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Survival outcomes after surgery for type A aortic dissection: a contemporary Dutch nationwide registry study

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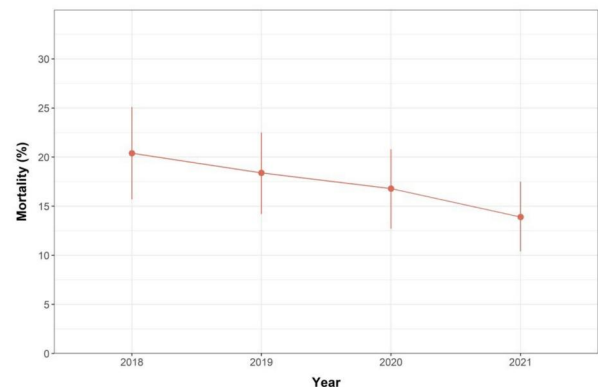
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Survival Outcomes After Surgery for Type-A Aortic Dissection: A Contemporary Dutch Nationwide Registry Study

Summary

All patients who underwent surgery for TAAD in the Netherlands between 2018 and 2021 were identified. In-hospital mortality decreased from 20.4% in 2018 to 13.9% in 2021. Patients who survived for one year after surgery seldomly died from the consequences of their dissection, but from other causes, such as cardiovascular diseases and cancer.



Legend: The figure presents in-hospital mortality for all Type-A Aortic Dissection (TAAD) operated patients in The Netherlands

[†]The first two and the last two authors contributed equally to this work.

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Abstract

OBJECTIVES: To describe the nationwide survival outcomes after surgery for type A aortic dissection.

METHODS: All patients who underwent surgery for type A aortic dissection in the Netherlands between 2018 and 2021 were identified in the Netherlands Heart Registration (NHR) database. The NHR data were linked to lifelong survival data from Statistics Netherlands (98% match). Time trends for in-hospital and mid-term mortality were described, and age- and sex-adjusted regression analysis was performed. The cause and location of death were reported and stratified according to survival time intervals.

RESULTS: The study population consisted of 1317 patients with a mean age of 63.1 years (11.8). The number of surgeries increased from 284 in 2018 to 375 in 2021. The surgery included the ascending aorta in 99%, aortic arch in 73%, aortic root in 32.5% and the descending aorta in 5% of cases. In-hospital mortality decreased from 20.4% in 2018 to 13.9% (95% CI: [10.4%, 17.4%]) in 2021. A total of 318 deaths were recorded, and the majority (70%) of patients died from the consequences of their dissection. However, among 365-day survivors, only 14% died related to their dissection, while 37% of deaths were related to cardiovascular disease and 17% to cancer. The majority (84%) of patients died in the hospital, but deaths after 365 days occurred most frequently (37%) at home.

CONCLUSIONS: Over the recent years, the number of surgeries for type A dissections in the Netherlands has increased, and in-hospital mortality has decreased. For patients surviving 1 year after surgery, the main cause of death was not dissection, but other causes such as cardiovascular disease or cancer.

Keywords: type A aortic dissection • nationwide registry • the Netherlands • cause of death

ABBREVIATIONS

ARR	Aortic root replacement
CBS	Centraal Bureau voor de Statistiek
GERAADA	German Registry for Acute Aortic Dissection Type A
ICD-10	International Classification of Disease—10
IRAD	International Registry of Acute Aortic Dissection
NHR	Netherlands Heart Registration
NORCAAD	Nordic Consortium for Acute Type A Aortic Dissection
TAAD	Type A aortic dissection

INTRODUCTION

Acute type A aortic dissection (TAAD) is a medical emergency that requires urgent surgery [1–3]. Despite extensive research over the past decades, the in-hospital and early mortality rates for TAAD remain high [4–8]. Registries, such as the International Registry of Acute Aortic Dissection (IRAD) [6, 7, 9, 10], Nordic Consortium for Acute Type A Aortic Dissection (NORCAAD) [11, 12] and population-based cohorts such as the Oxford Vascular Study [13], Danish nationwide data [5, 14] and German Registry for Acute Aortic Dissection Type A (GERAADA) [15–17] provide important data on the incidence and outcomes of TAAD. These studies have analysed risk factors, surgical complications and mortality/reintervention rates; however, detailed information on the cause and location of death of TAAD is lacking. We use nationwide registry data to describe contemporary survival outcomes, including the cause and location of death, of all patients who underwent surgery for TAAD in the Netherlands between 2018 and 2021. These insights are valuable for both patients and for clinicians who provide treatment and follow-up.

