4.63±2.04	467 (71.74%)	4.22±2.07	69 (69.00%)	0.319
Comorbidity (%)					
Congenital disorders	22 (3.38%)	0 (0.00%)	1 (1.00%)	0 (0.00%)	0.330
Hypertension	374 (57.45%)	0 (0.00%)	38 (38.00%)	0 (0.00%)	<0.001

Continued

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Comm College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Community College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 1 Continued

Variable	Survival (n=651) excluding missing data	Missing (%)	Death (n=100) excluding missing data	Missing (%)	*p* value*
Diabetes	64 (9.83%)	0 (0.00%)	11 (11.00%)	0 (0.00%)	0.717
Heart failure	102 (15.67%)	0 (0.00%)	27 (27.00%)	0 (0.00%)	0.005
Obstructive lung disease	91 (13.98%)	0 (0.00%)	15 (15.00%)	0 (0.00%)	0.785
Aortic rupture	8 (1.23%)	0 (0.00%)	2 (2.00%)	0 (0.00%)	0.875
Shock	44 (6.76%)	0 (0.00%)	22 (22.00%)	0 (0.00%)	<0.001
Renal dialysis status	37 (5.68%)	0 (0.00%)	22 (22.00%)	0 (0.00%)	<0.001
Monitoring data					
Mean HR (bpm)	79.27±12.43	0 (0.00%)	84.94±16.18	0 (0.00%)	0.001
SD HR (bpm)	7.03±4.35	2 (0.31%)	9.15±5.47	0 (0.00%)	<0.001
Mean SBP (mmHg)	122.66±15.15	0 (0.00%)	116.96±24.75	0 (0.00%)	0.027
Mean DBP (mmHg)	62.34±9.84	0 (0.00%)	61.22±20.07	0 (0.00%)	0.584
SD SBP (mmHg)	13.28±8.84	2 (0.31%)	16.75±11.98	0 (0.00%)	0.006
SD DBP (mmHg)	8.44±5.42	2 (0.31%)	10.02±7.82	0 (0.00%)	0.055
Mean 24 hours intake (dL)	28.09±19.61	0 (0.00%)	43.38±45.16	0 (0.00%)	0.001
Mean 24 hours output (dL)	16.68±11.77	0 (0.00%)	12.43±12.43	0 (0.00%)	0.002
Mean 24 hours fluid balance (dL)	11.40±16.86	1 (0.15%)	30.95±41.65	0 (0.00%)	<0.001
Medication					
Antihypertensives use (%)	597 (91.71%)	0 (0.00%)	80 (80.00%)	0 (0.00%)	<0.001
ACEI/ARBs use (%)	271 (41.63%)	0 (0.00%)	16 (16.00%)	0 (0.00%)	<0.001
β-blockers use (%)	563 (86.48%)	0 (0.00%)	58 (58.00%)	0 (0.00%)	<0.001
CCBs use (%)	391 (60.06%)	0 (0.00%)	39 (39.00%)	0 (0.00%)	<0.001
Diuretics use (%)	430 (66.05%)	0 (0.00%)	47 (47.00%)	0 (0.00%)	<0.001
Direct vasodilators use (%)	388 (59.60%)	0 (0.00%)	33 (33.00%)	0 (0.00%)	<0.001
Others (%)	128 (19.66%)	0 (0.00%)	12 (12.00%)	0 (0.00%)	0.090
Antihypertensives start time (h)	14.92±35.17	70 (10.75%)	28.28±89.09	34 (34.00%)	0.232
Outcomes					
Length of ICU stay (day)	6.24±7.53	0 (0.00%)	7.68±8.32	0 (0.00%)	0.105
Length of hospital stay (day)	13.07±13.33	0 (0.00%)	11.17±10.14	0 (0.00%)	0.098
Data Source (%)					
MIMIC-IV	470 (72.20%)	0 (0.00%)	60 (60.00%)	0 (0.00%)	0.013
eICU	181 (27.80%)	0 (0.00%)	40 (40.00%)	0 (0.00%)	

*Student t-test for continuous data and chi-square test for categorical data.
ACEI, angiotensin-converting enzyme inhibitors; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; ARBs, angiotensin receptor blockers; AST, aspartate aminotransferase; CCBs, calcium channel blockers; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; PT, prothrombin time; RBC, red blood cell; RDW, red cell distribution width; SD, standard deviation; WBC, white blood cell.

heart failure, the antihypertensive administration, the mean and SD of HR and SBP and the mean fluid management also demonstrated significant differences between the two groups.

