



## Clinical Research

# Prevalence of Incidentally Identified Thoracic Aortic Dilations: Insights for Screening Criteria

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### ABSTRACT

**Background:** Systematic screening for ascending thoracic aortic aneurysms and dilations does not exist currently with unknown prevalence and diagnostic yields. We evaluated the prevalence of ascending thoracic aortic dilation.

**Methods:** Computed tomography scans including the chest in adult patients carried out during 2016 were reviewed at our institution. Aortic dilation was defined as the ascending thoracic aorta diameter  $\geq 4.0$  cm, with sensitivity analyses using height-indexed values and thresholds of 3.5, 4.25, and 4.5 cm. The prevalence of aortic dilation was evaluated by age and sex. Potential diagnostic yield along the continuum of age threshold was calculated by sex.

**Results:** Of the 5662 scans from unique patients, the prevalence of aortic dilation was 2.1% overall, 3.2% for males and 0.9% for females. Patients with aneurysms were significantly older ( $70.2 \pm 9.9$  vs  $58.3 \pm 16.4$  years,  $P < 0.001$ ) and more likely to be male (81.0% vs 54.2%,  $P < 0.001$ ). The highest diagnostic yield of aneurysm  $\geq 4.5$  cm in females occurred at the age threshold of  $\geq 73$  years, with the yield of

### RÉSUMÉ

**Contexte :** En l'absence actuelle d'un dépistage systématique des anévrismes et des dilatations de l'aorte thoracique ascendante, la prévalence et le rendement diagnostique de ces anomalies sont inconnus. Nous avons évalué la prévalence de la dilatation de l'aorte thoracique ascendante.

**Méthodologie :** Nous avons passé en revue les tomодensitogrammes couvrant la région thoracique réalisés chez des patients adultes en 2016 dans notre établissement. La dilatation aortique a été définie par un diamètre de l'aorte thoracique ascendante  $\geq 4,0$  cm et les analyses de sensibilité ont utilisé des valeurs indexées en fonction de la hauteur et des seuils de 3,5, de 4,25 et de 4,5 cm. La prévalence de la dilatation aortique a été évaluée selon l'âge et selon le sexe. Le rendement diagnostique potentiel d'un bout à l'autre du continuum des seuils d'âge a été calculé selon le sexe.

**Résultats :** L'analyse des 5662 tomодensitogrammes, correspondant chacun à un patient différent, a révélé que la prévalence de la dilatation aortique était de 2,1 % globalement, soit de 3,2 % chez les

In thoracic aortic aneurysms, aortic diameter is used as a threshold for prophylactic operative interventions to prevent aortic dissections or rupture.<sup>1,2</sup> Preemptive detection of thoracic aortic aneurysms poses a challenge, as aneurysms are typically asymptomatic. Ultrasound screening has been implemented in the detection of abdominal aortic aneurysms for men 65 years or older, with an associated decrease in abdominal aortic aneurysm rupture.<sup>3</sup> However, the majority of the thoracic aortic territory cannot be screened by ultrasound, leaving computed tomography (CT) as the most practical modality for this purpose. The existing population-

based studies are outdated and limited in the cohort size, so the contemporary incidence of thoracic aortic aneurysm is unknown.<sup>4</sup> The lack of knowledge of the prevalence associated with thoracic aortic aneurysm also constitutes a hurdle in establishing a cost-effective, targeted identification of patients at risk of dissection and rupture. To this extent, we conducted a review of all CT scans involving the chest obtained during the calendar year 2016 at a tertiary care centre in the United States to evaluate the prevalence of incidentally identified ascending thoracic aortic dilation, and to identify a patient group with the highest yield for CT-mediated diagnosis by the use of sex and age thresholds.

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See page 898 for disclosure information.

### Methods

#### Setting and patient population

Yale-New Haven Hospital is a tertiary care centre in the United States. The electronic medical records were queried to

0.5%. The highest diagnostic yield of aneurysm  $\geq 4.5$  cm in males occurred at age  $\geq 84$  years, with the yield of 5.7%. In males, the diagnostic yields at age thresholds of  $\geq 50$ ,  $\geq 60$ , and  $\geq 70$  years were 1.3%, 1.6%, and 2.2%, respectively.

