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1 Burden and causes of readmissions following initial discharge after aortic syndromes

Mario D’Oria¹, Indrani Sen¹, Courtney N. Day², Jay Mandrekar², Salome Weiss³, Thomas C.
Bower¹, Gustavo S. Oderich¹, Philip P. Goodney⁴, Randall R DeMartino¹

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3 ¹Division of Vascular and Endovascular Surgery, Gonda Vascular Center, Mayo Clinic,
4 Rochester MN

5 ²Department of Health Sciences Research, Mayo Clinic, Rochester MN

6 ³Department of Cardiovascular Surgery, Bern University Hospital, University of Bern,
7 Switzerland

8 ⁴Section of Vascular Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, NH

9

10 **Corresponding author**

11 Randall R DeMartino, MD, MS

12 Email address: DeMartino.Randall@mayo.edu

13 Physical address: Division of Vascular and Endovascular Surgery – Gonda Vascular Center –
14 200 1st Street SW – Rochester MN 55905 – USA

15

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3 None.

4

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2 Article Highlights

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4 Type of research

5 Retrospective, population-based study.

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7 Key findings

8 Out of a total of 117 patients with diagnosis of aortic syndrome (AS) who survived the index
9 event, 79 patients (68%) experienced at least one readmission following initial discharge. The
10 median time to first any-cause, cardiovascular and aortic readmission was 143, 861 and 171
11 days, respectively. The cumulative incidence of any-cause readmissions at 2, 4 and 10 years was
12 45%, 55% and 69%, respectively. The cumulative incidence of cardiovascular readmissions at 2,
13 4 and 10 years was 15%, 20% and 28%, respectively. The cumulative incidence of aortic
14 readmissions at 2, 4 and 10 years was 38%, 46% and 59%, respectively.

15

16 Take-home message

17 Readmissions following initial discharge after diagnosis of AS are common and not different
18 across specific disease types. While aortic-related rehospitalization occur in more than half of
19 patients but tend to be earlier, cardiovascular-related rehospitalizations tend to happen later in
20 about one third of subjects.

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3 Table of Contents Summary

4 In a population-based study of patients with diagnosis of aortic syndrome (AS), readmissions
5 following initial discharge after diagnosis of AS are common and not different across specific
6 disease types. While aortic-related rehospitalization occur in more than half of patients but tend
7 to be earlier, cardiovascular-related rehospitalizations tend to happen later in about one third of
8 subjects. This may suggest the need for early follow-up focused on aortic complications while
9 later follow-up should address cardiovascular events.

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3 **Abstract**

4

5 **Introduction**

6 Aortic syndromes (AS), including aortic dissection (AD), intramural hematoma (IMH), and
7 penetrating aortic ulcer (PAU), carry significant morbidity and mortality; little data exist
8 regarding burden and causes of related rehospitalizations following initial discharge.

9

10 **Methods**

11 The study was conducted using the Rochester Epidemiology Project (REP). All adult residents
12 (age \geq 18 years) with an incident diagnosis of AD/IMH/PAU (1995-2015) were identified from
13 the REP using the International Classification of Disease (ICD), 9th and 10th revision, codes and
14 Hospital Adaptation of the ICD, 2nd edition, codes. Assessment of any-cause
15 (aortic+cardiovascular), aortic-related, or cardiovascular-related readmissions was determined
16 following date of hospital discharge or diagnosis date (i.e. the index event).

17

18 **Results**

1 A total of 117 patients out of 130 cases of AD/IMH/PAU included in the initial study population
2 survived the index event and were evaluated. The median age of diagnosis was 74 years and 70
3 (60%) were male. A total of 79 patients (68%) experienced at least one readmission. The median
4 time to first any-cause, cardiovascular and aortic readmission was 143, 861 and 171 days,
5 respectively. The cumulative incidence of any-cause readmissions at 2, 4 and 10 years was 45%,
6 55% and 69%, respectively. The cumulative incidence of cardiovascular readmissions at 2, 4 and
7 10 years was 15%, 20% and 28%, respectively. The cumulative incidence of aortic readmissions
8 at 2, 4 and 10 years was 38%, 46% and 59%, respectively. Overall survival for the entire cohort
9 at 2, 4 and 10 years was 84%, 75% and 50%, respectively.

10

11 **Conclusion**

12 Readmissions following initial discharge after diagnosis of AS are common and not different
13 across specific disease types. While aortic-related rehospitalization occur in more than half of
14 patients but tend to be earlier, cardiovascular-related rehospitalizations tend to happen later in
15 about one third of subjects. This may suggest the need for early follow-up focused on aortic
16 complications while later follow-up should address cardiovascular events.

