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Modelling years of life lost due to acute type A aortic dissection in the German healthcare setting: a predictive study

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ABSTRACT

Objectives This study aimed to develop a patient-centred approach to the burden of acute type A aortic dissection (ATAAD) through modelling. The main objective was to identify potential improvements in managing this life-threatening cardiovascular condition and to provide evidence-based recommendations to optimise outcomes.

Design We developed a predictive model along patient pathways to estimate the burden of ATAAD through the years of life lost (YLLs) metric. The model was created based on a systematic review of the literature and was parameterised using demographic data from the German healthcare environment. The model was designed to allow interactive simulation of different scenarios resulting from changes in key impact factors.

Setting The study was conducted using data from the German healthcare environment and results from the literature review.

Participants The study included a comprehensive modelling of ATAAD cases in Germany but did not directly involve participants.

Interventions There were no specific interventions applied in this study based on the modelling design.

Primary and secondary outcome measures The single outcome measure was the estimation of YLL due to ATAAD in Germany.

Results Our model estimated 102 791 YLL per year for ATAAD in Germany, with 62 432 and 40 359 YLL for men and women, respectively. Modelling an improved care setting yielded 93 191 YLL or 9.3% less YLL compared with the current standard while a worst-case scenario resulted in 113 023 or 10.0% more YLL. The model is accessible at https://acuteaorticdissection.com/ to estimate custom scenarios.

Conclusions Our study provides an evidence-based approach to estimating the burden of ATAAD and identifying potential improvements in the management of pathways. This approach can be used by healthcare decision-makers to inform policy changes aimed at optimising patient outcomes. By considering patient-centred approaches in any healthcare environment, the model has the potential to improve efficient care for patients suffering from ATAAD.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Used comprehensive modelling to estimate acute type A aortic dissection's years of life lost in Germany.
- ⇒ Based on systematic review and demographic data analysis.
- ⇒ Assumptions and modelling may not fully capture real-world variability.
- ⇒ Study's applicability is limited to Germany's health-care context.
- ⇒ Future research is needed to incorporate broader data and contexts.

INTRODUCTION

Acute type A aortic dissection (ATAAD) is an urgent, life-threatening condition that poses a significant risk of early mortality if not promptly treated. Given the nature of the disease's pathophysiology and the sudden onset of symptoms, the first point of medical contact is typically through local ambulance services or emergency department staff. However, the initial clinical manifestation can often be ambiguous and challenging, leading to a high rate of misdiagnosis.[1] Epidemiological studies report an incidence rate of approximately 1.85–11.9 cases per 100 000 population annually in Europe,[2–6] whereas data from Berlin emergency departments suggest an estimated incidence of 5.93–24.92 cases per 100 000 patients annually.[7] Remarkably, the clinical diagnosis of ATAAD is likely to be overlooked in up to 78.3% of instances even within the emergency department.[1 8] Although the diagnostic gold standard is an electrocardiogram-triggered CT angiogram,[9] patients with a confirmed diagnosis of acute aortic syndrome are typically transferred either within the hospital to the cardiac surgery department or to a suitable cardiac surgical centre in the vicinity, presenting a common logistical challenge. These critical stages of the care pathway are highly dependent on local circumstances, and reliable data on this process are scarce. To better understand patient pathways, we have segmented the preclinical process into distinct phases, including transfers between different hospitals and the time required for diagnosis. We note that in rare circumstances like multimorbidity, high age or explicit patient will, medical treatment may be applied, reducing the chances of survival significantly.[10] These cases are not considered in detail in this study.

Several factors influence the likelihood of an ATAAD occurrence and the subsequent outcomes, as demonstrated by a systematic review of the literature. Among these are underlying risk factors,[11] the time from the onset of pain to surgical incision ('pain-to-cut-time', PCT[1,12]), and the relationship between surgical volume and outcome.[13] While these factors have been individually investigated, no model currently exists that captures the cumulative impact of these factors, thereby enabling a comprehensive evaluation of the implications of ATAAD. The aim of this study is to model specific conditions in the care of ATAAD to enhance understanding of potential improvements and their impact on the disease burden. A suitable metric for quantifying this burden is the years of life lost (YLLs), which recognises premature mortality and extends the conventional mortality measure with an age-dependent weighting of deaths, making it an appropriate tool for assessing the impact of risk factors and diseases. Adopting a structured approach to modelling the care pathway and assessing outcomes is crucial for gaining a deeper understanding of ATAAD, despite the inherent challenges in capturing its full complexity.

