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ORIGINAL RESEARCH

# Development and Validation of a Predictive Model to Identify Patients With an Ascending Thoracic Aortic Aneurysm

Makoto Mori, MD; Geliang Gan, PhD; Yanhong Deng, MPH; Sameh Yousef, MD; Gabe Weininger, BS; Krishna R. Daggula, MS; Ritu Agarwal, MD, MS; Michael Shang, BS; Roland Assi, MD, MMS; Arnar Geirsson, MD; Prashanth Vallabhajosyula, MD, MS

**BACKGROUND:** Screening protocols do not exist for ascending thoracic aortic aneurysms (ATAAs). A risk prediction algorithm may aid targeted screening of patients with an undiagnosed ATAA to prevent aortic dissection. We aimed to develop and validate a risk model to identify those at increased risk of having an ATAA, based on readily available clinical information.

**METHODS AND RESULTS:** This is a cross-sectional study of computed tomography scans involving the chest at a tertiary care center on unique patients aged 50 to 85 years between 2013 and 2016. These criteria yielded 21 325 computed tomography scans. The double-oblique technique was used to measure the ascending thoracic aorta, and an ATAA was defined as >40 mm in diameter. A logistic regression model was fitted for the risk of ATAA, with readily available demographics and comorbidity variables. Model performance was characterized by discrimination and calibration metrics via split-sample testing. Among the 21 325 patients, there were 560 (2.6%) patients with an ATAA. The multivariable model demonstrated that older age, higher body surface area, history of arrhythmia, aortic valve disease, hypertension, and family history of aortic aneurysm were associated with increased risk of an ATAA, whereas female sex and diabetes were associated with a lower risk of an ATAA. The C statistic of the model was 0.723±0.016. The regression coefficients were transformed to scores that allow for point-of-care calculation of patients' risk.

**CONCLUSIONS:** We developed and internally validated a model to predict patients' risk of having an ATAA based on demographic and clinical characteristics. This algorithm may guide the targeted screening of an undiagnosed ATAA.

**Key Words:** comorbidity ■ computed tomography ■ risk prediction ■ risk score ■ thoracic aortic aneurysm

Ascending thoracic aortic aneurysms (ATAAs) are associated with the risk of catastrophic aortic complications, including aortic dissection and rupture.[1] To mitigate the risk of such complications, guidelines recommend prophylactic surgical replacement of an aneurysmal aorta based on the size threshold.[2] However, preemptive detection of an aneurysm is challenging, because most patients with an aortic aneurysm are asymptomatic. Therefore, the current diagnosis of an ATAA relies on incidental findings aside from workup based on high-risk genetic conditions such as Marfan syndrome or familial history of aneurysm and dissections. Although risk-based screening for an abdominal aortic aneurysm using ultrasound has led to a decrease in aneurysm-related mortality,[3,4] targeted screening protocol has not been realized for an ATAA. Barriers to risk-based targeted screening for an ATAA includes the limited understanding of risk factors for an ATAA and consequently the lack of an instrument that quantifies a patient's potential risk of having an ATAA.[5] Additionally, in the absence of a risk-prediction model that accounts for different effect sizes of various risk

Correspondence to: Prashanth Vallabhajosyula, MD, MS, Yale Aortic Institute, Yale School of Medicine, BB204, 330 Cedar Street, P.O. Box 208039, New Haven, CT 06510. E-mail: prashanth.vallabhajosyula@yale.edu

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## CLINICAL PERSPECTIVE

### What Is New?

- From 21 325 computed tomography scans, we developed a risk-prediction model to quantify individual patient risk of having an ascending thoracic aortic aneurysm based on commonly available demographic and comorbidity data.

### What Are the Clinical Implications?

- Using this risk-prediction tool, clinicians can now identify patients at increased risk of having an ascending thoracic aortic aneurysm, allowing for selective screening for an ascending thoracic aortic aneurysm using computed tomography scans.
- Such targeted screening may mitigate the current underdiagnosis and undertreatment of ascending thoracic aortic aneurysm, a major cause of aortic catastrophes.

### Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **ATAA** | ascending thoracic aortic aneurysm |

factors, it is difficult to apply known predictors in a clinical setting.

An echocardiogram cannot measure the entire thoracic aorta, and the measurement may be susceptible to operator-dependent error.[6] Therefore, the dependence on computed tomography (CT) with radiation exposure to visualize the entire thoracic aorta may present a higher threshold for recommending a population-scale screening.