**Conclusions:** Aortic dilation was identified in 2.8% of individuals with age  $\geq 50$  years. In females, aneurysm was uncommon. In males, there was an incremental increase in the diagnostic yield with age. Male patients with age  $\geq 50$  years may be the demographic group with a high prevalence of dilation.

identify patients with age  $\geq 18$  years who received CT scans including the chest for any indications during the calendar year 2016. There were 7910 CT scans including the chest that were performed in the year. After excluding multiple scans obtained on the same patient during the year, there were 6088 scans obtained on unique patients. In patients with multiple scans, the scan with the latest date was used for the analysis. Because the clinical benefit conferred by preemptive identification of aortic aneurysms and dilations diminishes in patients with advanced age, scans obtained on patients older than 85 years were excluded. In addition, patients who underwent CT for the surveillance of known thoracic aortic aneurysm were excluded. The final cohort consisted of 5662 patients with age less than 85 years without known thoracic aortic aneurysms before the index scans. Indications for obtaining the CT scans were categorized into the following groups: oncologic workup excluding lung nodule follow-up and lung cancer screening, infection-related workup, trauma workup, lung nodule follow-up, lung cancer screening, pain workup, and preoperative workup for nonaortic surgeries. The Institutional Review Board at Yale University approved this study.

### Definition of ascending thoracic aortic aneurysm

As the risk of rupture and dissection differs in ascending and descending thoracic aneurysm, we evaluated only dilations involving the ascending aorta in this study. Ascending thoracic aortic dilation was defined as a thoracic aorta of diameter  $\geq 4.0$  cm by the centre-line 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 the average of diameters measured at  $60^\circ$  apart from each other (Supplemental Fig.S2). The threshold of 4.0 cm is quite inclusive, but as this study intended to broadly identify potential screening targets, this definition was adopted for our primary analysis. Because the definition of aneurysm and dilation differs across studies,<sup>5</sup> from those using varying diameters to those using indexed values, by the body surface area or height, subsequent analyses in this study used additional size thresholds of 3.5, 4.25, and 4.5 cm. In addition, analysis using the recently reported aortic height index was performed. The aortic height index, defined as the aortic diameter in centimetres divided by the patient's

height in metres, has been shown to have better test characteristics in predicting adverse events when compared with diameter alone or indexing by body surface area.<sup>6</sup>

**Conclusions :** Une dilatation aortique a été observée chez 2,8 % des individus âgés de 50 ans ou plus. Chez les femmes, l'anévrisme était rare. Chez les hommes, on a constaté une augmentation graduelle du rendement diagnostique avec l'âge. Les patients de sexe masculin âgés de 50 ans ou plus pourraient être le groupe démographique affichant la prévalence de la dilatation la plus élevée.

### Statistical analysis

Differences in the patient characteristics were compared with the 2-tailed *t* test for continuous variables, the  $\chi^2$  test for categorical variables, and Fisher's exact test for categorical variables with cell size  $\leq 5$ . Continuous variables are summarized by mean with standard deviation, unless otherwise specified. Scatter plots were used to depict distributions of aneurysm by the diameter and patient age. Correlations between age and diameter were evaluated with a linear model using the  $R^2$  value. To evaluate the diagnostic yield at a range of age thresholds, the prevalence of dilation above specified age thresholds was calculated across the range of age 50 to 85 years. The correlation between the prevalence and age threshold was evaluated with a quadratic model using the  $R^2$  value. The multivariable logistic regression model was fitted for the dependent variable of aortic dilation of  $\geq 4.0$  cm and the following independent variables: age, sex, race, history of hypertension, dyslipidemia, smoking, and pack-years of smoking. The *P* value of  $< 0.05$  was used to define a statistically significant difference. All analysis was conducted with SAS 9.4 (SAS Institute Inc, Cary, NC).