METHODS

Systematic literature search

A comprehensive literature search in the PubMed database until April 2023 was conducted before starting the modelling process, visualised in figure 1. The search included articles using the keywords 'acute type A aortic

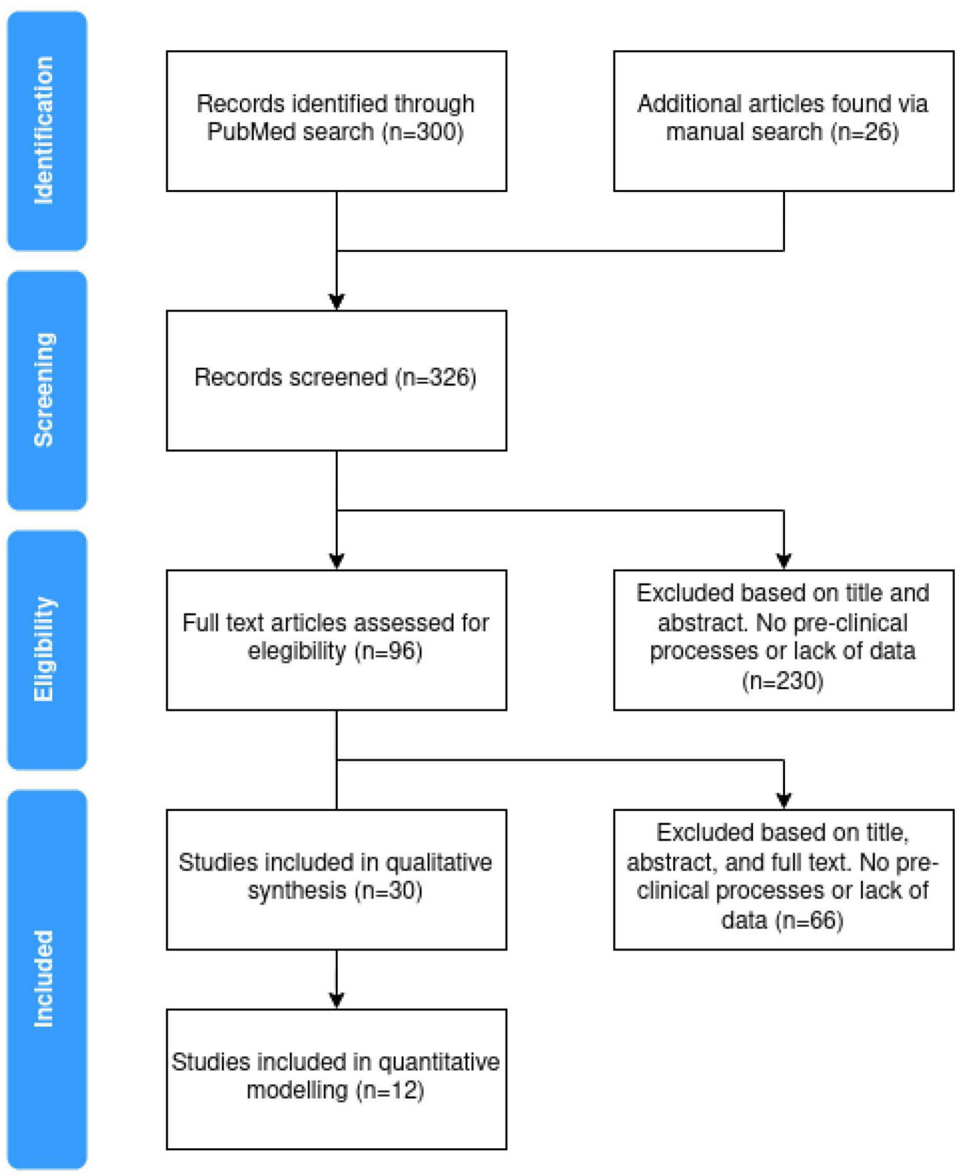

Figure 1 Systematic review flow chart. Visual representation of the review methodology.