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18 **Keywords**

19 Aortic syndrome; Readmissions: Epidemiology; Population-based.

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3 **Introduction**

4 Aortic syndromes (AS), which include aortic dissection (AD), intramural hematoma (IMH), and
5 penetrating aortic ulcer (PAU) are uncommon aortic pathologies with an incidence of 7.7 per
6 100,000 person-years¹. Although rare, they are associated with significant aortic and
7 cardiovascular morbidity and mortality². Depending on the location and type of AS, acute
8 management may be surgical, endovascular or medical. Following the acute management,
9 lifelong surveillance is advocated since secondary aortic procedures are common over time,
10 especially after aortic dissection. However, there is a paucity of data regarding burden and causes
11 of hospitalizations following initial diagnosis of these pathologies. Previous work has shown
12 mortality rate after AS diagnosis has remained relatively similar over the past several decades.
13 Additionally, over 60% of deaths are attributable to cardiac or aortic causes. To improve the
14 longitudinal care of patients with AS, understanding the cause for recurrent hospitalizations may
15 identify patterns and etiologies for targeted intervention. Thus, the study aim was to evaluate the
16 burden and pattern of readmissions following an initial diagnosis of AS using a population-based
17 approach.

18

19 **Methods**

20 *Study design*

21 The present study was part of a retrospective, population-based study aimed to assess AS
22 (AD/IMH/PAU) in Olmsted County, Minnesota (MN). The study was conducted using the

1 Rochester Epidemiology Project (REP), a medical record linkage system that includes virtually
2 all residents and local health care providers in Olmsted County, MN. Because of the unique
3 isolated nature of the region and few providers, billing data on all medical services are collated
4 through the REP^{3,4}. This enables identification of incident diagnosis of medical conditions and
5 permits review of treatments, evaluations, autopsy reports, and death certificates for decedents.
6 The Mayo Clinic and Olmsted Medical Center Institutional Review Boards approved this study
7 and granted a consent waiver for minimal risk. In addition, per Minnesota statutes, each patient
8 identified with AS had provided authorization for the use of their medical record for research. No
9 patients with AS were excluded because of lack of research authorization.

10

11 *Cohort identification*

12 Cohort identification has been previously described¹. Briefly, all adult residents (age \geq 18 years)
13 with an incident diagnosis of AD/IMH/PAU over two decades (1995 - 2015) were identified
14 from the REP using the International Classification of Disease (ICD), 9th and 10th revision,
15 codes and Hospital Adaptation of the International Classification of Diseases, 2nd edition, codes.
16 To be included in the study, the diagnosis must be confirmed by imaging or, for immediate
17 decedents, AS had to have been confirmed by autopsy or be listed on the death certificate as the
18 main/primary diagnosis. AD/IMH/PAU were defined using current clinical practice guidelines⁵.
19 All identified pathologies that met the inclusion criteria were evaluated regardless of the acuity
20 of presentation. The AS was defined as acute if diagnosed and/or treated within 14 days of the
21 onset of symptoms. Thereafter, it was defined as sub-acute between 2 weeks and 3 months, and
22 chronic after 3 months.

1 For the present study only the patients surviving the index event/hospitalization were included.
2 Comorbidities and medical events known before the index AS event were considered pre-
3 existing, and subsequent events were defined as the outcome events. For assessment of
4 comorbidities, the Charlson Comorbidity Index (CCI) was implemented⁶. For identification of
5 the CCI comorbidities, the ICD and Hospital Adaptation of the International Classification of
6 Diseases diagnostic codes were used. To be assigned as a comorbidity, two instances of the
7 predefined code(s) within 5 years before the AS diagnosis date were necessary, as described in
8 prior publications⁷. Censoring of all patients was done on March 31, 2019.

9

10 *Events appraisal*

11 Events (readmissions and mortality) assessment was done through two mechanisms. First, the
12 REP data sources were queried for mortality status (with death certificates reviewed for cause)
13 and readmissions. Second, vital status and death date information was queried using an
14 institutionally approved fee-based Internet research location service (Accurint, accurint.com) to
15 ensure that vital status was complete for all included subjects. If death occurred outside
16 Minnesota, death certificates were retrieved as permissible by the vital records statutes within the
17 state in which the decedent passed away. Events were classified as aortic (because of new-onset
18 acute complications from AS or need for secondary treatment of AS-related complications either
19 planned or not), cardiovascular (myocardial infarction MI, new-onset congestive heart failure
20 CHF, new-onset atrial fibrillation AF, stroke, deep venous thrombosis/pulmonary embolism
21 DVT/PE or cardiac arrest), or because of other reasons. In the case of acute thoracic pain leading
22 to hospitalization, the event was classified as aortic if appropriate diagnostic tests ruled out
23 cardiovascular events as above defined without any further evidence for alternate cause.

1 Assessment of any-cause (aortic and cardiovascular), aortic-related, or cardiovascular-related
2 readmissions was determined following date of hospital discharge or diagnosis date (i.e. the
3 index event).