Considering such unique challenges in ATAA, developing an algorithm to predict the patient's risk of having an ATAA is a critical step to targeted screening. Such an instrument to mitigate underdiagnosis and undertreatment of an ATAA is important, considering the observation that the incidence of thoracic aortic dissections may be increasing despite a concurrent increase in the number of prophylactic thoracic aortic replacements performed.[7] Large claims-based data sets have fallen short of reliably characterizing ATAA risk factors, because claims data alone lack aortic size measurement, which is critical in having a standardized definition of ATAA given that the size threshold used to define ATAA varies widely across studies and providers.[6,8]

To inform a risk-based screening protocol for ATAA, we leveraged a large CT database including standardized measurement of aortic diameter to develop and validate a prediction model to help identify patients with an ATAA, based on readily available demographic and comorbidity information.

## METHODS

The data and codes that support the findings of this study are available from the first author upon reasonable request.

### Patient Population and Data Source

This cross-sectional study was conducted at Yale-New Haven Hospital, a tertiary-care center in the United States. The institutional electronic medical record system was queried to identify patients aged ≥50 and <85 years who received CT scans, including the chest, for any indications between February 1, 2013 and December 31, 2016, either during inpatient, outpatient, or emergency department encounters. We set the lower age limit of 50 years because thoracic aortic aneurysm below age 50 years is extremely rare,[9] and the upper age limit was set because the potential benefit of detection leading to intervention decreases at older age. In patients with multiple scans, the scan with the earliest date was analyzed. These criteria yielded 21 325 CT scans with or without contrast obtained on unique patients. The institutional review board at Yale University approved this study, and individual consent was waived for the minimal risk nature of the study (institutional review board protocol ID: 2000020932, approval date: August 10, 2017).

### Definition of ATAA

ATAA was the outcome of interest and was defined as an ascending thoracic aorta of a diameter ≥4.0 cm by the double oblique technique measurement, in which the plane perpendicular to the long-axis of the aorta was defined in 3-dimensional space and the cross-sectional aorta was measured via average of outer-to-outer wall diameters measured at 60° apart from each other (Figure 1). The threshold of 4.0 cm was chosen to increase the sensitivity of detecting an enlarged aorta in the screening context, acknowledging that studies have defined aneurysm variably.[6,10] The largest portion of the aorta between the sinotubular junction and the proximal take-off of the innominate artery was measured. We did not index the aortic diameter by the body size, because the current guideline recommendations for surgical intervention is based on the diameter without indexing.[2] Because the scans included both cardiac-gated and nongated scans, we only considered aneurysms occurring in the ascending aorta, because the aortic root measurement is susceptible to motion artifacts along the cardiac cycle. Measurements were