### Results

Of the 5662 scans obtained from unique patients, 121 (2.14%) were incidentally found to have ascending thoracic aortic dilation of size  $\geq 4.0$  cm in diameter. Patient characteristics are outlined in Table 1. Patients with aortic dilation were significantly older compared with those without dilation ( $70.2 \pm 9.9$  vs  $58.3 \pm 16.4$  years,  $P < 0.001$ ) and more likely to be male (81.0% vs 54.2%,  $P < 0.001$ ). A higher proportion of Caucasian patients were found in the dilation cohort compared with the cohort without dilation (81.8% vs 71.3%,  $P = 0.043$ ), and a lower proportion of African American patients were present in the dilation cohort (12.4% vs 15.2%,  $P = 0.043$ ). Clinical settings (outpatient, inpatient, and emergency department) in which the CT scan was obtained did not differ significantly between the groups

**Table 1. Patient characteristics by aortic dilation ( $\geq 4.0$  cm) and no dilation**

Variables	No dilation (n = 5541)	Percentage or standard deviation	Dilation (n = 121)	Percentage or standard deviation	Overall (n = 5662)	Percentage or standard deviation	P value
Age (y)	58.3	16.4	70.2	9.9	58.6	16.4	<b>&lt; 0.001</b>
$\geq 65$ and $< 85$	2177	39.3%	90	74.4%	2267	40.0%	<b>&lt; 0.001</b>
$\geq 50$ and $< 65$	1904	34.4%	28	23.1%	1932	34.1%	
$< 50$	1460	26.3%	3	2.5%	1463	25.8%	
Male	3003	54.2%	98	81.0%	3101	54.8%	<b>&lt; 0.001</b>
Race							
Caucasian	3953	71.3%	99	81.8%	4052	71.6%	<b>0.043</b>
African American	842	15.2%	15	12.4%	857	15.1%	
Asian	95	1.7%	3	2.5%	98	1.7%	
Other	560	10.1%	4	3.3%	564	10.0%	
Missing/declined to report	91	1.6%	0	0.0%	91	1.6%	-
Clinical settings							
Outpatient	2098	37.9%	51	42.1%	2149	38.0%	<b>0.035</b>
Inpatient	1984	35.8%	51	42.1%	2035	35.9%	
Emergency	1435	25.9%	19	15.7%	1454	25.7%	
Comorbidity							
Hypertension	3197	57.7%	79	65.3%	3276	57.9%	0.10
Dyslipidemia	2366	42.7%	44	36.4%	2410	42.6%	0.17
Cocaine use	22	0.4%	0	0.0%	22	0.4%	0.47
Smoking history	1779	32.1%	53	43.8%	1832	32.4%	<b>0.0063</b>
Pack-year*	27.3	23.2%	29.8	25.1%	27.3	23.3	0.42

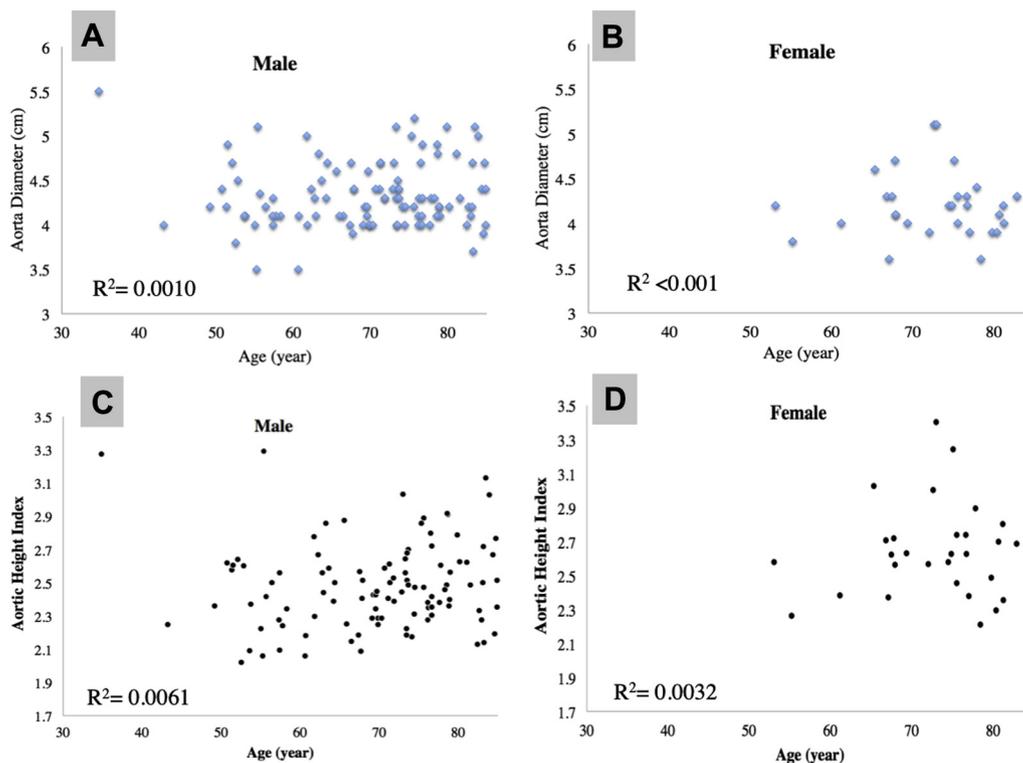
P values are calculated from comparisons between aneurysm and no aneurysm groups. Dilation cohort is defined as those with ascending aortic aneurysm  $\geq 4.0$  cm in diameter. Bold front indicates  $P < 0.05$ .