4

5 *Statistical analysis*

6 Baseline characteristics were assessed overall with categorical data reported as number and
7 percentage while continuous data was reported as median and IQR. In the time-to-event
8 analyses, only the first readmission was considered. The cumulative incidence of readmissions
9 was estimated while considering the competing risk of death. Discharge date or diagnosis date
10 for those not admitted to hospital was considered as time 0. Analysis was conducted at 30 days,
11 90 days and 1 year. Trends in readmission (total number of readmission per year/total number of
12 patients eligible per year) was assessed using univariate linear regression. Frequency of
13 readmissions was grouped by patient's diagnosis year (i.e. time 0); if there was either death in
14 first year or less than 1 year of follow-up, patient's readmissions were not included. Factors
15 associated with readmissions were assessed using univariate Cox proportional hazard regression.
16 Covariates for the models were entered before analysis, with only those considered to be most
17 relevant based on current literature included (age, gender, type of AS, acuity of disease, Charlson
18 Comorbidity Index CCI, previous cerebrovascular disease, initial management, in-hospital
19 complications). Two, four, and ten-year survival was estimated using the Kaplan-Meier method.
20 All statistical analyses were performed with the SAS statistical software (SAS 9.4, SAS Institute,
21 Cary, NC, USA). A 2-sided P-value <0.05 was considered statistically significant.

22

23 **Results**

1 *Study cohort*

2 A total of 117 patients out of 130 included in the initial study population survived the index AS
3 event and were included into the study. The median age of diagnosis was 74 years (IQR 61-80,
4 range 28-93) and 70 (60%) were male (**Table 1**). Overall, AD was identified in 65 (56%),
5 followed by PAU in 32 (27%) and IMH in 20 (17%). The median CCI for the entire cohort was 2
6 (IQR1-4, range 0-11) and the initial management was medical in 85 (73%).

8 *Number, causes, and frequency of readmissions*

9 A total of 79 patients (68%) experienced at least one readmission with a median time to first any-
10 cause readmission of 143 days (IQR 15-1244, range 1-5664). The percentage of the cohort
11 experiencing first any-cause readmission at 30 days, 90 days and 1 year was 26%, 32% and 41%,
12 respectively. Pain and complications (from disease or treatment) were the main causes for
13 readmission at 30 and 90 days (**Table 2 & Appendix Table 1**). A cardiovascular readmission
14 was noted in 37 patients (32% of the entire cohort) with a median time to first cardiovascular
15 readmission of 861 days (IQR 111-3006, range 1-5664). The percentage of the cohort
16 experiencing first cardiovascular readmission at 30 days, 90 days and 1 year was 2%, 8% and
17 14%, respectively. An aortic readmission was noted in 66 patients (56% of the entire cohort)
18 with a median time to first aortic readmission of 171 days (IQR 15-1213, range 1-5686). The
19 percentage of the cohort experiencing first aortic readmission at 30 days, 90 days and 1 year was
20 22%, 26% and 33%, respectively. Frequency of readmissions is reported in **Table 3**. Analysis of
21 trends in readmissions showed that during the study period there was no significant decrease in
22 the median number of overall readmissions (-0.04 per year, SE 0.03, p=.28), cardiovascular

1 readmissions (-0.02 per year, SE 0.02, $p=.27$), or aortic readmissions (-0.015 per year, SE 0.03,
2 $p=.64$).

3

4 *Cumulative incidence of readmissions*

5 With death as competing risk, the cumulative incidence of any-cause readmissions at 2, 4 and 10
6 years was 45% (95%CI 36-55), 55% (95%CI 46-65) and 69% (95%CI 60-79), respectively
7 (**Figure 1**). The cumulative incidence of cardiovascular readmissions at 2, 4 and 10 years was
8 15% (95%CI 10-23), 20% (95%CI 14-29) and 28% (95%CI 20-38), respectively (**Figure 2**). The
9 cumulative incidence of aortic readmissions at 2, 4 and 10 years was 38% (95%CI 30-48), 46%
10 (95%CI 37-56) and 59% (95%CI 50-69), respectively (**Figure 3**).

11

12 *Factors associated with readmissions*

13 Univariate Cox Proportional Hazard showed that in-hospital complications were associated with
14 both any-cause readmissions (HR 2.0, 95%CI 1.2, 3.2, $p=.007$) and aortic readmissions (HR 1.9,
15 95%CI 1.1, 3.2, $p=.02$), but not for cardiovascular readmissions (HR 1.5, 95%CI 0.7, 3.0, $p=.30$)
16 (**Appendix Table 2**). Similarly, initial management ($p=.04$) was associated with any-cause
17 readmissions (Open: HR 1.9, 95%CI 1.2, 3.0, $p=.01$ and Endo: 1.7, 95%CI 0.4, 6.9, $p=.48$, each
18 vs. Medical) and aortic readmissions ($p=.01$) (Open: HR 2.2, 95%CI 1.3, 3.6, $p=.003$ and Endo:
19 HR 2.1, 95%CI 0.5, 8.9, $p=0.30$), but not for cardiovascular readmissions ($p=0.31$). Conversely,
20 CCI was associated with cardiovascular readmissions (HR 1.2, 95%CI 1.1, 1.3, $p=.004$), but not
21 for any-cause readmissions (HR 1.0, 95%CI 0.9, 1.1, $p=.68$) or aortic readmissions (HR 1.0,

1 95%CI 0.9, 1.1, $p=.71$). Type of AS and acuity of disease (at index presentation) were not
2 significantly associated with any-cause, cardiovascular or aortic readmissions.