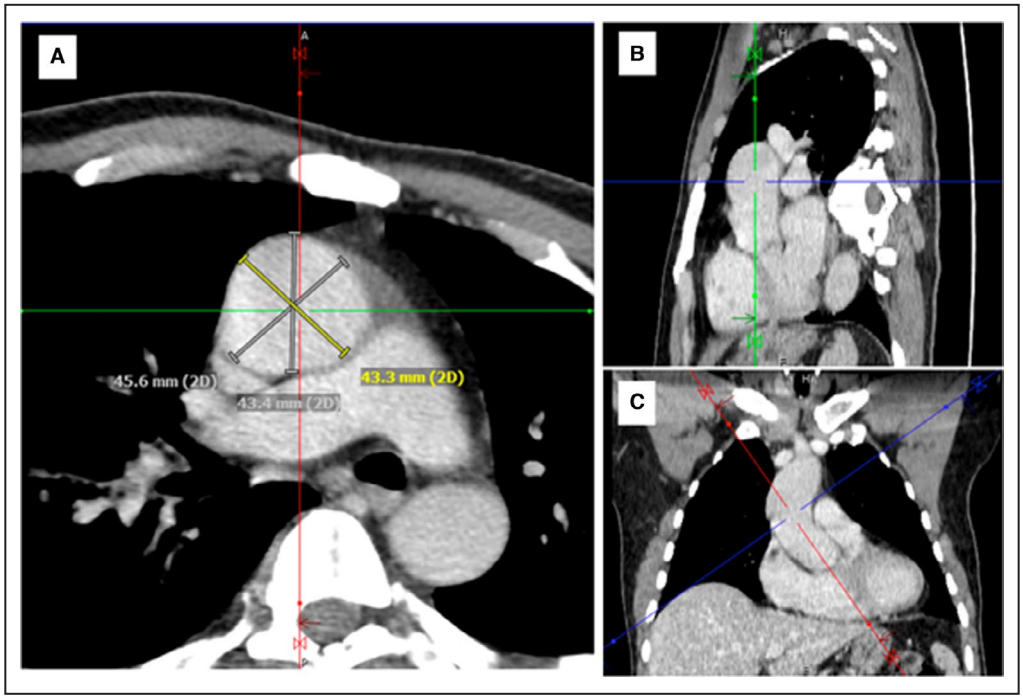


**Figure 1. Double-oblique measurement of ascending aortic aneurysm.**
The image displays an example of ascending thoracic aortic measurement using the double-oblique technique to identify the cut perpendicular to the direction of the flow of the aorta (**A**), using sagittal (**B**) and coronal (**C**) planes. Measurements are taken on 3 axes for robustness, and the average is reported. 2D, two dimensional.

performed using Visage imaging software (Visage Imaging, Richmond, Australia) by an author (S.Y.) trained by a senior member of the radiology faculty who specialized in cardiac and thoracic imaging. This investigator's measurements were compared with those of the radiologist's measurement of the aneurysm, yielding a 0.3-mm mean difference.[8]

## Predictor Variables and Missing Data

Candidate predictor variable were demographics (age, sex, race), family history of aortic aneurysm, and clinical characteristics (body surface area [BSA], pack-year smoking history, history of aneurysms outside of the aorta [*International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) code I72], and comorbidities that constituted the Elixhauser Comorbidity Index[11]) (Table S1). BSA showed a nonlinear relationship with the risk of an ATAA. On the basis of the inflexion points identified in the risk of an ATAA across BSA, we allowed the model to incorporate piecewise linear effect between BSA 1.7 to 2.2 and >2.2 $m^2$. We chose the Elixhauser Comorbidity Index to capture comorbidities that are potentially predictive of an ATAA, because the prior knowledge on the clinical risk factors for ascending aortic aneurysm was extremely sparse, and the established comorbidity index provided a list of major comorbidities capturing risks in many disease states.[12] Patients' past medical history at the time of scan were coded into *ICD-10-CM* codes, which were grouped according to Elixhauser Comorbidity Index. Given the prior knowledge of aortic valve pathologies being a risk factor for an ATAA, we substituted the valvular disorders variable in the Elixhauser Comorbidity Index with nonrheumatic aortic valve and mitral valve disorders defined by the corresponding *ICD-10-CM* codes I35 and I34. Patients who had scans before the intuitional transition to *ICD-10-CM* codes had conversion of the codes using the General Equivalence Mapping published by the Centers for Medicare and Medicaid Services and the Centers for Disease Control and Prevention.[13] The initial list of candidate variables were further refined via stepwise variable selection. There were no missing values in the demographic variables in this data set linked to the institutional electronic health record system. Because the presence or absence of comorbidities were defined by referencing the patient's past medical history list, there were also no missing values in the comorbidity variables.

## Variable Selection, Model Development, and Validation

Association between an ATAA and patient demographics and comorbidities were first evaluated using

bivariate logistic regression then multivariable logistic regression. The parsimonious model was chosen based on stepwise variable selection optimizing the Akaike information criterion value. The model performance was evaluated by stratified splitting of the data set randomly into 30:70 testing and development samples iterated over 20 times. The CIs of the performance metrics were evaluated at 5, 10, 15, 20, 25, 30, and 50 times to ensure plateauing of the confidence interval change after 20 iterations. Discrimination and calibration metrics were calculated from each of the 20 testing samples to generate 95% CIs of each performance estimate.

### Performance Metrics

We evaluated the model discrimination using the area under the receiver operating characteristic curve, which characterizes model discrimination and ranges between 0 and 1, with a higher value corresponding to better discrimination.[14] Area under the receiver operating characteristic curve is the proportion of the times patients with an event were accurately classified to have a higher probability of event within all possible pairs of patients with and without an event.[14] Calibration was characterized using the Brier score and calibration plot of the decile risks. Brier score is the mean squared error of predicted probability of event (range, 0–1) and observed event (binary 0 or 1), with lower values corresponding to higher accuracy of the prediction.[15]

### Statistical Analysis

To facilitate clinical implementation, we linearly transformed the regression coefficients for each predictor variable in the final logistic regression model and provided conversion of the total points for each patient and corresponding risk of an ATAA. The coefficients are an unexponentiated form of the odds ratio and relate to a point that can be transformed to the probability of having an ATAA, thereby allowing clinicians to enter risk factors present in a patient and obtain the risk of the patient having an ATAA. A 2-tailed $P<0.05$ was considered as statistically significant. All analyses were performed using RStudio 1.3.1073 (PBC, Boston, MA) packages "rms[16]" and "gtsummary,[17]" and SAS 9.4 (SAS Institute, Cary, NC).