Primary outcome

After excluding variables with high levels of missing data (ie, pH, lymphocytes, APTT, albumin and phosphate) or potential mediation (ie, haemoglobin and RDW for RBC), we also included the age, white blood cell (WBC), diabetes and obstructive lung disease as covariates given their underlying clinical relevance.[7 20 21] Among all variables included in multivariable logistic regression, mean 24-hour intake (OR 1.029, 95% CI (1.018, 1.041), p<0.001) and output (OR 0.941, 95% CI (0.914, 0.968), p<0.001) exhibited the strongest relationships with in-hospital death. There were also significant adjusted associations between heart failure and in-hospital death (OR 2.430, 95% CI (1.286, 4.590), p=0.006). Besides, the results were not affected by data from different databases after adjustment (table 2). In the analysis focusing

Table 2 Multivariable logistic regression including intake and output for odds to in-hospital death

	Coefficient	OR	95% CI	*p* value
Age (years)	0.009	1.009	(0.989, 1.028)	0.377
Sex	0.175	1.192	(0.710, 2.000)	0.507
Location: thoracic†	0.643	1.902	(0.674, 5.369)	0.224
Location: both	0.709	2.032	(0.617, 6.684)	0.243
Location: unspecified	0.652	1.920	(0.529, 6.977)	0.322
WBC counts (K/µL)	0.003	1.003	(0.989, 1.017)	0.681
RBC counts (M/µL)	−0.246	0.782	(0.575, 1.062)	0.116
Platelets (K/µL)	−0.002	0.998	(0.996, 1.001)	0.274
Creatinine (mg/dL)	0.006	1.006	(0.855, 1.183)	0.944
Bicarbonate (mmol/L)	−0.053	0.948	(0.876, 1.026)	0.185
Chloride (mmol/L)	−0.012	0.988	(0.907, 1.076)	0.784
Sodium (mmol/L)	0.062	1.064	(0.963, 1.176)	0.221
Hypertension	−0.431	0.65	(0.371, 1.138)	0.132
Diabetes	−0.012	0.988	(0.416, 2.344)	0.977
Heart failure	0.888	2.430	(1.286, 4.590)	0.006**
Obstructive lung disease	0.649	1.914	(0.936, 3.917)	0.075
Mean HR (bpm)	0.019	1.019	(0.996, 1.043)	0.105
SD HR (bpm)	0.034	1.034	(0.980, 1.091)	0.217
Mean SBP (mmHg)	−0.015	0.986	(0.967, 1.005)	0.139
Mean DBP (mmHg)	−0.005	0.995	(0.956, 1.036)	0.822
SD SBP (mmHg)	0.005	1.005	(0.980, 1.031)	0.700
SD DBP (mmHg)	0.024	1.024	(0.976, 1.076)	0.332
Mean 24 hours intake (dL)	0.029	1.029	(1.018, 1.041)	<0.001***
Mean 24 hours output (dL)	−0.061	0.941	(0.914, 0.968)	<0.001***
Antihypertensives use	−0.161	0.852	(0.393, 1.846)	0.684
Database‡	0.412	1.501	(0.618, 3.690)	0.366
Constant	−8.403	0.0002	(0.000, 5.007)	0.100

*p<.05, **p<.01, ***p<.001
†Compared to abdominal aortic dissection.
‡Data from different databases: MIMIC-IV = 1 and eICU = 2.
CI, confidence interval; DBP, diastolic blood pressure; HR, heart rate; OR, Odds ratio; RBC, red blood cell; SBP, systolic blood pressure; SD, standard deviation; WBC, white blood cell.

on fluid balance (table 3), similar results were found in mean 24-hour fluid balance (OR 1.030, 95% CI (1.019, 1.042), p<0.001) and heart failure (OR 2.495, 95% CI (1.333, 4.672), p=0.004). On comparison, a cut-off for the mean 24-hour fluid balance of 5.12 dL showed the highest AUC of 0.778 (OR 3.066, 95% CI (1.634, 5.753), p<0.001).