3

4 *Overall survival*

5 Overall survival for the entire cohort at 2, 4 and 10 years was 84% (95%CI 77, 91), 75% (95%CI
6 67, 83) and 50% (95%CI 40, 62), respectively (**Supplementary Figure 1**). Univariate Cox
7 Proportional Hazards showed that age (HR 1.7, 95%CI 1.3, 2.2, $p<.001$), CCI (HR 1.1, 95%CI
8 1.0, 1.2, $p=.02$), and CVD (HR 2.17, 95%CI 1.22, 3.87; $p=.008$). were associated with death
9 (**Appendix Table 3**).

10

11 **Discussion**

12 Despite the advancement in medical and surgical management of aortic disease, AS (including
13 AD, IMH and PAU) still carry a significant risk of early and long-term morbidity and mortality,
14 which has remained substantially unchanged over the last 20 years⁴. They require lifelong
15 clinical and imaging surveillance to detect secondary adverse events and address subsequent
16 reinterventions during follow-up. Thus, rehospitalizations following initial discharge are a
17 common event during the lifespan of AS patients and represent a significant cost for both
18 patients and society. However, detailed data on the causes and burden of readmissions are
19 lacking but will potentially highlight ways to improve the longitudinal care of this patients'
20 group.

1 In this contemporary population-based assessment, we examined incidences of, reasons for, and
2 factors associated with, readmissions after initial diagnosis of AS or discharge for AS. The
3 following main findings were evident from this study. First, about two third of all patients with
4 AS will experience at least one readmission during follow-up. Second, although readmissions
5 seem to occur relatively early, as indicated by a median time to the first readmission of 143 days,
6 a bimodal pattern appears to exist. Aortic readmissions were more common in the first year of
7 follow-up, while cardiovascular readmissions mostly cumulated during the second year of
8 follow-up. Third, different factors are associated with different types of readmissions, which may
9 inform on how to tailor specific follow-up protocols according to the individual patient's
10 presentation. Taken altogether, these findings would suggest a pattern of early intensive care for
11 aortic complications and later care needs for cardiovascular events. Furthermore, they are similar
12 to those from a recent series at the University of Bologna (Italy) detailing the long-term follow-
13 up of 242 consecutive patients with final diagnosis of acute AS between 2010-2016, which
14 reported that two thirds of these individuals will eventually develop at least one aortic or non-
15 aortic event during long-term follow-up⁸. We believe follow-up should be based on careful
16 multidisciplinary assessment, to be made on a case by case basis, and eventually lead to a
17 patient-tailored protocol encompassing at least the frequency and consistency of imaging (with a
18 balance to be achieved between the need to detect even subtle changes of the disease pattern and
19 the necessity to keep radiation and contrast exposure as low as reasonable), early referral for
20 intervention and strict management of cardiovascular risk factors.

21 In this study, neither type of AS (AD/IMH/PAU) nor acuity of disease were associated with
22 aortic readmissions. Conversely, in-hospital complications and open surgery were significantly
23 associated with their occurrence. These data may be attributable to different plausible causes.

1 First, they could be surrogate markers for more aggressive disease requiring more invasive
2 treatment that lead to increased rate of complications and rehospitalizations. Second, since open
3 surgery is usually reserved for AS involving the ascending aorta and/or aortic arch, this will
4 indicate that, even after successful exclusion of the more proximal disease, AS might not be fully
5 exempt from long-term adverse events. Indeed, a recent Swedish study focusing on long-term
6 survival and frequency of reinterventions of patients undergoing proximal thoracic aortic surgery
7 has showed that while aneurysm surgery normalizes mortality (in comparison with age-matched
8 and sex-matched peers), dissection surgery still carries a high long-term mortality rate caused by
9 disease progression⁹. These findings emphasize the need for close post-operative monitoring of
10 AS patients to promptly address potential complications.

11 In our cohort, the cause for first readmission within 90 days was aneurysmal
12 degeneration/expansion in 9%, rupture in 6% and planned intervention in 3%. Although difficult
13 to ascertain, these data seem concordant with the existing evidence that incidence of
14 reintervention after thoracic endovascular aortic repair (TEVAR) for AD is relatively high during
15 midterm follow-up (mean rate of 15% at 3 years), with the three most common reasons for
16 reintervention being endoleaks, false lumen perfusion (with/without aortic dilation), and new
17 dissection^{10, 11}. In fact, TEVAR has become the mainstay of treatment for AS involving the
18 descending aorta in the presence of anatomic and/or clinical complications, mainly because of
19 the early surgical benefit¹². Furthermore, a recent statewide study from the California Office of
20 Statewide Hospital Planning Development database reporting outcomes after acute
21 uncomplicated type B AD (9.165 cases, mean age 66 years, 39% female) would suggest an
22 independent survival benefit for TEVAR over medical therapy¹³, a finding which may support a
23 paradigm shift towards more aggressive management of acute type B AD even in the absence of