## RESULTS

Among the 21 325 patients with CT scans of the chest, there were 560 (2.6%) patients who had an ATAA based on the diameter threshold of 40 mm. On unadjusted comparisons, patients with an ATAA were older, more likely to be men, with higher BSA, and with a family history of aortic aneurysm. Frequencies of comorbidities were higher in patients with an ATAA for the history of heart failure, arrhythmia, mitral and aortic valve diseases, hypertension, and renal failure. History of depression were less frequent in patients with an ATAA than those without an ATAA (Table 1).

The multivariable model demonstrated that older age (odds ratio [OR], 1.03; 95% CI, 1.02–1.04 per 1-year increase; $P<0.01$), higher body surface area (OR, 1.09; 95% CI, 1.03–1.15; $P<0.01$ per 0.1 $m^2$ increase above 1.7 up to 2.2; OR, 1.19; 95% CI, 1.09–1.28; $P<0.01$ per 0.1 $m^2$ increase above 2.2), history of arrhythmia (OR, 1.35; 95% CI, 1.11–1.64; $P<0.01$), aortic valve disease (OR, 3.17; 95% CI, 2.39–4.15; $P<0.01$), hypertension (OR, 1.47; 95% CI, 1.20–1.80; $P<0.01$), and family history of aortic aneurysm (OR, 1.22; 95% CI, 1.01–1.48; $P=0.04$) were associated with increased risk of an ATAA, whereas female sex (OR, 0.46; 95% CI, 0.37–0.57; $P<0.01$) and diabetes (OR, 0.69; 95% CI, 0.55–0.86; $P<0.01$) were associated with lower risk of an ATAA (Table 2).

Our model achieved a good predictive discrimination with area under the curve of 0.723±0.016. The Brier score of the final model was 0.0251. The calibration plot demonstrated a good alignment with the line of perfect calibration across the deciles of the risk (Figure 2). The coefficients were transformed to a score that can be translated into the probability of individual patient having an ATAA (Figure 3). The scores assigned to each risk factor are summarized in Table 3, with Figure 3 showing the conversion between the overall points and the predicted probability of an ATAA. The sensitivity and specificity of the model were 71.8% and 63.3%, 32.5% and 90.1%, 14.3% and 96.1%, and 7.9% and 98.5%, at thresholds of 2.5%, 5.0%, 7.5%, and 10.0% predicted risks, respectively.

## DISCUSSION

The current lack of instruments to facilitate targeted screening of patients with increased risk of ATAA is concerning given the US observation that increasing per capita case volume of ascending aortic operations for aneurysm has not resulted in the expected decrease in the incidence of acute aortic dissection.[7] This contrasts with abdominal aortic aneurysm, for which successful implementation of primary care screening led to the reduction in aneurysm-related mortality.[3] To facilitate systematic risk-based screening for an ATAA, we developed and internally validated an instrument to predict patients' risk of having an ATAA based on readily available demographic and comorbidity information. The performance judged by the C statistics and calibration were favorable,