MATERIALS AND METHODS

Ethics statement

This is an observational population-based cohort study of prospectively collected data registered within the Netherlands Heart Registration (NHR) and of data from Statistics Netherlands ('Centraal Bureau voor de Statistiek (CBS)' in Dutch). The study was approved by the institutional review board MEC-U (W19.270) and conducted in agreement with the principles of the Declaration of Helsinki. A waiver for informed consent was obtained. The data underlying this article were provided by the NHR with permission from all participating hospitals and by Statistics Netherlands; data are available upon reasonable request to the corresponding author and representatives of the data sources.

Study data

The NHR is a nationwide, physician-driven and patient-focused quality registry that contains procedural and outcome data of all invasive cardiac interventional, electrophysiological and cardiothoracic surgical procedures from all Dutch hospitals [18, 19]. The aim of the NHR is to contribute to the maintenance and improvement of the quality and transparency of care for cardiac patients. For each intervention, a limited set of patient characteristics, procedural data and outcome data is collected by the hospitals and submitted to the NHR. Patients who underwent surgery for TAAD between 1 January 2018 and 31 December 2021 were selected. Reinterventions on the aorta were excluded. CBS contains, among other data outside the scope of this study, survival data of all inhabitants of the Netherlands. The NHR data were linked to data of Statistics Netherlands based on postal code and date of birth. From the NHR data, patient and procedural characteristics were obtained, while data from CBS were used to retrieve lifelong survival information including the date, cause and location of death.

The causes of death were identified based on International Classification of Disease–10 (ICD-10) codes.

Statistical analysis

All statistical analyses were performed using the R software (R Foundation for Statistical Computing, Vienna, Austria, www.r-project.org). Numerical variables were reported as mean (\pm standard deviation) or median (interquartile range) according to their distribution, and categorical variables as counts (percentages). Per the privacy regulations of Statistics Netherlands, cells were merged if they contained counts fewer than 5 to prevent possible identification of individuals. Time trends for in-hospital and mid-term mortality were graphically illustrated. Follow-up started on the day of surgery for TAA. Furthermore, the age- and sex-adjusted associations between the mortality outcomes and the intervention years were quantified using binary logistic and Cox proportional hazards regression (R package *survival*). A graphical overview of the causes of death was provided for the entire study population, as well as for 30-day and 365-day survivors (R package *mstate*).

RESULTS

In total, 1357 TAA operations, performed between 1 January 2018 and 31 December 2021, were identified in the NHR database; 1325 (98%) of these could be matched to the CBS follow-up data based on postal code and date of birth. Of these 1325 operations, 8 (0.6%) were reoperations, leaving 1317 unique patients who underwent primary surgery for TAA in The Netherlands. The number of TAA operations increased over the 4-year study period: 284 in 2018, 332 in 2019, 328 in 2020 and 373 in 2021.

The average age at surgery was 63 ± 12 years, 59% was male, and the median EuroSCORE II was 10.1 [5.5, 19.7] (Table 1). Mean LVEF was 53%, and diabetes mellitus and chronic lung disease were reported in 4.2% and 6.8%, respectively. Sixty-four patients (7%) had connective tissue disease and 69 (5%) had a history of previous cardiac surgery; 392 patients (30%) were in a critical medical condition when they arrived in the operation room as defined by the need for cardiopulmonary resuscitation, intubation, inotropic support, or preoperative renal failure with urinary production <10 ml/h. Preoperative aspirin and direct oral anticoagulant were used by 12.5% and 8.4%, respectively.

Regarding the procedural details (Table 2), the average cross-clamp time was 141 min, and 88% of the patients underwent circulatory arrest. Concomitant surgery on the aortic valve was performed in 39%. The valve was repaired in 11% and replaced in 28% (5% stentless bioprosthesis, 13% stented bioprosthesis and 10% mechanical prosthesis). Concomitant root surgery was performed in 32.5%, using either a Bentall, David or (partial) Yacoub procedure. Complete arch replacement (three vessels) was performed in 128 (10%) and zone 2 (2 vessels) arch replacement in 155 (12%). Six hundred thirty-five (49.6%) underwent hemi arch replacement and 317 (24%) underwent no arch surgery. In 61 (5%) patients, surgery was performed on the descending aorta, for example by using an (frozen) elephant trunk.