To partially mitigate the impact of congenital aetiology and the extensive fluid resuscitation caused by aortic rupture, shock and renal dialysis, we excluded few patients with these comorbidities and conducted sensitive analyses (online supplemental table 3). It is found that fluid management and in-hospital mortality remained significantly correlated, stressing the importance of fluid balance in AD patients.

Secondary outcomes

Multivariable linear regression revealed a significant association between the mean 24-hour output and the length of ICU stay (coefficient 0.067, 95% CI (0.003, 0.131), p=0.039), but not with the intake (coefficient −0.015, 95% CI (−0.037, 0.007), p=0.179) (online supplemental table 4). In the multivariable analysis of fluid balance, no significant difference was found in the mean 24-hour fluid balance (coefficient −0.020, 95% CI (−0.041, 0.002), p=0.073) (online supplemental table 5). Additionally in both regressions, the length was positively correlated with dissected thoracic aorta, mean HR and antihypertensives use while negatively correlated with the SD of HR, SBP and DBP. However, note that the decision for patients to leave the ICU may not always signify an improvement in

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Comm College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 3 Multivariable logistic regression including fluid balance for odds to in-hospital death

	Coefficient	OR	95% CI	*p* value
Age (years)	0.011	1.011	(0.992, 1.031)	0.250
Sex	0.119	1.127	(0.677, 1.876)	0.646
Location: thoracic†	0.525	1.69	(0.626, 4.568)	0.301
Location: both	0.663	1.941	(0.607, 6.204)	0.263
Location: unspecified	0.586	1.798	(0.508, 6.355)	0.363
WBC counts (K/μL)	−0.0003	0.9997	(0.986, 1.014)	0.966
RBC counts (M/μL)	−0.182	0.833	(0.618, 1.124)	0.232
Platelets (K/μL)	−0.001	0.999	(0.996, 1.001)	0.349
Creatinine (mg/dL)	0.039	1.039	(0.881, 1.227)	0.648
Bicarbonate (mmol/L)	−0.050	0.952	(0.880, 1.029)	0.212
Chloride (mmol/L)	−0.018	0.982	(0.905, 1.066)	0.660
Sodium (mmol/L)	0.062	1.064	(0.966, 1.173)	0.206
Hypertension	−0.538	0.584	(0.335, 1.018)	0.058
Diabetes	0.074	1.077	(0.468, 2.477)	0.861
Heart failure	0.914	2.495	(1.333, 4.672)	0.004**
Obstructive lung disease	0.624	1.867	(0.917, 3.802)	0.085
Mean HR (bpm)	0.017	1.017	(0.993, 1.042)	0.156
SD HR (bpm)	0.031	1.032	(0.978, 1.089)	0.252
Mean SBP (mmHg)	−0.013	0.987	(0.968, 1.006)	0.183
Mean DBP (mmHg)	−0.006	0.994	(0.953, 1.036)	0.771
SD SBP (mmHg)	0.004	1.004	(0.979, 1.030)	0.763
SD DBP (mmHg)	0.029	1.029	(0.980, 1.081)	0.244
Mean 24 hours fluid balance (dL)	0.030	1.030	(1.019, 1.042)	<0.001***
Antihypertensives use	−0.311	0.733	(0.330, 1.625)	0.444
Database‡	0.738	2.091	(0.912, 4.793)	0.081
Constant	−8.520	0.0002	(0.000, 3.884)	0.091

*p<.05, **p<.01, ***p<.001
†Compared to abdominal aortic dissection.
‡ Data from different databases: MIMIC-IV = 1 and eICU = 2.
CI, confidence interval; DBP, diastolic blood pressure; HR, heart rate; OR, Odds ratio; RBC, red blood cell; SBP, systolic blood pressure; SD, standard deviation; WBC, white blood cell.

their condition, it could also involve transfers between different departments. Therefore, the length of ICU stay alone may not fully reflect the severity of a patient's condition.