\*Pack-year calculated only for those with positive smoking history.

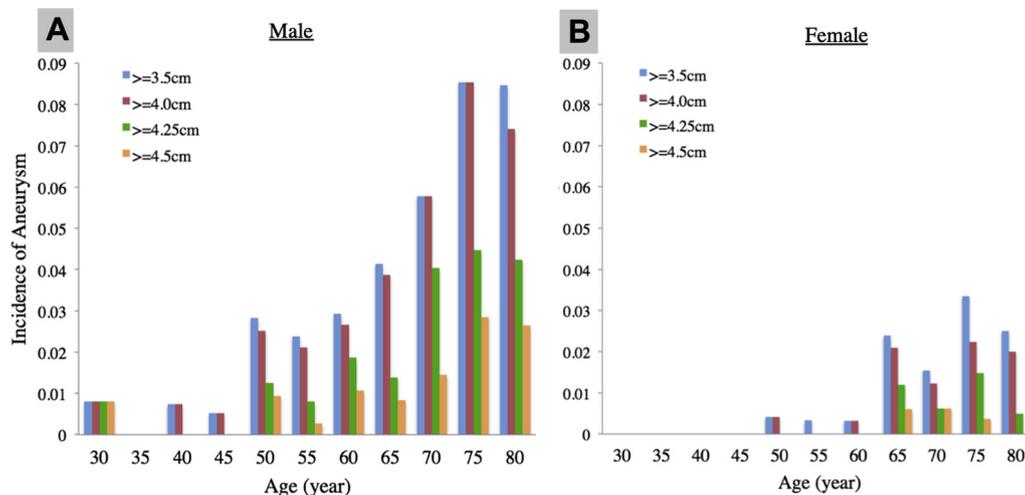
(Table 1). Hypertension was more common in the aortic dilation cohort, whereas dyslipidemia, cocaine use, smoking history, and pack-years of smoking were similar between the groups.

Distributions of ascending aorta size by age, stratified by sex, are summarized in Figure 1. The size by diameter and by

aortic height index are demonstrated. There were no correlations between the age and aortic diameter or aortic height index ( $R^2 < 0.01$  for all). Compared with the number of CT scans obtained in the population with age  $\geq 50$  years, scans obtained in the population with age  $< 50$  years were expectedly less (4199 vs 1463 scans,  $P < 0.001$ ), and the



**Figure 1.** Scatter plot diagrams of the aneurysm size and age, stratified by sex. (A, B) Distribution by the aorta diameter (male and female, respectively). (C, D) Distribution by the aortic height index (male and female, respectively).  $R^2$  values are of linear fits.