Table 1: Baseline characteristics of 1317 patients who underwent surgery for acute type A aortic dissection in the Netherlands between 2018 and 2021

Characteristics	Overall	Missing data
Age (years)	63.1 (11.8)	0 (0%)
Male sex	770 (59%)	0 (0%)
BMI (kg/m ²)	26.5 (4.7)	75 (6%)
BSA (m ²)	2 (0.2)	75 (6%)
Intervention year		0 (0%)
2018	284 (22%)	
2019	332 (25%)	
2020	328 (25%)	
2021	373 (28.3%)	
EuroSCORE II	10.1 [5.5, 19.7]	106 (8%)
LVEF (%)	53.6 (6.4)	47 (4%)
Creatinine (μ mol/l)	98 (47.1)	54 (4%)
Diabetes mellitus	54 (4%)	25 (2%)
Atrial fibrillation	104 (9%)	178 (14%)
Connective tissue disease	64 (7%)	367 (28%)
Chronic lung disease	89 (7%)	6 (1%)
Previous CVA	62 (5%)	17 (1%)
Previous ECVD	230 (18%)	6 (0.5%)
Previous cardiac surgery	69 (5%)	2 (0.2%)
Critical state	392 (30%)	3 (0.2%)
Urgency setting		0 (0%)
Elective	15 (1%)	
Urgent	110 (9%)	
Emergency	1016 (77%)	
Salvage	176 (13%)	
Preoperative aspirin use	128 (8%)	293 (22%)
Preoperative DOAC use	34 (4%)	350 (27%)

Data are presented as *n* (%); mean (\pm SD); median [interquartile range].

BMI: body mass index; BSA: body surface area; CVA: cerebrovascular accident; ECVD: extracardiac vascular disease; DOAC: direct oral anticoagulant; LVEF: left ventricular ejection fraction.

Table 2: Procedural details of 1317 patients who underwent surgery for acute type A aortic dissection in the Netherlands between 2018 and 2021

Characteristics	Overall	Missing data
ECC	1303 (99%)	4 (0.3%)
ECC time (min)	257.4 (101.5)	105 (8%)
Cross clamp time (min)	141.4 (69.4)	100 (8%)
Circulatory arrest	1148 (88.3%)	2 (0.2%)
Circulatory arrest time	43.6 (28.6)	159 (12%)
Concomitant CABG TAA surgery extend	107 (8%)	0 (0%)
AV repair or replacement	520 (39%)	0 (0%)
Root	428 (32.5%)	45 (4%)
Aortic arch	961 (73%)	0 (0%)
Descending aorta	68 (5%)	1 (0.1%)
Minimum central temperature	23.4 (4)	192 (15%)
Number of arch vessels repaired		38 (3%)
0 vessels	953 (75%)	
1 vessel	42 (3%)	
2 vessels	155 (12%)	
3 vessels	128 (10%)	

Data are presented as *n* (%); mean (\pm SD). Times are reported in min.

AV: aortic valve; CABG: coronary artery bypass graft; ECC: extra corporeal circulation.