The total hospital stay duration was also analysed, which similarly indicated that the length was significantly associated with mean 24-hour output (coefficient 0.123, 95% CI (0.024, 0.222), p=0.015) rather than intake (coefficient −0.023, 95% CI (−0.057, 0.010), p=0.174) (online supplemental table 6). In the multivariable analysis of fluid balance, a negative association was found between the length of hospital stay and the mean 24-hour fluid balance (coefficient −0.032, 95% CI (−0.064 to −0.001), p=0.045) (online supplemental table 7). In both two regressions, factors such as higher WBC counts, lower RBC counts, platelet levels, presence of dissected thoracic aorta and comorbid heart failure were associated with a longer hospital stay.

DISCUSSION

In the management of acute aortic syndromes, such as AD, current clinical practices largely revolve around pharmacological blood pressure control. However, the fluid intake generated during the treatment process also exerts a significant impact on blood pressure dynamics, which is a complex yet crucial aspect in the context of patient management.[22] Notably, this relationship is not linear and may be subject to intricate regulatory mechanisms within the body.[23] The dynamic arterial elastance, serving as an effective predictor for arterial pressure response to fluid expansion, could potentially undergo

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Comm College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

inevitable alterations after AD.[24] Thus, understanding the direct interrelation between fluid balance and mortality is pivotal for effective clinical decision-making and patient care.

This study highlights and provides further evidence that in the management of AD, excessive fluid resuscitation is not recommended. The 2010 guidelines from ACCF/AHA, along with other societies, suggest that volume administration should be titrated to improve blood pressure due to the potential to cause false lumen propagation.[25] In our multivariable logistic regression adjusted for potential confounders, the mean 24-hour fluid intake and output during an ICU stay outperform the SBP and DBP in predicting in-hospital mortality, as indicated by their *p* values. This finding suggests that fluid balance could be an important and vital adjunct to arterial blood pressure management in clinical care. Therefore, a treatment strategy based solely on pharmacological control of blood pressure may be insufficient.

However, it is possible that our findings may be affected by AD patients who undergo substantial fluid resuscitation due to specific comorbidities or imminent death. Limited to the format of the ICU databases, identifying cases where fluid intake occurred due to life-saving efforts was challenging, and we were only able to perform sensitivity analyses by excluding patients with confirmed ruptures. Even though these factors did not alter our conclusions, some bias may still exist. A prospective study is warranted to further assess the impact of fluid balance after excluding the aforementioned factors on the mortality of AD patients. In addition to fluid balance, we observed a positive correlation between heart failure and in-hospital mortality, which is likely attributed to acute severe aortic regurgitation caused by the involvement of the aortic root in dissection.[8] As the database diagnoses were solely based on discharge information, we cannot determine whether heart failure occurred during the hospitalisation due to AD. Nevertheless, some studies have shown that whether it is newly or previously diagnosed, heart failure may have significant implications for the care and outcomes of dissection patients.[6]

Notably, in the initial anti-impulse treatment of AD patients, the guidelines predominantly recommend β-blockers as the preferred antihypertensive agents based on post-discharge follow-up outcomes in patients with a chronic state of AD.[7 8 26] For hospitalised patients, particularly those in the ICU, β-blockers can indeed reduce cardiac output by lowering HR and contractility, thereby alleviating the impact of arterial pulsation on the dissected vessels while minimally affecting fluid balance.[27] However, another commonly used antihypertensive medication, diuretics, can lower blood pressure by reducing fluid overload, which may also offer protective benefits in acute heart failure. Considering the discussion above, whether diuretics represent a more rational choice for improving acute phase outcomes such as in-hospital mortality remains a question that merits further investigation.[28 29] Concurrently, meticulous tracking and restriction of a patient's fluid balance, alongside antihypertensive treatment, are pivotal for achieving the meticulous equilibrium that addresses malperfusion while preventing the progression or rupture of the dissection.