1 frank complications. However, TEVAR might not be able to prevent all aortic events during
2 follow-up as indicated from the INSTEAD trial data¹⁴ with subsequent consensus document¹⁵
3 and further confirmed by a recent systematic review¹⁶. Thus, a more in-depth evaluation of the
4 anatomy and physiology of patients with and without aortic degeneration might provide helpful
5 data to assist with patients' selection, techniques implementation and surveillance strategies that
6 may achieve higher clinical effectiveness and cost effectiveness as compared with "one-fits-all"
7 algorithms¹⁷. Due to the limited number of patients treated with TEVAR over our 20-years
8 review, we cannot comment on the impact TEVAR has for these aortic pathologies nor on the
9 selection of patients' subgroups that might benefit the most from endovascular treatment.

10 As previously demonstrated, patients with AS have a significantly higher risk of non-aortic
11 cardiovascular death and first-time non-fatal cardiovascular events as compared with population
12 referents, a risk which did not seem to decrease even after excluding events occurring during the
13 acute period¹⁸. The findings from the present study further elucidate the timing and likely
14 predisposing factors of these events. Indeed, cardiovascular readmissions were prevalent in the
15 second year of follow-up and were predicted by higher CCI. Thus, it is likely that a greater
16 burden of comorbidities will predispose this patients' group to higher risk of cardiovascular, but
17 not aortic events. This was also expected to some extent, given that when compared with local
18 controls, patients with AS have higher rates of cardiac, vascular and pulmonary disease, and
19 carry a higher comorbidity burden⁴. Our findings further underline the need for measures aimed
20 at reduction of the overall cardiovascular risk in individuals with AD, a need that has been
21 recognized also in recent clinical practice guidelines from the European Society for Vascular
22 Surgery⁵. Among cardiovascular risk factors, hypertension is the most commonly found in
23 patients with AD and IMH, with a prevalence rate up to 80%, and thought to play a role in the

1 development and progression of the disease(s)^{19,20}. However, it has also been showed that AD
2 patients may be poorly compliant with their antihypertensive regimen, and further work to
3 improve medication adherence and to understand its impact on disease progression is vital to
4 deliver the best outcomes for ASs patients²¹.

5 Observations coming from this report must also be examined considering previously reported
6 data from the same cohort. Indeed, we had already observed 5-, 10-, and 15-year survival rates of
7 62%, 43%, and 30%, respectively, with a significantly higher long-term risk of any-cause death
8 for patients with AS compared to population referents even after exclusion of acute deaths⁴. In
9 line with previously reported data²²⁻²⁴, most patients (32%) in our cohort died of aortic causes,
10 while cardiovascular causes were the primary diagnosis of death in 29% of the study subjects.
11 However, further analysis of non-acute deaths only (>2 weeks following the index event),
12 cardiovascular causes were more common than aortic causes in our cohort¹⁸. The findings from
13 this study further strengthen these data, as indicated by the fact that only age at diagnosis and
14 baseline CCI (i.e. baseline comorbidity burden) were independent predictors for death. Although
15 overall management of AS has significantly improved during the last decades, medical therapy
16 and follow-up protocols for AS patients might still not be appropriate or strict enough to prevent
17 the occurrence of aortic and cardiovascular deaths, thereby improving overall life expectancy
18 and need for rehospitalizations. With these data, future work can focus on defining targets to
19 improve the quality of care and prognosis of these complex aortic pathologies.

20 Epidemiologic studies of AS are usually difficult to conduct, as many reports for patients with
21 AS predominantly come from multicenter registries²⁵, claims data^{26,27}, or single-center series²⁸,
22 which might bias the findings as more severe cases are generally referred to specialized centers.
23 Furthermore, as patients follow-up might be undertaken at several locations, this could result in

1 heterogeneous and incomplete data. As a result, these methodologies, although specific may lack
2 sensitivity²⁹. In contrast, our results are strengthened by the fact that, within the United States,
3 the REP provides unmatched conditions for the conduct of population-based research. Because
4 Olmsted County is a relatively isolated geographical area, where all main health care providers
5 in the county are included in the REP, virtually all health care delivered to Olmsted County
6 residents can be reliably and consistently captured. Although Olmsted County displays a
7 predominantly white population, previous REP studies showed high comparability in
8 demographic and ethnic characteristics of the Olmsted County residents with those of Minnesota
9 and the upper Midwest, as well as close mortality rates for Olmsted County and the United States
10 overall³⁰.

11

12 *Study limitations*

13 Some limitations to our study must be acknowledged. First, owing to the relatively small
14 subgroups of IMH and PAU, we may not have had enough power to detect a difference among
15 these groups. We acknowledge that these are three separate but pathophysiological related
16 pathologies. However, the study aim was to obtain a broad assessment on the burden and pattern
17 of readmissions after initial AS diagnosis. Further studies with larger cohorts are warranted to
18 identify specific subgroups of individuals that may warrant tailored protocols for follow-up and
19 intervention. Owing to the retrospective, population-based nature of the research, the patients
20 were managed by several providers and follow-up protocols were not standardized. Therefore, we
21 could not identify specific shortcomings in the medical management of these patients, which
22 should be the object of future research. Also, we acknowledge that the true autopsy rate in
23 Olmsted County is not known, so it is possible that some patients may have died without

1 diagnosis. However, this would only impact incidence and not readmissions (as these patients
2 would have been excluded from the present study). Lastly, our composite definition of aortic or
3 cardiovascular readmissions did not allow us to differentiate the relative strength of single
4 pathological entities.