**Figure 2.** Histograms of the incidence of aneurysm, calculated by the number of aneurysm divided by the number of computed tomography scans within the 5-year incremental age groups. (A) Male and (B) female data. Size thresholds by the diameter are color coded.

prevalence of dilation in patients with age < 50 years was exceedingly rare (0.21%), with only 3 male patients having dilations among 1463 unique patients with scans. The distribution of the number of scans obtained in each age group by sex is displayed in Supplemental Figure S1. Within the population with age ≥ 50 years, the prevalence of dilation ≥ 4.0 cm was 2.81% (118/4199) overall, 4.3% (95/2212) for males and 1.2% (23/1987) for females. Figure 2 displays the prevalence of aneurysm above a range of aneurysm size threshold by age and sex. In males, the prevalence of aortic dilation ≥ 4.0 cm increased incrementally towards older age groups, peaking at a prevalence of 8.5% in the group aged 75-80 years. Across all age groups, the prevalence in females was lower than that of males, with the prevalence peaking in the group aged 75-80 years, at 2.1%.

Table 2 outlines the size characteristics of aortic dilation. Of 121 patients with diameter ≥ 4.0 cm, 87 (71.9%) had sizes ≥ 4.0 and < 4.5 cm, and 34 (28.1%) had size ≥ 4.5 cm. The rate of diagnostic yield of ascending thoracic aortic dilation above age thresholds is displayed in Figure 3. In all size categories, the male group assumed quadratic fit with positive slope, indicating an incremental increase in the diagnostic yield as the age threshold increased. However, the female group assumed quadratic fit with negative slope, indicating an incremental decrease with increasing age threshold. The diagnostic yield of dilation ≥ 4.5 cm in females was remarkably low: the highest yield occurred at the age threshold of ≥ 73 years, with the yield of 0.46%. The highest diagnostic yield of dilation ≥ 4.5 cm in males occurred at age ≥ 84 years, with the yield of 5.66%. In males, the diagnostic yields at age thresholds of ≥ 50, ≥ 60, and ≥ 70 years were 1.26%, 1.58%, and 2.18%, respectively.

Results of the multivariable logistic regression model are summarized in Table 3. An increase in age and male sex were strongly associated with the increased risk of having an aortic dilation of ≥ 4.0 cm. Dyslipidemia was the only comorbidity that demonstrated a trend towards association with the decreased risk of having aortic dilation.