In conformity with the recommended tests from the ESC 2014 guideline, our univariate analyses revealed significant differences in blood pH, bicarbonate and phosphate, reflecting potential metabolic disorders and oxygenation status.[7] Moreover, decreased RBC counts, haemoglobin, and increased HR indicated circulatory blood loss, including bleeding and false lumen blood accumulation, which are closely associated with patient prognosis.[8] The occurrence of end-organ malperfusion typically signified complicated dissection.[6] Evidence from the International Registry of Acute Aortic Dissection suggested that patients who died during hospitalisation had a higher incidence of malperfusion complications.[30] Differences in creatinine and renal dialysis status could be attributed to the presence of renal malperfusion. Mesenteric malperfusion was recognised as one of the most severe complications of AD, with elevated liver function test results serving as important indicators. However, our study did not observe differences in AST and ALT, possibly due to the low incidence of mesenteric malperfusion (approximately 4%) and insufficient cases in our sample.[31]

Although our study emphasised the significant correlation between fluid balance and the hospital outcomes of AD patients, we were not able to establish a direct causal relationship between them, as fluid intake and output could serve as markers reflecting the load on the circulatory system. Additionally, we focused solely on the total fluid volume, without analysing the specific components of these fluid intake (eg, parenteral nutrition and vasoactive medications). Moreover, the absence of specialised descriptions for aortic dissection (eg, Stanford classification and detailed surgery) within the ICD codes further complicated matters.[6] Furthermore, the primary outcome of this study was all-cause mortality, which may not be exclusively caused by AD. These limitations hinder the generalisability of our results to broader clinical scenarios and warrant further validation through well-designed prospective studies.

CONCLUSION

In this study, detailed monitoring data from two recognised ICU databases were collected, and multivariable regressions adjusted for potential confounders were employed. These analyses underscore the critical importance of maintaining a strict fluid balance during the in-patient management of acute AD, emphasising the need to avoid both over-resuscitation and under-resuscitation, beyond the conventional focus on blood pressure and HR management.

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Comm College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Author affiliations
[1]Department of Vascular Surgery, Shanghai Jiao Tong University School of Medicine Affiliated Ninth People's Hospital, Shanghai, China
[2]Department of Economics, University of Waterloo, Waterloo, Ontario, Canada
[3]Big Data Research Lab, University of Waterloo, Waterloo, Ontario, Canada
[4]Department of Anthropology, Economics and Political Science, MacEwan University, Edmonton, Alberta, Canada
[5]Senior Research Fellow, Labor and Worklife Program, Harvard University, Cambridge, Massachusetts, USA

Acknowledgements We express our gratitude to all the individuals, including both healthcare professionals and patients, who have contributed to the MIMIC-IV and eICU databases.

Contributors JL: Methodology, Software, Formal analysis, Writing—Original Draft, Visualisation. ZZ: Methodology, Software, Formal analysis, Writing—Original Draft. YL: Software, Formal analysis, Validation, Writing—Original Draft. ZW: Data Curation, Writing—Review and Editing. HP: Software, Validation, Writing—Review and Editing. ZX: Software, Visualisation, Writing—Review and Editing. XY: Software, Writing —Review and Editing. PQ: Conceptualisation, Writing—Review and Editing, Funding acquisition. TC: Conceptualisation, Methodology, Validation, Writing—Review and Editing. XL (guarantor): Conceptualisation, Supervision, Writing—Review and Editing, Funding acquisition.