**Table 1. Patient Characteristics by Those With and Without Ascending Thoracic Aortic Aneurysm**

| Variables | No aneurysm, N=20 765 | Aneurysm, N=560 | *P* value |
|---|---|---|---|
| Age, y | 66 (59, 74) | 70 (64, 77) | <0.001 |
| Sex (Women) | 9123 (44%) | 133 (24%) | <0.001 |
| Race | | | 0.061 |
| White | 16 619 (80%) | 469 (84%) | |
| Black | 2226 (11%) | 44 (7.9%) | |
| Asian | 303 (1.5%) | 11 (2.0%) | |
| Other | 1617 (7.8%) | 36 (6.4%) | |
| Body surface area, $m^2$ | 1.88 (1.69, 2.08) | 1.98 (1.78, 2.15) | <0.001 |
| Smoking pack-years | 0 (0, 20) | 0 (0, 20) | 0.9 |
| Congestive heart failure | 2211 (11%) | 93 (17%) | <0.001 |
| Arrhythmia | 3892 (19%) | 174 (31%) | <0.001 |
| Mitral valve disease | 647 (3.1%) | 28 (5.0%) | 0.012 |
| Aortic valve disease | 644 (3.1%) | 69 (12%) | <0.001 |
| Peripheral vascular disorders | 1375 (6.6%) | 42 (7.5%) | 0.4 |
| Hypertension, uncomplicated | 12 643 (61%) | 413 (74%) | <0.001 |
| Hypertension, complicated | 1421 (6.8%) | 40 (7.1%) | 0.8 |
| Paralysis | 120 (0.6%) | 2 (0.4%) | 0.8 |
| Other neurological disorders | 1346 (6.5%) | 30 (5.4%) | 0.3 |
| Chronic pulmonary disease | 6258 (30%) | 148 (26%) | 0.059 |
| Diabetes, uncomplicated | 4106 (20%) | 98 (18%) | 0.2 |
| Diabetes, complicated | 581 (2.8%) | 18 (3.2%) | 0.6 |
| Hypothyroidism | 2108 (10%) | 56 (10%) | >0.9 |
| Renal failure | 1610 (7.8%) | 64 (11%) | 0.001 |
| Liver disease | 1832 (8.8%) | 44 (7.9%) | 0.4 |
| Peptic ulcer disease | 341 (1.6%) | 9 (1.6%) | >0.9 |
| AIDS/HIV | 194 (0.9%) | 4 (0.7%) | 0.6 |
| Lymphoma | 1137 (5.5%) | 21 (3.8%) | 0.075 |
| Metastatic cancer | 3891 (19%) | 90 (16%) | 0.11 |
| Solid tumor without metastasis | 6321 (30%) | 161 (29%) | 0.4 |
| Rheumatoid arthritis/ collagen vascular disease | 921 (4.4%) | 17 (3.0%) | 0.11 |
| Coagulopathy | 636 (3.1%) | 14 (2.5%) | 0.4 |
| Fluid and electrolyte disorders | 827 (4.0%) | 23 (4.1%) | 0.9 |
| Blood loss anemia | 23 (0.1%) | 1 (0.2%) | 0.5 |
| Deficiency anemia | 263 (1.3%) | 5 (0.9%) | 0.4 |
| Alcohol use disorder | 823 (4.0%) | 20 (3.6%) | 0.6 |
| Drug use disorder | 484 (2.3%) | 7 (1.2%) | 0.092 |
| Psychoses | 316 (1.5%) | 6 (1.1%) | 0.4 |
| Depression | 3044 (15%) | 60 (11%) | 0.009 |
| Nonaortic aneurysm | 98 (0.5%) | 6 (1.1%) | 0.056 |
| Family history of aortic aneurysm | 4823 (23%) | 158 (28%) | 0.006 |

Continuous variables are expressed as median (first, third quartile).

**Table 2. Risk Factors for Ascending Thoracic Aortic Aneurysm**

| Variables | Odds ratio | 95% CI | *P* value |
|---|---|---|---|
| Age, per 1-y increase | 1.03 | 1.02–1.04 | <0.001 |
| Women, reference men | 0.46 | 0.37–0.57 | <0.001 |
| Body surface area, per 0.1-$m^2$ increase above 1.7 up to 2.2 | 1.09 | 1.03–1.15 | 0.004 |
| Body surface area, per 0.1-$m^2$ increase above 2.2 | 1.19 | 1.09–1.28 | <0.001 |
| Aortic valve disease | 3.17 | 2.39–4.15 | <0.001 |
| Arrhythmia | 1.35 | 1.11–1.64 | 0.002 |
| Hypertension | 1.47 | 1.20–1.80 | <0.001 |
| Chronic pulmonary disease | 0.83 | 0.68–1.00 | 0.054 |
| Diabetes | 0.69 | 0.55–0.86 | 0.001 |
| Lymphoma | 0.69 | 0.43–1.05 | 0.1 |
| Family history of aortic aneurysm | 1.22 | 1.01–1.48 | 0.04 |

especially in the current absence of a risk prediction instrument for an ATAA.

Potential clinical implications of this instrument are the following. First, the parsimonious nature of the model is regulated to only 10 variables required to calculate the predicted risk. Such a simple model has advantages in implementation. Complex models that leverage large number of variables could improve model performance, but manual entry of variables become prohibitive and has a substantial overhead to integrate into the electronic health record systems to automate such data entry. Integration across multiple health systems that use different electronic health record systems would pose further challenges to such a model.[18,19] In contrast, our risk prediction algorithm with the scores can be used via simple addition of points with the corresponding predicted probability of a patient having an ATAA. Integration of such simple calculation in an app platform is also feasible. This likely would facilitate broad adoption, including external validation at different hospitals and in various patient groups. Second, comorbidity and demographic data are readily available without the need to perform specific laboratory tests or imaging. Therefore, such information is essentially available for any patient who had or is having a clinical encounter.