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dissection' in combination with 'incidence', 'transportation', 'delay', 'heart surgery', 'misdiagnosis' and 'volume outcome'. No restrictions were placed on language or publication type using the strategy:

("acute type A aortic dissection" [Title/Abstract]) AND ("incidence" [Title/Abstract] OR "transportation" [Title/Abstract] OR "delay" [Title/Abstract] OR "heart surgery" [Title/Abstract] OR "misdiagnosis" [Title/Abstract] OR "volume-outcome" [Title/Abstract]).

A total of 300 results were obtained. Additionally, we manually searched the reference lists of relevant articles to identify any additional studies. After removing duplicates, the remaining studies were assessed for inclusion and relevance by at least two independent reviewers using strict criteria. We included studies that offered detailed insights into the incidence, epidemiology, outcomes and treatment efficacy of ATAAD, particularly those providing population-based data and exploring diagnostic and treatment delays. Exclusion criteria targeted case reports, editorial comments, review articles without original data and studies not directly focusing on ATAAD or applicable to a broad healthcare context. Additionally, each study underwent careful evaluation to ensure the reliability and validity of our analysis, with a particular focus on the study populations and measurements. This meticulous selection and evaluation process led to a refined list of studies foundational for our predictive model development, anchoring our analysis in relevant and high-quality research.

Modelling approach

The initial step of the modelling process involved describing the management of pathways during an ATAAD event (figure 2) according to the literature search. This pathway was divided into five segments: the immediate ATAAD event (1), transportation to the primary hospital (2), diagnosis (3), transportation to the hospital of definitive care (4) and surgery (5). For each segment, a standard case was defined based on parameters obtained from published evidence. Additionally, best-case and worst-case scenarios were developed with adjusted parameter values. By calculating the mortality rate for each segment, we could determine the overall mortality of an ATAAD event. Although patient-level data and uncertainty quantifications were lacking for some inputs, the best, standard and worst-case scenarios provided an initial understanding of the results' variability. Moreover, the model allows for the incorporation of alternative parameterisations, enabling readers to simulate different settings based on the healthcare system of their respective regions.

Standard-case scenario

According to Howard *et al*[2] and Landenhed *et al*,[11] the mortality rate before the first medical contact in a dissection event is estimated to be up to 35.1% (segment I). If left untreated, the mortality rate is 0.5%–2% per hour.[9 14 15] Thus, PCT is a crucial factor influencing ATAAD patient mortality.[1 12] After a correct initial diagnosis, the average PCT is approximately 5.5 hours and reflected in the transportation and diagnosis segments in figure 2 (segments 2–4). However, due to challenges in accurately diagnosing ATAAD, cases are often initially misdiagnosed as acute coronary syndromes, with a clinical misdiagnosis rate of up to 78.3%.[1 8] Initial misdiagnosis not only has an immediate negative impact but also extends the PCT by an average of 3.3 hours to establish a correct diagnosis.[1] Similar findings have been reported by Harris *et al*[16] using data from the International Registry of Acute Aortic Dissection. This conservative analysis assumed that an increased PCT due to misdiagnosis contributes to mortality (segment III) but excluded any direct negative impact from incorrect medication. The volume of ATAAD surgeries performed by the surgeon at the receiving hospital was identified as another significant factor for mortality (segment V). Reutersberg *et al*[13] reported in-hospital mortality rates of 22.3% in low-volume hospitals, 19.0% in medium-volume hospitals and 16.5% in high-volume centres. Similar trends were observed by Knipp *et al*[17] (in the USA) and Benedetto *et al*[18] (in the UK). The study by Reutersberg *et al*[13] also highlighted age as an influential factor for in-hospital mortality, with an OR of 1.14 per 5 years of age. This finding was also supported by Fukui *et al*[19] and Rylski *et al*.[20] Therefore, we incorporated age as a variable in our mortality model, using the baseline mortality rates for a person of average age (45.1 years) with adjustment based on the OR identified by Reutersberg *et al*.[13]

YLL modelling

To model the YLL due to ATAAD, we obtained the most recent population pyramid of Germany, with detailed information on the national age distribution.[21] Additionally, we acquired conditional life expectancy data,[22] representing the expected remaining years of life for individuals at any age (eg, as of 2020, a woman in Germany who has reached the age of 85 years has an expected remaining life expectancy of 6.5 years). The age structure and conditional life expectancy data by sex are illustrated in online supplemental figure.