Funding This work was supported by these funding as follows: the National Natural Science Foundation of China [Nos. 82170509, 82170411, 82300540], Clinical Research Program of 9th People's Hospital [JYLJ202010, JYLJ202204], Translational Medicine Science and Technology Infrastructure Opening Project [TMSK-2021-121], Shanghai Science and Technology Innovation Action Plan [20Y11909600, 21S31904300], Shanghai Municipal Health Bureau Project [202040434, 20224Y0170, 202240145], Fundamental research program of 9th People's Hospital [JYZZ153, JYZZ170, JYYC004, JYLJ202204], Shanghai 9th People's Hospital Nursing Fund Project [JYHL20213D07] and the Fundamental Research Funds for the Central Universities [KLSB2023KF-04]. The funding sources had no involvement in study design, data collection, analysis and interpretation, writing of the report and the decision to submit the article for publication. The National Natural Science Foundation of China [Grant No. 82300540], under the administration of Dr. Peng Qiu, are added and will be allocated to cover the article processing charges (APC) for this publication.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants, but the Ethics Committee of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine exempted ethics approval for this study because patients were drawn from two public databases. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Data are available upon reasonable request. The two public databases were available in PhysioNet for CITI Program credentialed researchers with signed data use agreement (https://physionet.org/content/mimiciv/2.0/;https://physionet.org/content/eicu-crd/2.0/). The codes for data extraction and analyses were available from the corresponding authors upon reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iD
Xinwu Lu http://orcid.org/0000-0001-6503-5210

REFERENCES

1 Melvinsdottir IH, Lund SH, Agnarsson BA, *et al*. The incidence and mortality of acute thoracic aortic dissection: results from a whole nation study. *Eur J Cardiothorac Surg* 2016;50:1111–7.
2 Lee J, de Louw E, Niemi M, *et al*. Association between fluid balance and survival in critically ill patients. *J Intern Med* 2015;277:468–77.
3 Monnet X, Lai C, Teboul JL. How I personalize fluid therapy in septic shock? *Crit Care* 2023;27:123.
4 Mentz RJ, Stevens SR, DeVore AD, *et al*. Decongestion strategies and renin-angiotensin-aldosterone system activation in acute heart failure. *JACC Heart Fail* 2015;3:97–107.
5 Hoeper MM, Benza RL, Corris P, *et al*. Intensive care, right ventricular support and lung transplantation in patients with pulmonary hypertension. *Eur Respir J* 2019;53:1801906.
6 Lombardi JV, Hughes GC, Appoo JJ, *et al*. Society for Vascular Surgery (SVS) and Society of Thoracic Surgeons (STS) reporting standards for type B aortic dissections. *J Vasc Surg* 2020;71:723–47.
7 Erbel R, Aboyans V, Boileau C, *et al*. 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. *Task Force Diagn Treat Aortic Dis Eur Soc Cardiol (ESC) Eur Heart J* 2014;35:2873–926.
8 Isselbacher EM, Preventza O, Hamilton Black J 3rd, *et al*. 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation* 2022;146:e334–482.
9 Evangelista A, Isselbacher EM, Bossone E, *et al*. Insights From the International Registry of Acute Aortic Dissection: A 20-Year Experience of Collaborative Clinical Research. *Circulation* 2018;137:1846–60.
10 Trimarchi S, Mandigers TJ, Bissacco D, *et al*. Twenty-five years of observations from the International Registry of Acute Aortic Dissection (IRAD) and its impact on the cardiovascular scientific community. *J Thorac Cardiovasc Surg* 2024;168:977–89.
11 Johnson AEW, Bulgarelli L, Shen L, *et al*. MIMIC-IV, a freely accessible electronic health record dataset. *Sci Data* 2023;10:1.
12 Johnson A, Bulgarelli L, Pollard T, *et al*. MIMICIV (version 2.0). PhysioNet; 2022. Available: https://doi.org/10.13026/7vcr-e114 [Accessed 8 Feb 2023].
13 Pollard TJ, Johnson AEW, Raffa JD, *et al*. The eICU Collaborative Research Database, a freely available multi-center database for critical care research. *Sci Data* 2018;5:180178.
14 Pollard T, Johnson A, Raffa J, *et al*. EICU collaborative research database (version 2.0). PhysioNet; 2019. Available: https://doi.org/10.13026/C2WM1R [Accessed 8 Feb 2023].
15 Goldberger AL, Amaral LA, Glass L, *et al*. PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals. *Circulation* 2000;101:E215–20.
16 Goldstein BA, Chang TI, Winkelmayer WC. Classifying individuals based on a densely captured sequence of vital signs: An example using repeated blood pressure measurements during hemodialysis treatment. *J Biomed Inform* 2015;57:219–24.
17 Hosseini-Nasab M, Mirzaei K Z. Functional analysis of glaucoma data. *Stat Med* 2014;33:2077–102.
18 Qiu P, Li Y, Liu K, *et al*. Prescreening and treatment of aortic dissection through an analysis of infinite-dimension data. *BioData Min* 2021;14:24.
19 Wu Z, Li Y, Qiu P, *et al*. Prognostic Impact of Blood Pressure Change Patterns on Patients With Aortic Dissection After Admission. *Front Cardiovasc Med* 2022;9:832770.
20 Liu H, Shi L, Zeng T, *et al*. Type 2 diabetes mellitus reduces clinical complications and mortality in Stanford type B aortic dissection after thoracic endovascular aortic repair: A 3-year follow-up study. *Life Sci (1962)* 2019;230:104–10.
21 Obel LM, Lindholt JS, Lasota AN, *et al*. Clinical Characteristics, Incidences, and Mortality Rates for Type A and B Aortic Dissections: A Nationwide Danish Population-Based Cohort Study From 1996 to 2016. *Circulation* 2022;146:1903–17.
22 Corrêa TD, Vuda M, Takala J, *et al*. Increasing mean arterial blood pressure in sepsis: effects on fluid balance, vasopressor load and renal function. *Crit Care* 2013;17:R21.