5

6 **Conclusion**

7 Readmissions following initial discharge after diagnosis of AS are common and not different
8 across specific disease types. While aortic-related rehospitalization occur in more than half of
9 patients but tend to be earlier, cardiovascular-related rehospitalizations tend to happen later in
10 about one third of subjects. This may suggest the need for early follow-up focused on aortic
11 complications while later follow-up should address cardiovascular events.

12

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20

21 Tables

22 Table 1. Baseline demographics and clinical characteristics.

23

1 Table 2. Number of readmissions within 1 year from start (Discharge date or Diagnosis date)

2

3 Table 3. Frequency of readmissions.

4

5 Appendix Table 1. Causes of readmissions.

6

7 Appendix Table 2. Univariate Cox Proportional Hazards Models for Readmissions. A. Any-
8 cause readmissions. B. Cardiovascular readmissions. C. Aortic readmissions.

9

10 Appendix Table 3. Univariate Cox Proportional Hazards Models for Death.

11

12 **Figures**

13 Figure 1. Cumulative Incidence of Any-Cause Readmissions (with Death as a competing risk).

14

15 Figure 2. Cumulative Incidence of Cardiovascular Readmissions (with Death as a competing
16 risk).

17

18 Figure 3. Cumulative Incidence of Aortic Readmissions (with Death as a competing risk).

19

20 Supplementary Figure 1. Kaplan-Meier Estimates for Overall Survival.

Table 1. Baseline demographics and clinical characteristics.

Variable	Total (N=117)
Type of AS	
AD	65 (55.6%)
IMH	20 (17.1%)
PAU	32 (27.4%)
Age at diagnosis	
Median	74.0
Q1, Q3	61.3, 80.3
Range	(27.8-93.4)
Gender	
Male	70 (59.8%)
Female	47 (40.2%)
Acute AS	64 (90.1%)
CCI	
Median	2.0
Q1, Q3	1.0, 4.0
Range	(0.0-11.0)
Previous MI	18 (15.4%)
Previous CHF	22 (18.8%)
Previous PVD	49 (41.9%)
Previous CVD	23 (19.7%)
Previous COPD	29 (24.8%)
Previous DM	21 (17.9%)
Initial management	
Medical	85 (72.6%)

Variable	Total (N=117)
Open	29 (24.8%)
Endovascular	3 (2.6%)

AS: aortic syndrome; AD: aortic dissection; IMH: intramural hematoma; PAU: penetrating aortic ulcer;
CCI: Charlson Comorbidity Index; MI: myocardial infarction; CHD: congestive heart failure; PVD:
peripheral vascular disease; CVD: cerebrovascular disease; COPD: chronic obstructive pulmonary
disease; DM: diabetes mellitus.

Table 2. Number of readmissions within 1 year from start (Discharge date or Diagnosis date).

Readmission Type	# of patients with readmission in 1 year	# of patients with readmission	Among those with readmission in 1 year	Among those with readmission in 1 year	Among those with readmission in 1 year
			Overall	Alive	Death
	N	N	Median (Q1, Q3)	Median (Q1, Q3)	Median (Q1, Q3)
Any	44	78*	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 1.0)
CV	14	37	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	--
Aortic	35	65*	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 1.0)

*1 patient with incomplete 1 year of follow-up

DVT: deep venous thrombosis; PE: pulmonary embolism; CHF: congestive heart failure; CV: cardiovascular.

Appendix Table 1. Causes of readmissions.

	Total (N=117)
ANY READMISSION	
Any readmission	
Yes	79 (67.5%)
Days to 1st any readmission (Among those with any readmission)	
Median	143.0
Q1, Q3	15.0, 1244.0
Range	(0.5-5664.0)
Any 30-day readmission	
Yes	29 (25.7%)
Cause for 30-day any readmission – First Cause (Among those with any readmission within 30 days)	
Pain	12 (46.2%)
Aneurysmal degeneration/expansion	2 (7.6%)
Complication	7 (26.9%)
Rupture	2 (7.7%)
Stroke	1 (3.8%)
DVT/PE	1 (3.8%)
Limb Ischemia	1 (3.8%)
Any 90-day readmission	
Yes	36 (31.9%)
Cause for 90-day Readmission – First Cause (Among those with any readmission within 90 days)	
Pain	12 (36.4%)
Aneurysmal degeneration/expansion	3 (9.0%)
Planned Intervention	1 (3.0%)
Complication	8 (24.2%)
Rupture	2 (6.1%)
New-onset CHF	2 (6.1%)
Stroke	2 (6.1%)
DVT/PE	2 (6.0%)
Limb Ischemia	1 (3.0%)