## Discussion

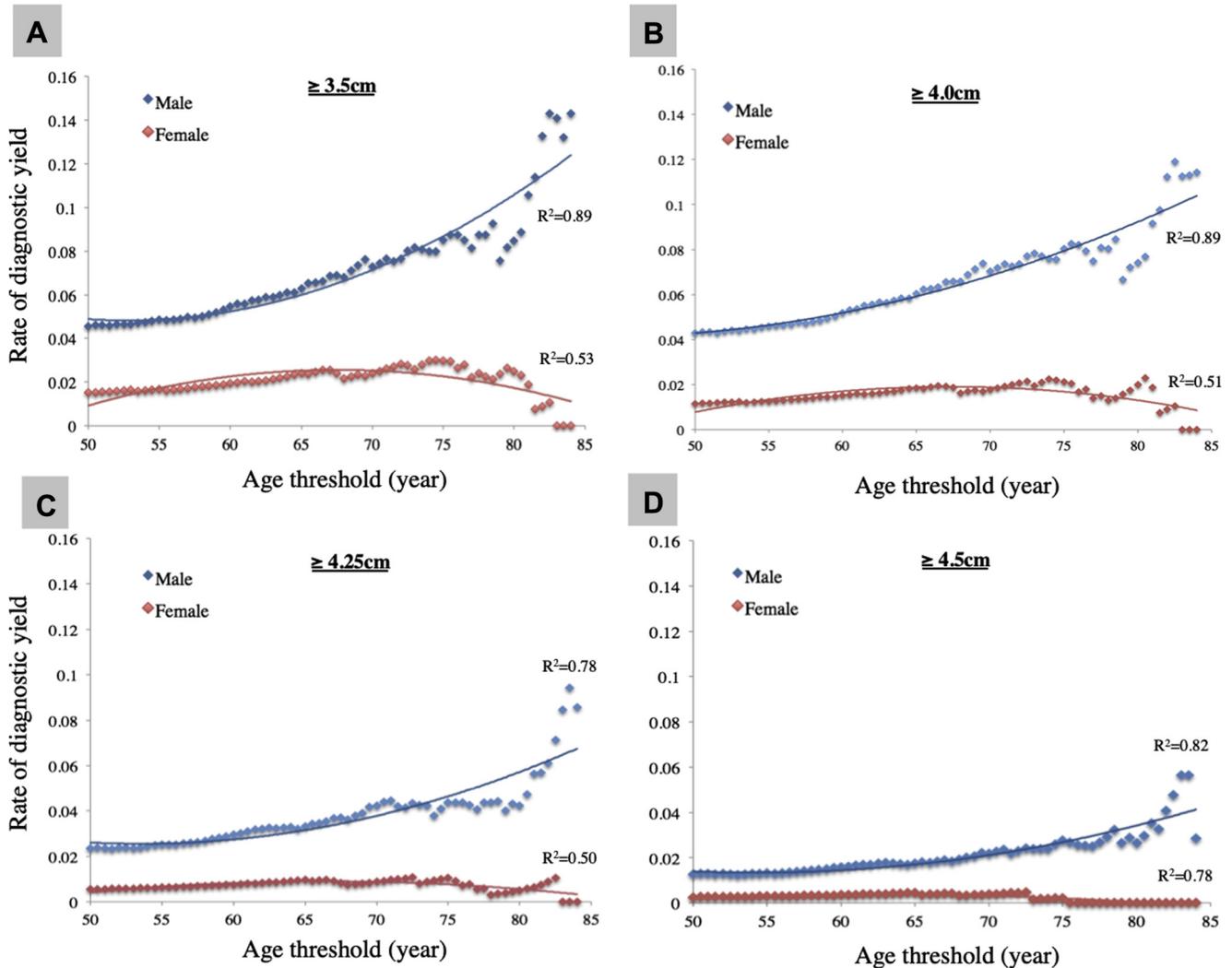
This cross-sectional review of all CT scans involving the chest obtained in patients with age ≥ 18 at a large tertiary academic centre revealed that the prevalence of incidentally identified ascending thoracic aortic dilation of ≥ 4.0 cm was 2.1%, with 97.8% of dilations occurring in patients with age ≥ 50 years. In females with age ≥ 50 years, clinically pertinent aneurysm (≥ 4.5 cm) was exceedingly uncommon at 0.3%. The prevalence of aortic diameter ≥ 4.5 cm was significantly higher in male with age ≥ 50 years at 1.3%. In males, there was a significant correlation between age and the prevalence of dilation, with a steady increase in diagnostic yield at higher age thresholds across the age range examined (50-85 years), peaking at the age threshold of ≥ 84 years with the yield of 5.7% for dilation ≥ 4.5 cm. Although these data may suggest that CT-mediated identification for thoracic

**Table 2. Aortic diameter, patient height, and scan indications**

Variables	Diameter ≥ 4.0 cm (n = 121)
Diameter, mean ± SD (cm)	4.4 ± 0.3
≥ 4.0 and < 4.5	87 (71.9%)
≥ 4.5	34 (28.1%)
Aortic height index,* mean ± SD	2.6 ± 0.3
< 2.4	38 (31.4%)
≥ 2.4 and < 2.7	56 (46.3%)
≥ 2.7 and < 3.0	18 (14.8%)
≥ 3.0	9 (7.4%)
CT scan indications	
Nonpulmonary oncologic	49 (40.5%)
Infection workup	17 (14.1%)
Trauma workup	14 (11.6%)
Lung nodule follow-up	12 (9.9%)
Lung cancer screening	9 (7.4%)
Pain workup	6 (5.0%)
Preoperative workup	0 (0%)
Miscellaneous	11 (9.1%)
Cardiac surgery referrals	9 (6.7%)

CT, computed tomography.