Several of the risk factors identified in this model have been suggested in large claims-based studies, including male sex, larger body habitus, higher age, diabetes, and hypertension.[20,21] Although claims data sets used in such studies lack the rigor of an ATAA diagnosis based on aortic measurement and are often limited by the *ICD-9* codes' inability to distinguish ascending from descending pathologies,[22] our findings based on ATAA diagnosis adjudicated by standardized measurement of the aorta may support these associations

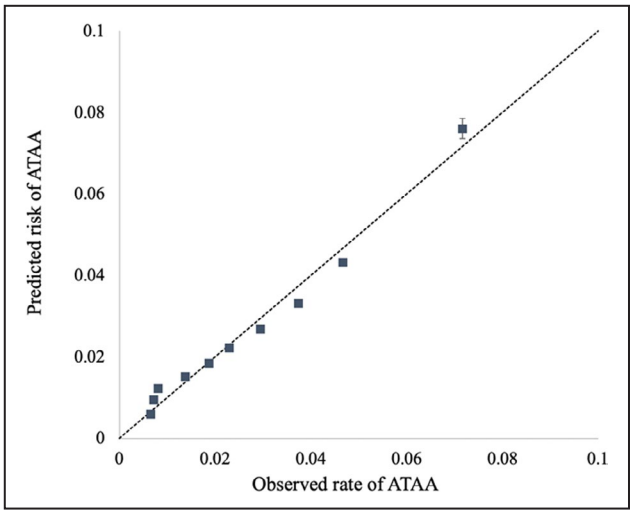


**Figure 2. Calibration plot.**
The figure shows a calibration plot of the logistic regression model predicting the risk of an ascending thoracic aortic aneurysm (ATAA) by the deciles. Confidence intervals (only visible for the top decile) were generated from iterating the random-sample split 20 times.

previously suggested. The causal pathways behind arrhythmia being associated with increased risk of an ATAA is unclear. A large observational study in Taiwan suggested an association between atrial fibrillation and abdominal aortic aneurysm,[23] but it is possible that atrial fibrillation was residually confounded with hypertension and larger body habitus.[24] Additionally, leveraging our electronic medical record system, we obtained an extensive family history. Expectedly, family history of aortic aneurysm was significantly associated with the risk of an ATAA.

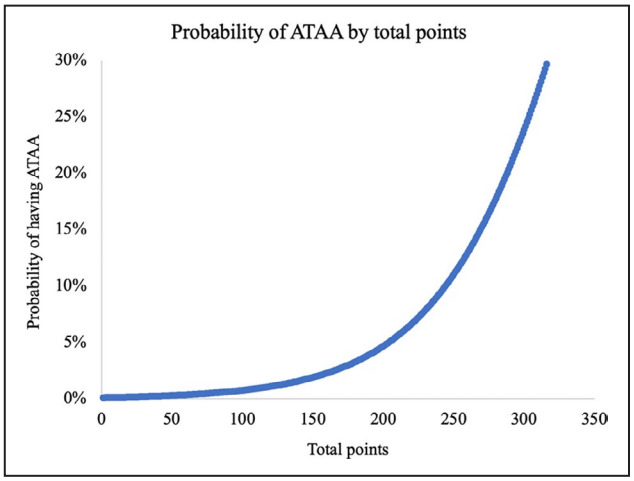


**Figure 3. Conversion between total points and predicted ascending thoracic aortic aneurysm (ATAA) risk.**
The figure shows the conversion relationship between the total points based on comorbidity and demographics outlined in Table 2 and the patient's predicted risk of having an ATAA.

**Table 3. Risk Algorithm for Ascending Thoracic Aortic Aneurysm**

| Variable | Value | Corresponding point |
|---|---|---|
| Age | Per 1-year increase above age 50 y | 7.5 |
| Sex | Women | 0 |
| | Men | 35 |
| Body surface area | Per 0.1-$m^2$ increase above 1.7 $m^2$ up to 2.2 $m^2$ | 4 |
| | Per 0.1-$m^2$ increase above 2.2 $m^2$ | 7.7 |
| Chronic pulmonary disease | Yes | 0 |
| | No | 9 |
| Diabetes | Yes | 0 |
| | No | 17 |
| Hypertension | Yes | 17 |
| | No | 0 |
| Arrhythmias | Yes | 14 |
| | No | 0 |
| Lymphoma | Yes | 0 |
| | No | 17 |
| Family history of aortic aneurysm | Yes | 9 |
| | No | 0 |
| Aortic valve disease | Yes | 52 |
| | No | 0 |

