

Supplementary Appendix

The authors have provided this appendix to give readers additional information on their work.

Supplementary Methods

Systematic Literature review

We performed a systematic literature review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, in line with the protocol approved by the authors¹. We summarized all published original articles, including patients with AAD type A. Two independent reviewers (GL and APE) identified all eligible articles by searching within the MEDLINE bibliographical database. Reference lists were systematically examined for the presence of relevant articles with the use of the “snowball” approach. Eligible studies were: 1) published in English, 2) retrospective clinical trials, 3) prospective clinical studies, and 4) registries. The excluded studies met the following criteria: 1) not published in English, 2) reviews and meta-analyses, 3) editorials, perspectives, and letters to the editor, 4) papers irrelevant to AAD type A.

We performed a MEDLINE search for records through Jan 2020, according to the PRISMA statement using the keyword “aortic dissection” to search all published studies on acute aortic dissection (AAD) that provided incidence, treatment strategy, or outcomes. The used algorithm for the literature search was: “(Aortic disease OR Acute aortic dissection) AND type A”. Studies were included in the systematic review if they met the following prespecified criteria: 1) published in English, 2) retrospective clinical studies 3) prospective clinical

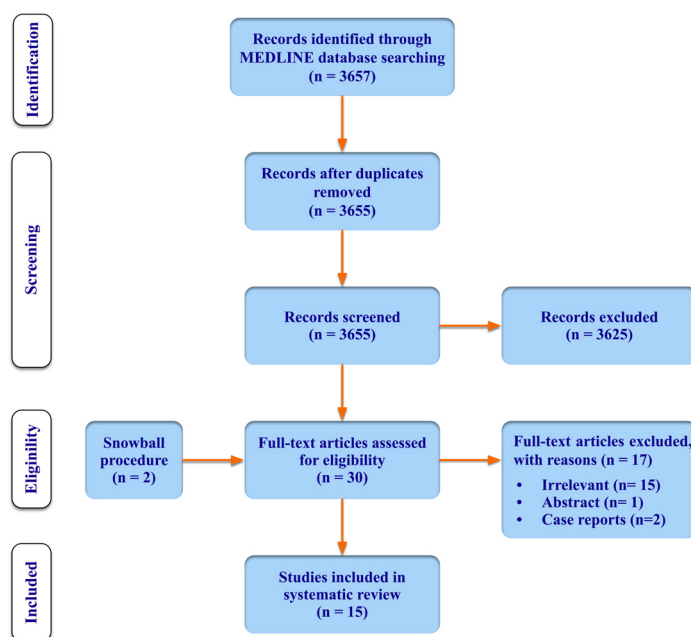
studies, and 4) registries. Excluded studies met at least one of the following criteria: 1) not published in English, 2) reviews and meta-analyses, 3) editorials, perspectives, and letters to the editor, 4) papers irrelevant to AAD type A.

Data Extraction and Tabulation

Standardized, pre-piloted forms were used for data extraction and tabulation. Data extraction was performed by two independent reviewers (GL and APE), and any discrepancies were identified and resolved through quality control discussions with another author (ST) whenever necessary.

Statistical Analysis

Continuous variables were summarized as means and standard deviations (SD) or when data followed a skewed distribution as medians and interquartile ranges (IQR). Categorical variables were summarized as frequencies and percentages accompanied by 95 % confidence intervals (95 % CI). When continuous data were presented as medians and range, we applied the Hozo et al² method to estimate the respective means and SDs. If the medians and interquartile ranges or mean and 95 % CI were reported within reviewed papers, we converted them to means and SDs according to the Cochrane Handbook³. All relative rates were estimated based on available data for each variable of interest, and available data were han-



Supplemental Figure 1: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the search strategy.

dled according to the principles stated in the Cochrane Handbook³. Data on outcomes of interest were tabulated and analyzed cumulatively. All relative rates were estimated based on available data for each variable of interest. Data analyses were performed with IBM SPSS Statistics 25 software (IBM Corp., Armonk, NY, USA).

Supplementary Results

The primary literature search yielded 3,657 potentially relevant articles. After the title/abstract screening, 30 articles were retrieved for full-text evaluation (Supplemental Figure 1). Two additional studies were identified through snowball methodology. Overall, 15 studies fulfilled the pre-determined inclusion criteria and were included in this systematic review⁴⁻¹⁸. The characteristics of enrolled patients are summarized in Supplementary Table 1. The 15 studies reported data on a total of 31,160 patients. 80.3 % (n =25,037/31,160) of them had been treated surgically, while only 16.9 % (n =5,255/31,160) had been treated conservatively. The rest, 2.8 % (n =877/31160) of patients, were managed either with unknown strategies or with a combination of strategies. The in-hospital mortality of the general population was 18.9 % (n =5,775/30,590), while for the surgically and conservatively treated was 11.03 % (n =2,717/24,620), and 37.8 % (n =1,910/5,062), respectively. The 5-year survival rate was 61.5 % (n =1,770/2,878) of patients, independently of the treatment strategy. Yet, the 5-year survival of surgically treated patients was 72.1 % (n =1,780/2,470).