\* Cutoffs for the strata of aortic height index were modified based on Zafar et al.<sup>6</sup>



**Figure 3.** Rates of diagnostic yield by computed tomography scans in identifying ascending thoracic aortic aneurysm above the given diameters: (A)  $\geq 3.5$  cm, (B)  $\geq 4.0$  cm, (C)  $\geq 4.25$  cm, and (D)  $\geq 4.5$  cm. The rate of diagnostic yield represents the prevalence of aneurysm above the age threshold by 0.5-year increment indicated in the horizontal axis. The data points are stratified by sex, with blue indicating male and red indicating female. The quadratic model was used to fit the data points, and  $R^2$  values are indicated in each figure.

aortic dilation may have the highest yield in male patients with age  $\geq 50$  years, further risk modelling is needed to identify additional risk factors for aneurysm to refine the criteria.

Risk factors for aortic abdominal aneurysms (AAA) have been fairly well characterized through large prospective cohorts, with increased age, male sex, non-black race, family history, atherosclerotic disease, and smoking history, all being associated with the increased risk of AAA. Surprisingly, our multivariable model did not demonstrate hypertension or smoking history to be a significant predictor of ascending aortic dilation. In addition, the history of dyslipidemia was associated with the decreased risk of having aortic dilatation. This may be reconciled by the observation that the pathogenesis of ascending and descending aortopathy differ from each other and that descending aortopathy is associated with the atherosclerotic process whereas ascending aorta may not. Because the prevalence of aortic dilation even at the threshold of 3.5 cm was low in this cohort, it is possible that certain

variables were underpowered for rigorous interrogation of such association. Age and sex were strongly predictive in accordance with prior reports.

The Multicentre Aneurysm Screening Study enrolling men aged 65-74 years for ultrasonographic AAA screening demonstrated a 53% reduction in aneurysm-related deaths by

**Table 3. Multivariable model for predictors of aortic dilation**

Variables	OR	95% CI	P value
Age (per 1 y increase)	1.06	1.04 - 1.09	<b>&lt; 0.001</b>
Male (ref: female)	4.15	2.61 - 6.60	<b>&lt; 0.001</b>
Asian race (ref: white)	1.36	0.41 - 4.52	0.61
Black race (ref: white)	1.15	0.65 - 2.04	0.63
Other race (ref: white)	0.59	0.21 - 1.62	0.30
Hypertension	1.27	0.84 - 1.92	0.25
Dyslipidemia	0.57	0.38 - 0.85	0.0054
Smoking history	1.05	0.63 - 1.74	0.86
Pack-year of smoking	1.00	0.99 - 1.01	0.86

CI, confidence interval; OR, odds ratio.

Bold font indicates  $P < 0.05$ .

screening.<sup>8</sup> Consequently, the current guideline on AAA screening by the US Preventive Services Task Force is 1-time screening for AAA with ultrasound in men aged 65-75 years who have ever smoked.<sup>9</sup> This combination of age and smoking history as screening criteria coincides with the current recommendation for lung cancer screening, which recommends low-dose CT screening in adults aged 55-80 years who have 30 pack-years of smoking history and currently smoke or have quit within the past 15 years.<sup>10</sup> This overlap likely provides an opportunity to further study cost-effective screening of thoracic aortic aneurysms by CT scans, although it should be noted that only 7.5% of the aneurysms were detected by the CT scans obtained for this indication in our study.

Although a clear association existed between the increased age and prevalence of ascending thoracic aortic dilations, there was no clear association between age and the size or the aortic height index of dilations (Fig. 1). A longitudinal study has demonstrated a diameter increase at the rate of 0.1 cm/y in thoracic aortic aneurysms.<sup>11</sup> This seeming discrepancy between the existing data and the current finding may be due to the significant variability in the growth rate among individuals and variable baseline aneurysm size<sup>12</sup> that may have rendered the correlation insignificant in this cross-sectional study. In addition, although longitudinal data may capture the size increase at an individual level, it is possible that this may not translate into the correlation between overall absolute size and age. The growth rate does appear to be accelerated in individuals with smoking history,<sup>12</sup> likely owing to the reduced tissue integrity associated with smoking. Integration of smoking status may aid in refining meaningful screening criteria for thoracic aortic aneurysms.