Probability of an ascending thoracic aortic aneurysm (ATAA) = $e^{(-6.1+\text{total point}/44.9)} / (1+e^{(-6.1+\text{total point}/44.9)})$. For an individual patient, the sum of the corresponding point base can be entered into the equation above in place of total point to yield the predicted probability of an ATAA. Multiplying the probability by 100 would yield the risk of an ATAA in percentage points. For example, a 65-year-old man with a body surface area (BSA) of 2 $m^2$, hypertension, no diabetes, arrhythmia, and aortic valve disease would have 112.5 (7.5 points×15) points for age, 35 points for male sex, 12 points for BSA (4 points×3), 17 points for hypertension, 17 points for no diabetes, 14 points for arrhythmia, and 52 points for aortic valve disease for a total of 259.5 points, which corresponds to a 13% predicted risk of having an ATAA.

Unlike the well-established association between smoking and abdominal aortic aneurysm,[25] smoking was not associated with increased risk of an ATAA in this study. This may be related to the predominantly nonatherosclerotic nature of the ascending aortic pathology compared with descending pathologies[26] and may highlight the importance of evaluating ascending and descending pathologies separately. In contrast to previous studies suggesting the association between aortic and extra-aortic aneurysms, history of nonaortic aneurysm was not significantly associated with the risk of an ATAA. This may support the notion that some extra-aortic aneurysms are atherosclerotic in nature, whereas that of the ascending aorta is predominantly degenerative, and the presence of an aneurysm may not necessarily increase the risk of having an aneurysm elsewhere.

Clinical implementation of the model requires caution, because the model has not been validated in

a prospective setting. Provided there are costs of CT scans and downstream effect of follow-ups and potential for inducing patient anxiety, we present the following scenario implementing screening CT scan in patients with >10% predicted risk of having an ATAA, a relatively high threshold considering the ATAA prevalence of 2.6%. Assuming 5-year rupture or dissection risk of 16% in ascending aortic diameter >4.0 cm,[27] 30-day mortality of 32% from acute type A aortic dissection (based on nationwide and Medicare beneficiary estimates),[28,29] 1 mortality would occur in every 3 dissections, and 1 dissection would occur in 5 years in every 7 untreated or undetected ascending aneurysms. If CT scans, at the estimated cost of $380,[30] are to be performed on patients with 10% predicted risk, 210 scans are required to prevent 1 in-hospital mortality. This equates to the cost of $79 800 per life saved. Considering that an ideal life-saving intervention would cost <$158 000 to save the life of a patient aged 80 years and <$540 000 for a patient aged 50 years,[31] we consider the monetary cost of CT scans a reasonable one, even accounting for the cost of aortic surgery bundle.

## Limitations

The generalizability of our model to the general population is unknown, because we did not restrict the cohort by the clinical indications for obtaining the CT scan. Additionally, our cohort was limited to those who underwent CT scan for a clinical indication, and may not reflect the relationship between the predictor variables and the risk of an ATAA in general adult populations in the community. However, the observed prevalence of ATAA is comparable to prior studies, suggesting that although our center is a tertiary center specializing in aortic care, our cohort was not enriched by those with higher risk of an ATAA.[32] The generalizability of this model developed in patients who had various indications for thoracic imaging to a broader community population requires further assessment.

Elixhauser Comorbidity Index variables used to develop the model have been well established in predicting short- and long-term mortality in various clinical contexts, but their importance in predicting an ATAA had not been known. Therefore, the resulting variables retained in the final model may not appear clinically granular enough to provide mechanistic insights. However, we modified the coding of valvular heart disease to those specific to aortic and mitral valves to provide additional granularity. Further study is needed to understand the mechanistic importance of clinical conditions identified in this model development process. Regardless, the comorbidity classification system combined with demographics and family history data provided a practical starting point to develop a risk model using a large data set containing image-based aortic diameter measurement.

# CONCLUSIONS

We developed and internally validated a risk model to identify patients aged between 50 and 85 years who are at increased risk of having an ascending aortic aneurysm based on demographic and clinical characteristics. Discrimination and calibration of the model were good. This prediction rule may guide the targeted screening of patients at increased risk of having an ascending aortic aneurysm.