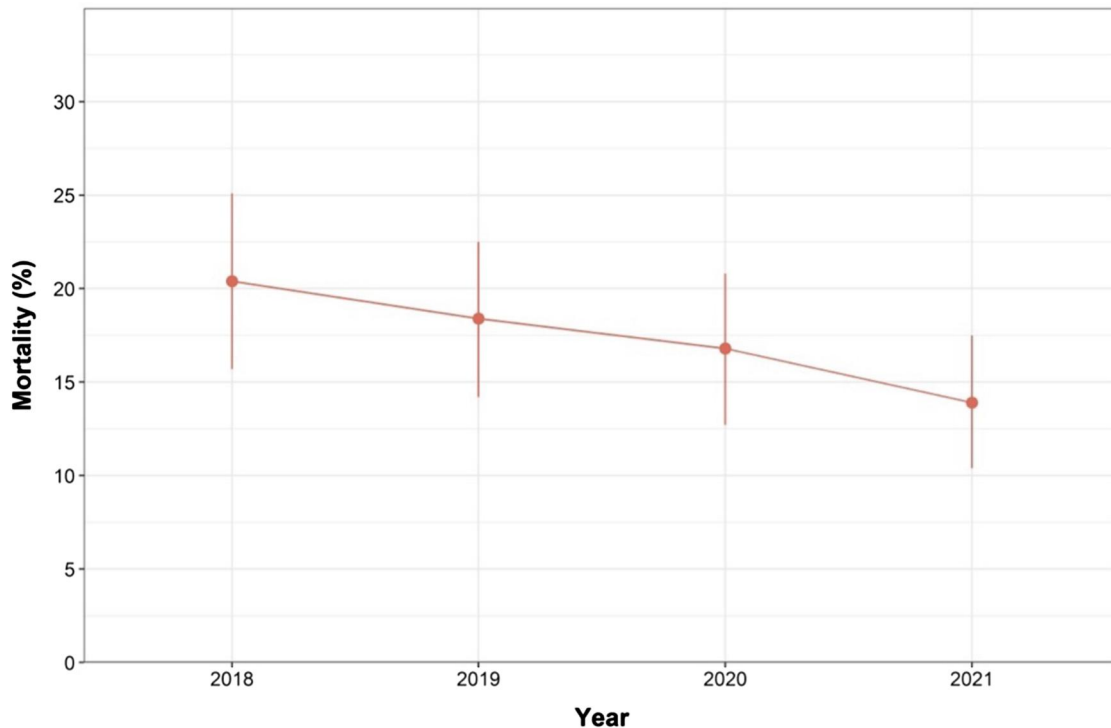


Figure 1: Yearly in-hospital mortality after surgery for acute type A aortic dissection in the Netherlands between 2018 and 2021. The dots represent the percentage of in-hospital mortality per intervention year, and the vertical bars represent the corresponding 95% confidence intervals.

The in-hospital mortality risk decreased over the 4-year study period (Fig. 1): 20.4% (95% confidence interval [CI] 13.8–25.1%) in 2018, 18.4% (95% CI 14.2–22.5) in 2019, 16.8% (95% CI 12.7–20.8%) in 2020 and 13.9% (95% CI 10.4–17.5%) in 2021. The age and sex-adjusted odds ratios for in-hospital mortality, with 2018 as reference, were 0.87 (95% CI 0.58–1.30) for 2019, 0.78 (95% CI 0.52–1.18) for 2020 and 0.63 (95% CI 0.41–0.95) for 2021 (Supplementary Material, Table S1). The mortality risk throughout the first 5 years after the index surgery is presented per intervention year in Fig. 2. The corresponding age- and sex-adjusted hazard ratios were 0.94 (95% CI 0.69–1.27) for 2019, 0.82 (95% CI 0.59–1.13) for 2020 and 0.82 (95% CI 0.59–1.12) for 2021 (Supplementary Material, Table S2).

A total of 318 patients died during follow-up and of them 226 (71.1%) died within 30 days. An overview of all the causes of death is provided throughout the entire study as well as during specific time periods in Table 3. Most of the patients who died, died from the consequences of their dissection ($N=222$, 69.8%). Interestingly, whereas 85% of the deaths within 30 days were attributed to dissections, only 14% of the deaths after 365 days were. Specifically, 365-day survivors died from other cardiovascular disease in 37%, malignancy in 16% and other undefined causes in 33%. Figure 3 illustrates this relation between the cause of death and survival time. The location of death is presented in Table 4 similar to the cause of death. In total, 267 (84%) patients died in the hospital, and after 365 days, a considerable amount of the deaths occurred at home or in a nursing home.

DISCUSSION

This nationwide registry study demonstrates that in-hospital mortality after surgery for type A dissection in The Netherlands

has decreased over recent years, while the number of surgeries has increased. Furthermore, patients who survive 1 year after surgery seldom die from the consequences of their dissection but die from other causes, such as cardiovascular diseases and cancer. This could be important information for the surgical and follow-up strategy.