The crude incidence rate of ATAAD was obtained through an analysis of autopsy reports, allowing for the inclusion of mortality data even at the prehospital stage.[3] The estimate was based on the analysis of a substantial sample size of approximately 30 million person-years from the Berlin-Brandenburg region, rendering the dataset suitable and appropriate to serve as a valuable reference. Applying the relative incidence rates per age group according to this distribution (figure 3) to the population data of Germany, we derived an annual incidence rate of 14.5 cases per 100 000 population. The model also allows to select alternative incidence distributions from different data sources or healthcare environments.

Next, we computed the YLL by integrating the previously mentioned data points. For each subgroup defined by age and sex, we determined the absolute number of incidences based on the incidence distribution. Using the mortality rates obtained from the pathway specifications

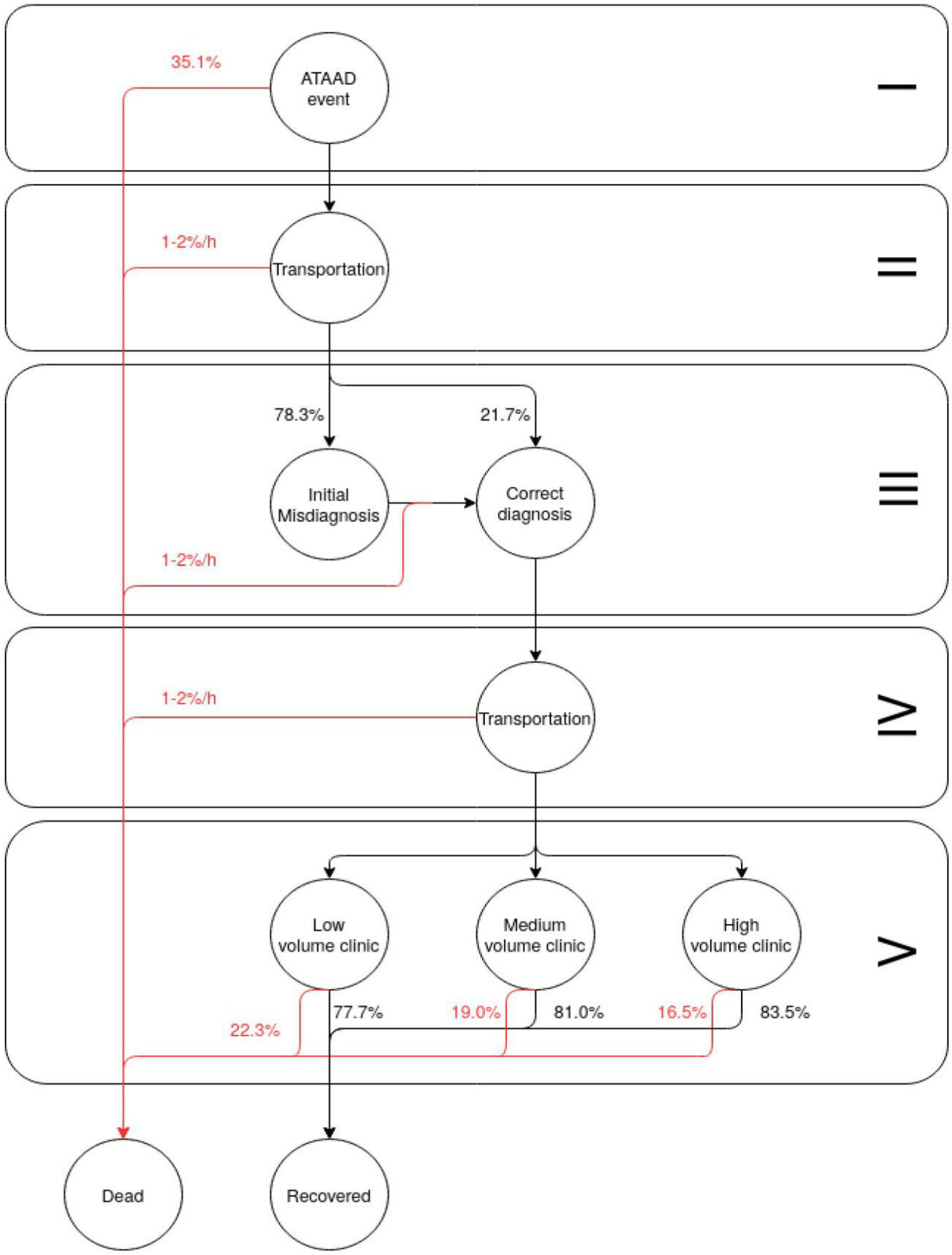

Figure 2 ATAAD flow chart. Visualisation of the patient flow after ATAAD event through the care segments alongside transition probabilities. ATAAD, acute type A aortic dissection.

depicted in figure 2, the absolute number of ATAAD-related deaths within each subgroup was estimated. By considering the expected remaining life expectancy and the mortality resulting from a probability-weighted outcome of the patient pathway the YLL was obtained for each subgroup, ultimately generating the absolute YLL distribution.

In line with standard practice in burden-of-disease studies, future YLLs were discounted at a rate of 3% per year.[23] Additionally, we considered two hypothetical scenarios to assess the potential impact of changes to the standard model.

Best-case scenario

The best-case scenario assumed highly efficient patient transportation and significantly improved diagnostic performance. The PCT in this scenario was set to the first quartile reported by Zaschke *et al.*[1] Furthermore, in line with the volume-outcome relationship, ATAAD cases were assumed to be treated exclusively in high-volume clinics, leading to a hypothetical in-hospital mortality rate of 14.0% based on the study by Umana-Pizano *et al.*[24]

Worst-case scenario

Conversely, the worst-case scenario simulated a deterioration in patient transportation, with the transport time set to the third quartile reported by Zaschke *et al.*[1] This scenario also accounted for a decrease in the volume-outcome effect, where ATAAD surgeries were performed only in low-volume centres.