A surprising finding was that although the male cohort demonstrated a clear increase in the diagnostic yield and prevalence at increasing age thresholds, this trend was not observed in female cohort (Fig. 3). The quadratically fitted curve in Figure 3 indicates that males have an incremental increase in both the diagnostic yield and the rate of increase in the diagnostic yield along the age continuum. In contrast, the same curve for females had a negative slope, indicating that there was an increase in diagnostic yield up to the age of 70-75 years, after which the yield declined. As Figure 2 demonstrates, the prevalence of aneurysm in females was low even at the peak age group of 70-75 years, and perhaps this rendered the data more susceptible to random noise. To our knowledge, such findings have not been reported, and this trend deserves further interrogation.

Efforts in identifying biomarkers as screening tools for thoracic aortic aneurysm have been largely disappointing due to their lack of specificity, although some, including matrix metalloproteinase, C-reactive protein, and lipoprotein(a), were deemed sensitive.<sup>13</sup> In contrast, some promising findings have been reported in genetic variants. Namely, 2 single-nucleotide polymorphisms in the *FBN-1* gene, which encodes fibrillin-1, have been associated with an odds ratio of 1.6-1.8 for thoracic aortic aneurysms and dissections.<sup>14,15</sup> With the advent of rapid sequencing technology at low cost, a genetic approach holds promise to augment the screening effort. Regardless of the screening approach, populational studies to further identify risk factors for thoracic aortic aneurysm are needed to guide a targeted, cost-effective screening effort. Ultimately,

such screening effort must be demonstrated to have a populational impact in altering the natural course of the disease and overall improvement in clinical outcomes.

Our study demonstrated an incremental increase in the prevalence of ascending thoracic aortic aneurysms with the increase in age in the male cohort, with the highest prevalence observed at the age threshold of  $\geq 84$  years, which is essentially at the upper limit of our inclusion criteria. These data pose a dilemma in determining the optimal upper age limit for the screening criteria, regardless of the modality used. Age is a major risk factor for adverse surgical outcomes, and many providers likely experience hesitations in recommending thoracic aortic surgeries to octogenarians for asymptomatic aneurysms. Although there exist single-centre reports on satisfactory outcomes for ascending thoracic aortic and arch surgeries in octogenarians,<sup>16</sup> the approach to proceed with surgery must be an individualized process. The epiaortic "wrap" technique, in which a durable synthetic material is anchored and wrapped over the dilated aorta without the use of cardiopulmonary bypass or cross-clamping,<sup>17</sup> may present a reasonable low-risk alternative to this population with advanced age to minimize the surgical risks while providing the mechanical support with a reasonable durability. With such potential low-risk therapeutic alternatives, we would advocate for setting a higher upper limit for the screening.

### Limitations

This study harbours limitations inherent to the single-centre study design. The tertiary-care setting of the centre may have biased the patient population towards more complex patients with a distinct set of comorbidities, although the relevance of such patient characteristics to the incidence of thoracic aortic dilation is unknown. As the purpose of the study was to characterize patients with aortic dilations that were incidentally identified, patients with the known history of aneurysms were excluded. This perhaps resulted in an underestimation of the true prevalence, although this exclusion was applied for the generalizability of the finding to centres without a dedicated aortic centre. The Aortic Institute at Yale-New Haven Hospital has seen 964 patients presented electively for the first time between 2011 and 2017. The extent of analysis in evaluating the incidence of thoracic aortic dilation is limited by the limited comorbidity data, although we believe that with the lack of epidemiological data for thoracic aortic aneurysms, demographics and incidences render themselves valuable. Further implications towards implementation of a cost-effective screening protocol must first consider improvement in patient outcomes related to preemptive detection of aortic aneurysms.

### Conclusions

The prevalence of ascending thoracic aortic dilation in individuals with age  $\geq 50$  years was 2.8%. In females, clinically pertinent aneurysm was exceedingly uncommon. In males, there was a significant correlation between age and the prevalence of dilation, with an incremental increase in the diagnostic yield at higher age thresholds. This correlation was not clearly observed in females. These data may argue for CT-mediated screening for thoracic aortic dilation and aneurysm to initially focus on male patients with age  $\geq 50$  years.

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## Disclosures

The authors have no conflicts of interest to disclose.

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## Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at [www.onlinecjc.ca](http://www.onlinecjc.ca) and at <https://doi.org/10.1016/j.cjca.2019.03.023>.