In our study, the 30-day mortality rate was 17.2% over the years 2018–2021. A recent nationwide Danish study reported a 30-day mortality rate of 24.0% between 2011 and 2016 [14]. The IRAD reported an overall in-hospital mortality of 18.4% for surgically treated TAAD patients between 2010 and 2013 [7], the Scandinavian multicentre study NORCAAD of 15.7% for 2005–2014 [11] and the nationwide German study GERAADA of 20.2% for 2006–2010 [17]. These mortality rates are difficult to compare as the corresponding surgical intervention year and study setting differ.

Our nationwide data show a steep decrease in in-hospital mortality from 20.4% in 2018 to 13.9% in 2021, which persisted after adjustment for age and sex. Such a significant improvement in short-term survival in only 4 years is hard to explain from a clinical standpoint. Possibly, although the number of surgeries increased, the selection of patients may have contributed to this finding. Moreover, the COVID-19 pandemic might also have influenced the results. The dissection registry of the NHR is currently expanding with more data including detailed perioperative characteristics, which will help better understand the observed improvements in outcomes in the future.

In a nationwide Danish study, the recorded deaths within 5 years of the initial TAAD operation were stratified into early death (≤ 30 days) and non-early death (>30 days) [14]. For the early deaths, 57%, 1.7% and 4.1% were aortic-, cardiac- and cancer-related, respectively. For non-early deaths, the authors reported 23.2%, 3.1% and 12.8% due to aortic-, cardiac- and

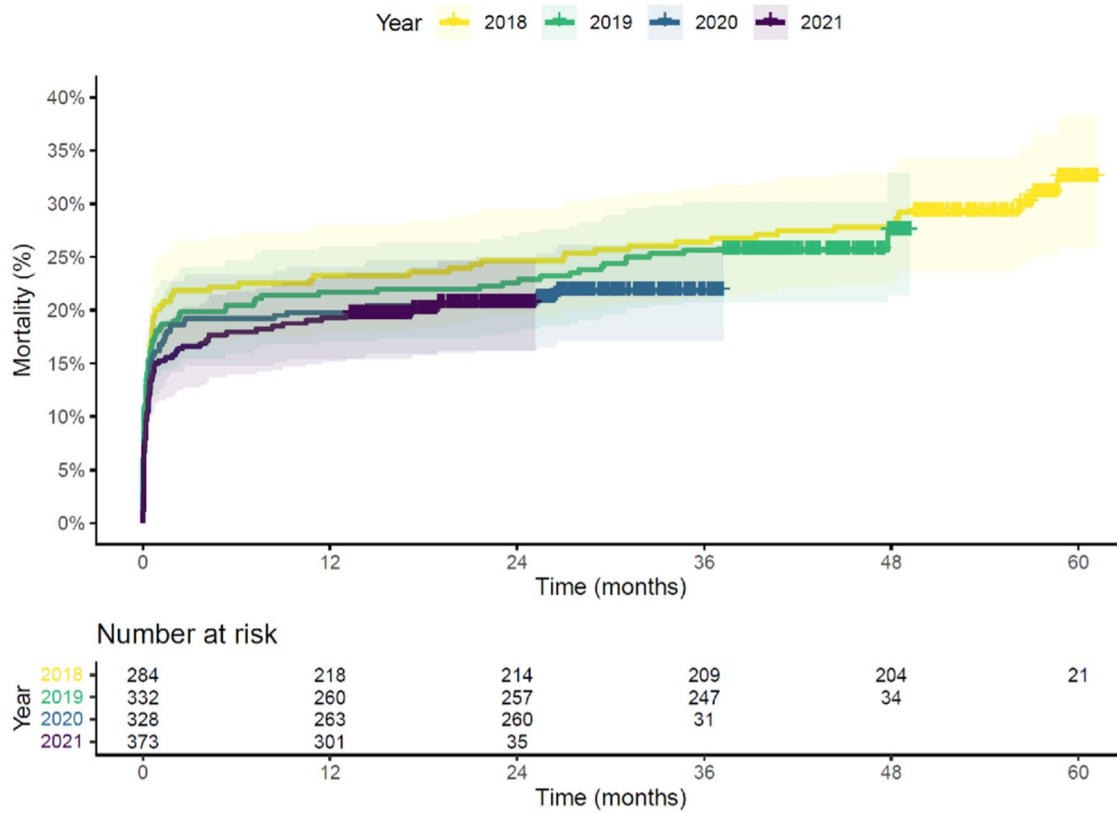


Figure 2: Kaplan-Meier survival curve per intervention year for patients who underwent surgery for acute type A aortic dissection in the Netherlands between 2018 and 2021. The coloured lines represent the cumulative incidences of mortality throughout 5-year follow-up, and the shaded areas represent the corresponding 95% confidence intervals. Censoring is indicated with the '+' sign. Follow-up time started on the day of surgery.