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Community College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

23 Guarracino F, Bertini P, Pinsky MR. Cardiovascular determinants of resuscitation from sepsis and septic shock. *Crit Care* 2019;23:118.
24 Zhou X, Pan W, Chen B, *et al*. Predictive performance of dynamic arterial elastance for arterial pressure response to fluid expansion in mechanically ventilated hypotensive adults: a systematic review and meta-analysis of observational studies. *Ann Intensive Care* 2021;11:119.
25 Hiratzka LF, Bakris GL, Beckman JA, *et al*. 2010 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. *Circulation* 2010;121:e266–369.
26 Chen S-W, Chan Y-H, Lin C-P, *et al*. Association of Long-term Use of Antihypertensive Medications With Late Outcomes Among Patients With Aortic Dissection. *JAMA Netw Open* 2021;4:e210469.
27 Suzuki T, Isselbacher EM, Nienaber CA, *et al*. Type-selective benefits of medications in treatment of acute aortic dissection (from the International Registry of Acute Aortic Dissection [IRAD]). *Am J Cardiol* 2012;109:122–7.
28 Jessup M, Marwick TH, Ponikowski P, *et al*. 2016 ESC and ACC/AHA/HFSA heart failure guideline update - what is new and why is it important? *Nat Rev Cardiol* 2016;13:623–8.
29 van der Meer P, Gaggin HK, Dec GW. ACC/AHA Versus ESC Guidelines on Heart Failure: JACC Guideline Comparison. *J Am Coll Cardiol* 2019;73:2756–68.
30 Berretta P, Trimarchi S, Patel HJ, *et al*. Malperfusion syndromes in type A aortic dissection: what we have learned from IRAD. *J Vis Surg* 2018;4:65.
31 Di Eusanio M, Trimarchi S, Patel HJ, *et al*. Clinical presentation, management, and short-term outcome of patients with type A acute dissection complicated by mesenteric malperfusion: observations from the International Registry of Acute Aortic Dissection. *J Thorac Cardiovasc Surg* 2013;145:385–90.

BMJ Open: first published as 10.1136/bmjopen-2024-083933 on 8 February 2025. Downloaded from http://bmjopen.bmj.com/ on February 17, 2026 at Grant Macewan Comm College City Centre Campus . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.