	Total (N=117)
Any 1-year readmission	
Yes	45 (40.9%)
CV READMISSION	
CV readmission	
Yes	37 (31.6%)
Days to 1st CV readmission (Among those with CV readmission)	
Median	861.0
Q1, Q3	111.0, 3006.0
Range	(0.5-5664.0)
CV 30-day readmission	
Yes	2 (1.8%)
CV 90-day readmission	
Yes	9 (8.3%)
CV 1-year readmission	
Yes	14 (13.6%)
AORTIC READMISSION	
Aortic readmission	
Yes	66 (56.4%)
Days to 1st aortic readmission (Among those with aortic readmission)	
Median	171.0
Q1, Q3	15.0, 1213.0
Range	(0.5-5686.0)
Aortic 30-day readmission	
Yes	25 (22.1%)
Aortic 90-day readmission	
Yes	29 (25.9%)
Aortic 1-year readmission	
Yes	36 (33.0%)

Table 3. Frequency of readmissions.

Year	N	Any Readmission		CV Readmission		Aortic Readmission	
		Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3
1995	4	1.5	0.5, 2.5	0.5	0, 1.5	1.0	0.5, 1.0
1996	6	2.0	1.0, 5.0	0.5	0, 1.0	1.5	0, 3.0
1997	2	0	0, 0	0	0, 0	0	0, 0
1998	7	1.0	0, 5.0	0	0, 0	1.0	0, 1.0
1999	2	1.5	0, 3.0	0.5	0, 1.0	1.0	0, 2.0
2000	3	4.0	1.0, 4.0	0	0, 0	3.0	1.0, 2.0
2001	11	2.0	1.0, 3.0	0	0, 1.0	1.0	1.0, 2.0
2002	9	2.0	1.0, 3.0	0	0, 1.0	1.0	0, 2.0
2003	7	1.0	0, 2.0	1.0	0, 2.0	0	0, 1.0
2004	4	0.5	0, 1.5	0.5	0, 1.0	0	0, 0.5
2005	2	1.0	0, 2.0	0	0, 0	1.0	0, 2.0
2006	8	2.0	0.5, 3.0	0.5	0, 1.0	0.5	0, 2.0
2007	4	2.0	1.0, 3.5	0.5	0, 1.0	1.5	0.5, 3.0
2008	2	1.0	0, 2.0	0	0, 0	1.0	0, 2.0
2009	3	0	0, 1.0	0	0, 0	0	0, 1.0
2010	7	1.0	0, 6.0	0	0, 1.0	1.0	0, 5.0
2011	4	0.5	0, 1.0	0	0, 0	0.5	0, 1.0
2012	7	1.0	1.0, 6.0	0	0, 1.0	1.0	1.0, 2.0
2013	6	0	0, 1.0	0	0, 0	0	0, 0
2014	5	1.0	0, 1.0	0	0, 1.0	0	0, 1.0
2015*	0						

*all patients in 2015 did not have enough follow-up to be considered

Appendix Table 2. Univariate Cox Proportional Hazards Models for Readmissions.**A. Any-Cause Readmission**

Variable	HR (95% CI)	p-value
Type of AS		Overall p=0.238
AD	1.0 reference	
IMH	1.33 (0.73, 2.44)	0.349
PAU	0.74 (0.43, 1.26)	0.264
Age at diagnosis (per 10 years)	1.02 (0.87, 1.20)	0.805
Gender		0.801
Male	1.06 (0.67, 1.68)	
Female	1.0 reference	
Acuity of disease		Overall p=0.640
Acute	1.0 reference	
Subacute	1.56 (0.48, 5.11)	0.461
Chronic	0.67 (0.16, 2.78)	0.581
CCI	1.02 (0.94, 1.10)	0.677
CVD		0.238
No	1.0 reference	
Yes	1.38 (0.81, 2.34)	
Initial Management		Overall p=0.039
Medical	1.0 reference	
Open	1.85 (1.15, 3.0)	0.012
Endovascular	1.68 (0.41, 6.93)	0.476
In-Hospital Complications		0.007
None	1.0 reference	
Any Complication	1.96 (1.20, 3.21)	

Median Follow-up for Any-Cause Readmission = 6.95 (2.99, 12.29) years

B. CV Readmission

Variable	HR (95% CI)	p-value
Type of AS		Overall p=0.572
AD	1.0 reference	
IMH	0.58 (0.20, 1.67)	0.310
PAU	0.82 (0.38, 1.78)	0.620
Age at diagnosis (per 10 years)	1.23 (0.95, 1.60)	0.125
Gender		0.155
Male	1.70 (0.82, 3.53)	
Female	1.0 reference	
Acuity of disease		Overall p=0.980
Acute	1.0 reference	
Subacute	0.81 (0.11, 6.09)	0.842
Chronic	0.99 (0.13, 7.43)	0.991
CCI	1.15 (1.05, 1.27)	0.004
CVD		0.019
No	1.0 reference	
Yes	2.35 (1.16, 4.79)	
Initial Management		Overall p=0.314
Medical	1.0 reference	
Open	1.69 (0.86, 3.33)	0.128
Endovascular	--	
In-Hospital Complications		0.301
None	1.0 reference	
Any Complication	1.46 (0.72, 2.96)	