Table 3: Causes of death for patients who died after surgery for acute type A aortic dissection in the Netherlands between 2018 and 2021

Cause of death	Overall; N = 318	<30 days; N = 226	30-365 days; N = 49	>365 days; N = 43
Dissection	222 (70%)	190 (84%)	26 (53%)	6 (14%)
Cardiovascular	52 (16%)	22 (9.7%)	14 (29%)	16 (37%)
Malignancy	9 (2.8%)	14 (6.2%) ^a	9 (18.1%) ^a	7 (16%)
Other	35 (11%)			14 (33%)

Data are presented as n (%).

^aTo protect privacy, low number of table entrances are combined.

cancer-related deaths, respectively. These trends are comparable to our results, particularly the significant rise in cancer- and cardiac-related deaths and reduction in dissection-related deaths.

Recently, aortic root replacement (ARR) has been described as a more extensive approach in TAAD operations that should be considered, even in an acute setting, in patients with acknowledged risk factors for late aortic complications or probable need for reinterventions [20]. Moreover, ARR is recommended by current guidelines to be performed in patients where dissection involves the root, and operative risk is acceptable [3]. In the

Netherlands, ARR was performed on 32.5% of all operations. ARR was reported in 30.8% in IRAD, 28.3% in GERAADA and 26% in NORCAAD [7, 15, 21].

The standard approach is an open distal anastomosis in most cases with a hemiarch replacement. Conflicting results have been published, but some studies have argued that complete arch replacement leads to decreased mortality and fewer late reinterventions [4, 17, 22-24]. A meta-analysis by Poon *et al.* [25] demonstrated no difference in mortality for patients who underwent hemiarch versus total arch repair. Partly conflicting, another meta-analysis by Ma *et al.* [4] showed that hemi-arch had lower early mortality rates than total arch repair, but higher late mortality rates. We observed in our study that, on average, in the Netherlands, 10% of all TAAD surgeries included complete arch replacement. The GERAADA study reported a higher, 16.1% complete arch, with 47.5% hemi arch reconstruction [17]. The IRAD study reported an increase in complete arch replacement from 16.4%, 21.5% and 22.1% for 1996-2003, 2004-2009 and 2010-2016, respectively [7, 9]. Surprisingly, the NORCAAD reported only 6% full arch for 2005-2014 [21]. These results show that the extent of arch is subject to discussion, as recently highlighted in current guidelines [2, 3].

The priority of TAAD operation is short-term survival, but extensive root and arch operations are performed in routine practice. It seems from our results that TAAD surgeries in the Netherlands extensively utilize a root approach while adopting a