Table 1 presents the parameter values used in our three scenarios.

Figure 3 Incidence. Distribution of ATAAD incidence by age and sex. ATAAD, acute type A aortic dissection.

Patient and public involvement

The study was purely modelling-based, using publicly available data. As a result, there was no direct involvement of patients or the public in the research process.

RESULTS

The simulation results for our predefined scenarios are outlined below. All estimates are primarily based on the incidence distribution reported by Kurz *et al*,[3] which reflects a German population. Alternative results are also provided, based on an incidence distribution presented in Howard *et al*[2] (originating from Oxfordshire, UK) and presented in parenthesis for comparative purposes.

Standard-case scenario

When assessing the model in the base case, we obtained a mortality rate of 53.6% for any individual of average age, considering immediate mortality as well as transport time and surgical mortalities. Applying the model to entire the population of Germany, we calculated a total of 102 791 (46 178) YLL in 2020. Among these, 62 432 (27 326) YLLs were attributed to males while 40 359 (18 852) YLLs were attributed to females. This accounts for 57.3% (60.6%) of the total expected residual life at the time of diagnosis. Figure 4 provides an overview of the YLL distribution across different age groups and sexes.

Best-case and worst-case scenarios

In the best-case scenario, the YLL decreased to 93 191 (41,703), representing a reduction of 9.3% (9.7%) compared with the base case, or 9600 (4,475) years. Conversely, the worst-case assumptions resulted in an increase of 10.0% (9.3%) and 113 023 (50,453) YLL. Thus, the overall impact of the different scenarios amounts to 19 832 (8750) YLL. A significant portion of the YLL, 62 916 (26 726), was attributed to immediate mortality from ATAAD before any medical intervention could take place. Excluding these cases, 39 875 (19 452) YLL out of the total 102 791 (46 178) YLL remained, representing the potential impact of patient management on the YLL. Therefore, the 9.3% (9.7%) reduction in total YLL in the best-case scenario corresponds to a notable improvement of 24.1% (23.0%) when excluding cases of immediate death. Conversely, the worst-case scenario indicates an increase of YLL by 25.7% (22.0%) when considering the adjusted metric excluding sudden death.