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Supplementary Table 1: Characteristics of published clinical studies and registries with AAD type A patients.

Author & year	Study Design	Period	Country	N of pts	Age	Onset-admission time, h, median (IQR)	Management	CNS deficit†, %	Follow-up, y	Early Mortality, %	5-year Survival, %
Wu 2019 ⁽⁵⁾	ROS	2011-2017	China	911	48.67 (11.3)	1.2 (1.0-3.0)	911 Surg	5	NA	11.6	79.0
Inoue 2020 ⁽¹¹⁾ -JRAD Registry	ROS	2011-2016	Japan	1217	67.9 (13.1)	3.3 (range: 0-283)	916 Surg 301 Med	18.9	1.5	11.6	NA
Chen 2019 ⁽¹⁴⁾	ROS	2004-2012	Taiwan	40	61.2 (12.9)	NA	18 Surg 22 Med	NA	10	7.5	72.5
Yamaguchi 2019 ⁽⁴⁾ -JROAD-DPC Registry	ROS	2012-2015	Japan	10131	69.8 (13.5)	NA	6682 Surg 61 TEVAR 45 Surg & TEVAR 3343 Med	NA	NA	24.3	NA
Wen 2019 ⁽⁶⁾	ROS	2012-2016	China	264	47.75 (9.98)	NA	NA	NA	NA	17.1	NA
Huang 2019 ⁽¹²⁾	ROS	2006-2008	China	570	46.9 (12.0)	NA	399 Surg 171 Med	NA	2.2	NA	63.9
Bashir 2019 ⁽¹⁵⁾ -NACSA Registry	POS	2007-2013	UK	507	75.3 (3.7)	NA	NA	11	5.0	22.5	55.0
Ahn 2019 ⁽¹⁶⁾ -ASAN-AAS Registry	ROS	1993-2015	Korea	394	56.5 (14.1)	NA	351 Surg 43 Med	NA	8.5	15.0	18.5
Ahlsson 2019 ⁽¹⁷⁾ -NORCAAD Registry	ROS	2005-2014	Sweden, Finland, Iceland, Denmark	1159	61.6 (12.2)	NA	1159 Surg	4.1	NA	18.0	NA
Abe 2019 ⁽¹⁸⁾ -JCVSD Registry	ROS	2000-2015	Japan	11843	68.7 (12.7)	NA	11843 Surg	10.9	NA	7.6	NA
McClure 2018 ⁽⁹⁾ – several databases	ROS	2002-2014	Canada	2289	68 (15.2)	NA	1204 Surg 1085 Med	NA	12.0	53.0	65.5*
Evangelista 2018 ⁽¹³⁾ -RESA-II Registry	ROS	2012-2014	Spain	443	64.6 (14.2)	NA	347 Surg 96 Med	8.4	NA	34.5	NA
Melvinsdottir 2016 ⁽⁸⁾	ROS	1992-2013	Iceland	101	65.6 (15.0)	NA	76 Surg 34 Med	8.0	20.0	56.4	33.6
Kimura 2011 ⁽¹⁰⁾	ROS		Japan	355	63 (12.1)		355 Surg	15.5	4.8	9.3	76.5
Trimarchi 2010 ⁽⁷⁾ -IRAD Registry	POS & ROS	1996-2004	IRAD	936	NA	NA	776 Surg 160 Med	NA	NA	29.9	NA

AAD: Acute Aortic Dissection, Surg: Surgical, Med: Medication, pts: patients, TEVAR: Thoracic Endovascular Aortic Repair, ROS: Retrospective Observational Study, POS: Prospective Observational Study, JRAD: Japan Registry Of Aortic Dissection, JROAD-DPC: Japanese Registry of All Cardiac and Vascular Diseases-Diagnostic Procedure Combination Database, AAS: Acute Aortic Syndrome, NORCAAD: Nordic Consortium for Acute Type A Aortic Dissection registry, JCVSD: Japan Cardiovascular Surgery Database, RESA-II: Spanish Registry of Acute Aortic Syndrome, IRAD: International Registry of Acute Aortic Dissection, NACSA: National Adult Cardiac Surgery Audit, NA: Not Available, d: days, y: years, IQR: Interquartile Range.

† CNS deficit is expressed as Stroke or TIA due to the AAD, *Mortality is expressed only in Surgically managed patients