# ARTICLE INFORMATION

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## Affiliations

Divison of Cardiac Surgery, Yale School of Medicine, New Haven, CT (M.M., S.Y., G.W., M.S., R.A., A.G., P.V.); Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, CT (M.M.); Yale Center for Analytical Sciences, New Haven, CT (G.G., Y.D.); Joint Data Analytics Team, Yale New Haven Health System, New Haven, CT (K.R.D., R.A.); and Yale Aortic Institute, Yale School of Medicine, New Haven, CT (R.A., P.V.).

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## Disclosures

Dr Geirsson receives a consulting fee as a member of the Medtronic Strategic Surgical Advisory Board. The remaining authors have no disclosures to report.

## Supplementary Material

Table S1

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# SUPPLEMENTAL MATERIAL

Table S1. ICD-10 code used to define comorbidities.

| Comorbidity | ICD10 code |
|---|---|
| Congestive heart failure | I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, 142.5-I42.9, I43.x, I50.x, P29.0 |
| Cardiac arrhythmias | I44.1-I44.3, I45.6, I45.9, I47.x-I49.x, ROO.O, ROO.1, ROO.8, T82.1, Z45.0, Z95.0 |
| Aortic valve disease | I34.x |
| Mitral valve disease | I35.x |
| Pulmonary circulation disorders | I26.x, I27.x, I28.0, I28.8, I28.9 |
| Peripheral vascular disorders | I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9 |
| Hypertension, uncomplicated | I10.x |
| Hypertension, complicated | I11.x-I13.x, I15.x |
| Paralysis | G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0-G83.4, G83.9 |
| Other neurological disorders | G10.x-G 13.x, G20.x-G22.x, G25.4, G25.5, G31.2, G31.8, G31.9, G32.x, G35.x-G37.x, G40.x, G41.x, G93.1, G93.4, R47.0, R56.x |
| Chronic pulmonary disease | I27.8, 127.9, J40.x-J47.x, J60.x-J67.x, J68.4, J70.1, J70.3 |
| Diabetes, uncomplicated | E10.0, E10.1, E10.9, E11.0, E11.1, E11.9, E12.0, E12.1, E12.9, E13.0, E13.1, E13.9, E14.0, E14.1, E14.9 |
| Diabetes, complicated | E10.2-E10.8, E11.2-E11.8, E12.2-E12.8, E13.2-E13.8, E14.2-E14.8 |
| Hypothyroidism | E00.x-E03.x, E89.0 |
| Renal failure | I12.0, I13.1, N18.x, NI9.x, N25.0, Z49.0-Z49.2,Z94.0, Z94.0, Z[1]99.2 |
| Liver disease | B18.x, I85.x, I86.4, I98.2, K70.x, K71.1, K71.3-K71.5, K71.7, K72.x-K74.x, K76.0, K76.2-K76.9. Z94.4 |
| Peptic ulcer disease excluding bleeding | K25.7, K25.9, K26.7, K26.9, K27.7, K27.9, K28.7, K28.9 |
| AIDS/H1V | B20.x-B22.x, B24.x |
| Lymphoma | C81.x-C85.x, C88.x, C96.x, C90.0, C90.2 |
| Metastatic cancer | C77.x-C80.x |
| Solid tumor without metastasis | C00.x-C26.x, C30.x-C34.x, C37.x-C41.x, C43.x, C45.x-C58.x, C60.x-C76.x, C97.x |
| Rheumatoid arthritis/ collagen vascular diseases | L94.0, L94.1, L94.3, M05.x, M06.x, M08.x, M12.0, M12.3, M30.x, M31.0-M31.3, M32.x-M35.x, M45.x, M46.1, M46.8, M46.9 |
| Coagulopathy | D65-D68.x, D69.1, D69.3-D69.6 |

| | |
|---|---|
| Obesity | E66.x |
| Weight loss | E40.x-E46.x, R63.4, R64 |
| Fluid and electrolyte disorders | E22.2, E86.x, E87.x |
| Blood loss anemia | D50.0 |
| Deficiency anemia | D50.8, D50.9, D51.x-D53.x |
| Alcohol abuse | F10, E52, G62.1, I42.6, K29.2, K70.0, K70.3, K70.9, T51.x, Z50.2, Z71.4, Z72.1 |
| Drug abuse | F11.x-F16.x, F18.x, F19.x, Z71.5. Z72.2 |
| Psychoses | F20.x, F22.x-F25.x, F28.x, F29.x, F30.2, F31.2, F31.5 |
| Depression | F20.4, F31.3-F31.5, F32.x, F33.x, F34.1, F41.2, F43.2 |
| Non-aortic aneurysms | I72.x |

The ICD-10 codes are defined based on Elixhauser comorbidity index.