To enhance the applicability of the model, we developed an interactive dashboard (accessible at https://

Table 1 Scenario parametrisation

	Base case	Best case	Worst case
Transportation time	5.5 hours	4.5 hours	7.9 hours
Time to correct diagnosis	3.1 hours	1.8 hours	8.5 hours
Low/medium/high-volume split	27%/60%/13%	0%/0%/100%	100%/0%/0%
Low/medium/high-volume mortality	22.3%/19.0%/16.5%	· / ·· /14.0%	22.3%/ ·· / ··

Data not relevant.

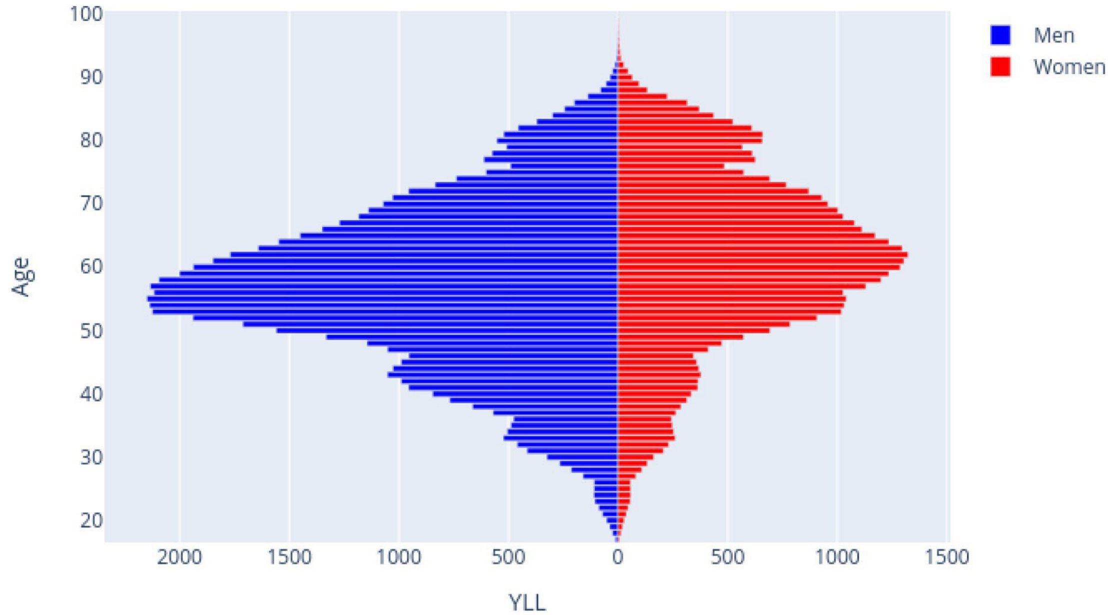

Figure 4 YLL due to ATAAD. Age distribution of YLL by sex. ATAAD, acute type A aortic dissection; YLL, years of life lost.

acuteaorticdissection.com/ for potential users). This dashboard allows users to simulate different scenarios of important parameters as derived from current literature and facilitates the demonstration of the interplay between key factors in the model.

DISCUSSION

Our analysis devises a data-informed model to estimate the burden of disease subsequent to ATAAD. This methodology introduces a unique analytical angle for evaluating ATAAD, enabling an association between patient outcomes and events throughout the primary care stages from symptom onset to treatment. It facilitates the assessment of the cumulative impact of varied interventions, supporting clinical and administrative decisions in public health. Our study used the German healthcare system as a representative example to quantify YLL. In the year 2020, ATAAD's immediate effects led to 102 791 YLL, of which 9600 could have been saved through improved care.

Earlier studies had cited 4 040 920 YLL in Germany in 2010 and attributed to a wide range of cardiovascular and circulatory diseases.[25] This suggests that ATAAD's strain on the healthcare system approximates 2.5% of that of cardiovascular diseases. Comparing the standard care against substandard care or an optimised care scenario, we simulate two hypothetical situations demonstrating significant effects on YLL. The analysis underscores several time-sensitive stages that add up to the total time to definitive care. Furthermore, as the surgical care volume is known to significantly influence outcomes, early diagnosis and prompt transfer to high-volume centres is recommended, even accepting longer transport times to optimise outcomes in ATAAD care.