C. Aortic Readmission

Variable	HR (95% CI)	p-value
Type of AS		Overall p=0.107
AD	1.0 reference	
IMH	1.52 (0.81, 2.87)	0.196
PAU	0.67 (0.36, 1.24)	0.202
Age at diagnosis (per 10 years)	0.96 (0.81, 1.14)	0.622
Gender		
Male	1.16 (0.70, 1.92)	0.573
Female	1.0 reference	
Acuity of disease		Overall p=0.507
Acute	1.0 reference	
Subacute	1.98 (0.60, 6.55)	0.264
Chronic	0.82 (0.20, 3.44)	0.789
CCI	0.98 (0.90, 1.07)	0.713
CVD		
No	1.0 reference	
Yes	1.30 (0.73, 2.33)	0.376
Initial Management		Overall p=0.011
Medical	1.0 reference	
Open	2.15 (1.29, 3.57)	0.003
Endovascular	2.13 (0.51, 8.86)	0.300
In-Hospital Complications		
None	1.0 reference	
Any Complication	1.90 (1.12, 3.21)	0.018

AS: aortic syndrome; AD: aortic dissection; IMH: intramural hematoma; PAU: penetrating aortic ulcer;

CCI: Charlson Comorbidity Index; CVD: cerebrovascular disease.

Appendix Table 3. Univariate Cox Proportional Hazards Models for Death.

Variable	HR (95% CI)	p-value
Type of AS		Overall p=0.451
Dissection	1.0 reference	
IMH	1.27 (0.60, 2.69)	0.540
PAU	1.47 (0.80, 2.69)	0.216
Age at diagnosis (per 10 years)	1.71 (1.32, 2.21)	<0.001
Gender		
Male	0.64 (0.38, 1.09)	0.102
Female	1.0 reference	
Acuity of Dx		0.803
Acute	1.0 reference	
Subacute	0.72 (0.10, 5.29)	0.743
Chronic	1.51 (0.36, 6.41)	0.577
CCI	1.11 (1.02, 1.20)	0.017
CVD		
No	1.0 reference	
Yes	2.17 (1.22, 3.87)	0.008
Initial Management		Overall p=0.688
Medical	1.0 reference	
Open	0.78 (0.42, 1.44)	0.425
Endovascular	0.67 (0.09, 4.89)	0.672
In-Hospital Complications		
None	1.0 reference	
Any Complication	0.90 (0.49, 1.66)	0.746

Median Follow-up for Death = 11.10 (4.82, 14.14) years

AS: aortic syndrome; AD: aortic dissection; IMH: intramural hematoma; PAU: penetrating aortic ulcer;

CCI: Charlson Comorbidity Index; CVD: cerebrovascular disease.

Table 3. Frequency of readmissions.

Year	N	Any Readmission		CV Readmission		Aortic Readmission	
		Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3
1995	4	1.5	0.5, 2.5	0.5	0, 1.5	1.0	0.5, 1.0
1996	6	2.0	1.0, 5.0	0.5	0, 1.0	1.5	0, 3.0
1997	2	0	0, 0	0	0, 0	0	0, 0
1998	7	1.0	0, 5.0	0	0, 0	1.0	0, 1.0
1999	2	1.5	0, 3.0	0.5	0, 1.0	1.0	0, 2.0
2000	3	4.0	1.0, 4.0	0	0, 0	3.0	1.0, 2.0
2001	11	2.0	1.0, 3.0	0	0, 1.0	1.0	1.0, 2.0
2002	9	2.0	1.0, 3.0	0	0, 1.0	1.0	0, 2.0
2003	7	1.0	0, 2.0	1.0	0, 2.0	0	0, 1.0
2004	4	0.5	0, 1.5	0.5	0, 1.0	0	0, 0.5
2005	2	1.0	0, 2.0	0	0, 0	1.0	0, 2.0
2006	8	2.0	0.5, 3.0	0.5	0, 1.0	0.5	0, 2.0
2007	4	2.0	1.0, 3.5	0.5	0, 1.0	1.5	0.5, 3.0
2008	2	1.0	0, 2.0	0	0, 0	1.0	0, 2.0
2009	3	0	0, 1.0	0	0, 0	0	0, 1.0
2010	7	1.0	0, 6.0	0	0, 1.0	1.0	0, 5.0
2011	4	0.5	0, 1.0	0	0, 0	0.5	0, 1.0
2012	7	1.0	1.0, 6.0	0	0, 1.0	1.0	1.0, 2.0
2013	6	0	0, 1.0	0	0, 0	0	0, 0
2014	5	1.0	0, 1.0	0	0, 1.0	0	0, 1.0
2015*	0						

*all patients in 2015 did not have enough follow-up to be considered