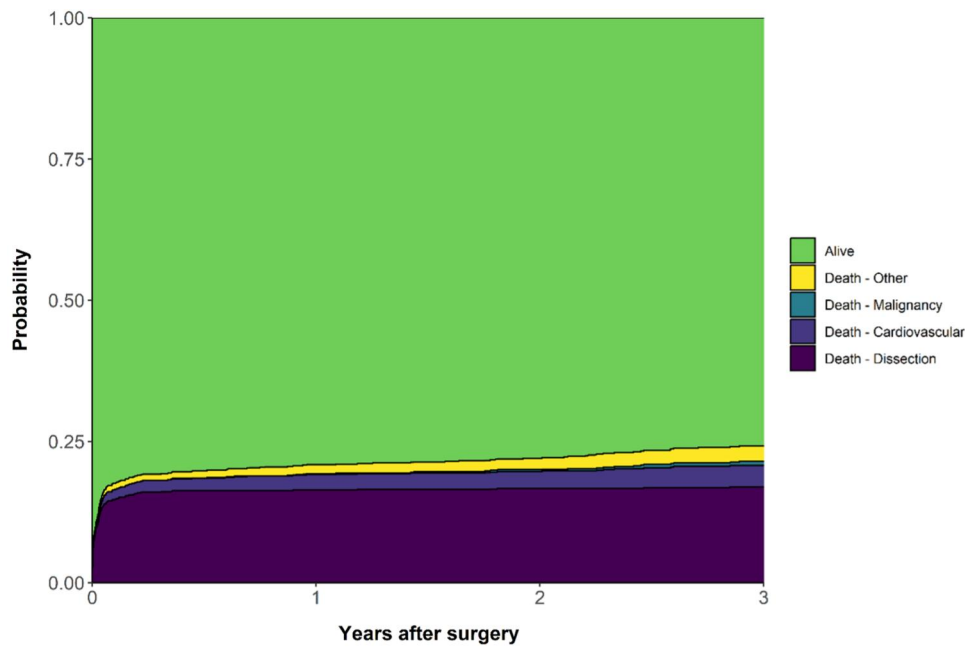


Figure 3: Graphical overview of the causes of death during 3-year follow-up after surgery for type A aortic dissection in the Netherlands. The vertical axis represents the probability to be in one of the defined states. All patients are in the 'Alive' state at the start of follow-up and move to one of the death states when they die of that particular cause.

Table 4: Location of death for patients who died after surgery for acute type A aortic dissection in the Netherlands between 2018 and 2021

Location of death	Overall; N = 318	<30 days; N = 226	30–365 days; N = 49	>365 days; N = 43
Hospital	267 (84%)	220 (97%)	32 (65%)	15 (35%)
Home	26 (8.2%)		9 (18%)	16 (37%)
Nursing home	12 (3.8%)	6 (3) ^a	4 (8.2%)	8 (19%)
Other	7 (2.2%)			
Unknown	6 (1.9%)		4 (8.1%) ^a	4 (9.3%) ^a

Data are presented as *n* (%).

^aTo protect privacy, low number of table entrances are combined.

more conservative approach for the arch. Extensive surgery may be beneficial for patients in the long run, but further research is needed.

Strengths and limitations

One of the key strengths of this study is the nationwide aspect. This creates a broad overview of the entire nation's healthcare system for a relatively rare disease, which is only possible in a medical system that has unified electronic health record or reliable nationwide registries. In addition, we observe very low rates of missing data. Yet, the inherent limitation when conducting nationwide registry-based studies is the validity of the registered diagnostic codes, for example in ICD-10 codes and the risk of misclassification/information bias in data of Statistics Netherlands. This information is often completed by general practitioners, and without an autopsy, the true cause of death

may be challenging to accurately determine. Finally, a minor limitation is that 2% of all TAAD could not be matched and were therefore excluded.

This study did not include data on all patients diagnosed with TAAD in the Netherlands, but exclusively those patients who underwent surgery. Hence, the results could be influenced by patient selection, especially during the COVID-19 pandemic. However, another nationwide study from the Netherlands reported no difference in overall number of acute aortic operations during the pandemic [26] and we saw an increase in surgeries over the 4-year study period.

CONCLUSIONS

This nationwide registry study demonstrates that in-hospital mortality after surgery for type A dissection in the Netherlands has decreased in recent years. Patients who survive 1 year after surgery seldom die from the consequences of their dissection but die from other causes, such as cardiovascular diseases and cancer. These new insights are valuable for patients and for clinicians who provide treatment and for follow-up guidelines.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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DATA AVAILABILITY

Data are available upon reasonable request to the corresponding author and representatives of the data sources.

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Author contributions

Patrick T. Timmermans: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing—original draft. **Bart J.J. Velders:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; writing—original draft. **Rolf H. H. Groenwold:** Supervision; Writing—review & editing. **Roemer J. Vos:** Investigation; Writing—review & editing. **Maaike M. Roefs:** Investigation; Resources; Validation; Writing—review & editing. **Jerry Braun:** Investigation; Supervision; Writing—review & editing. **Robert J. M. Klautz:** Investigation; Supervision; Writing—review & editing. **Gianclaudio Mecozzi:** Conceptualization; Investigation; Resources; Writing—review & editing. **Jesper Hjortnaes:** Conceptualization; Investigation; Methodology; Resources; Supervision; Writing—review & editing.

Reviewer information

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