Impact of delay

Outcomes of ATAAD are highly time-sensitive, with the first 48 hours after symptom onset accounting for the highest risk to patients, many of whom succumb before reaching medical facilities or receiving a diagnosis. With a routine usage of scores such as the Aortic Dissection Detection Score, or a low threshold for CT imaging, a swifter diagnosis is likely. Additionally, ultrasound screening may be used to enhance the diagnosis process even further. Even minor alterations to emergency room procedures or ambulance services could significantly enhance diagnostic accuracy. Important examples include bilateral blood pressure measurement, neurological symptom checks and a thorough check for a personal or family medical history for aortic diseases. Basic implementation of diagnostic algorithms to exclude acute aortic syndrome in chest, back or thoracic pain cases would also be crucial. Classifying patient treatment as an emergency until definitive care is reached can lead to prioritisation in disposition management and thus further reduce treatment time until treatment.[26] The Berlin STEMO concept[27] and the Aortentelefon in Berlin[12] serve as excellent examples of structured approaches to preclinical processes leading to improved patient outcomes, with similar observations noted in the UK.[28 29]

Volume factor

Beyond PCT, the quality and expertise of surgical intervention may significantly impact survival. As demonstrated in our best-case and worst-case scenario, patients are likely to benefit from surgical management at high-volume centres specialised in aortic dissection surgery. Particularly high-risk patients, where surgery may be deemed too risky, could benefit from the expertise available at high-volume centres, familiar with risk/benefit estimations and individual prognosis assessments.

Striving for undelayed onsite diagnosis followed by prompt transfer to specialist aortic teams in high-volume centres is recommended and in line with international efforts to manage acute conditions as well. Orchestrated centralised care has been linked with reduced 30-day mortality and improved long-term survival of dissection in the UK.[29] Evidence from Japan suggests that the benefits of high-volume care could potentially offset concerns over prehospital transfer distance.[30] A network of highly specialised centres has proven effective for acute myocardial infarction[31] and is likely to hold true for dissection. Making use of aerial transport can further improve the tradeoff in favour of high-volume centres.[32] The low incidence and more difficult onsite diagnosis of ATAAD need to be addressed by education and awareness, a task supported by the use of our analytical tool.

Limitations

Despite the significance of our findings, there are certain limitations. First, our study relied on modelling techniques and parameterisation using available published evidence, introducing potential biases and uncertainties associated with data quality and reliability. Second, our model incorporated assumptions and simplifications to model the complex pathway of ATAAD, which may not fully capture the heterogeneity and variability of real-world scenarios. Third, the lack of patient-level data and potentially imprecise quantifications for certain input variables required the use of best-case, standard-case and worst-case scenarios, which may not encompass the full range of the clinical spectrum. Furthermore, our study focused on the population of Germany, limiting generalisability and applicability to other regions with different healthcare systems and demographics. Lastly, our model did not consider potential changes in healthcare practices or technological advancements over time, which could impact the mortality and YLL associated with ATAAD. These limitations highlight the need for further research incorporating more comprehensive data and accounting for contextual factors to enhance the accuracy and applicability of future assessments of the ATAAD burden.

Conclusion

In conclusion, this analysis uses a comprehensive modelling approach to assess the burden of ATAAD in the population of Germany. By simulating predefined scenarios and incorporating data from published evidence, valuable insights into the mortality and YLL associated with ATAAD are provided.

Our findings show that ATAAD imposes a substantial burden in terms of mortality and YLL, with a base-case mortality rate of 53.6% and a total of 102 791 YLL in the year 2020. These results highlight the need for better management strategies to improve patient outcomes and reduce the impact of this life-threatening condition.

Furthermore, our analysis demonstrated the potential influence of various scenarios on the YLL, with the best-case scenario showing a 9.3% reduction and the worst-case scenario indicating a 10.0% increase compared with the base case. These findings underscore the importance of accurate early diagnosis, timely interventions, and the significance of specialised high-volume clinics in improving patient outcomes.

We also developed an interactive dashboard to facilitate easy interaction with the model and allow for simulations of various parameters and scenarios. This tool serves as a potential resource for healthcare professionals and strategists to explore the impact of different interventions and regional healthcare systems on the burden of ATAAD.

Overall, this analysis provides important insight into the burden of ATAAD in Germany and offers a foundation for further research and informed decision-making to enhance patient care and outcomes. By addressing the challenges of ATAAD comprehensively, the aim of reducing the mortality and YLL associated with this devastating condition may become more realistic.

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