Increased Aortic Diameters on Multidetector Computed Tomographic Scan Are Independent Predictors of Incident Adverse Cardiovascular Events

The Framingham Heart Study

Saadia Qazi, DO, MPH; Joseph M. Massaro, PhD; Michael L. Chuang, MD; Ralph B. D’Agostino, Sr., PhD; Udo Hoffmann, MD, MPH; Christopher J. O’Donnell, MD, MPH

Background—Adverse aortic remodeling, such as dilation, is associated with multiple cardiovascular disease (CVD) risk factors. We sought to determine whether measures of enlarged aortic diameters improve prediction of incident adverse CVD events above standard CVD risk factors in a community-dwelling cohort.

Methods and Results—Participants from the Framingham Offspring and Third Generation Cohorts (n=3318; aged 48.9±10.3 years), who underwent noncontrast thoracic and abdominal multidetector computed tomography during 2002 to 2005, had complete risk factor profiles, and were free of clinical CVD, were included in this study. Diameters were measured at 4 anatomically defined locations: the ascending thoracic aorta, descending thoracic aorta, the infrarenal abdominal aorta, and lower abdominal aorta. Adverse events comprised CVD death, myocardial infarction, coronary insufficiency, index admission for heart failure, and stroke. Each aortic segment was dichotomized as enlarged (diameter ≥ upper 90th percentile for age, sex, and body surface area) or not enlarged; the hazard of an adverse event for an enlarged segment was determined using multivariable-adjusted Cox proportional hazards models. Over a mean 8.8±2.0 years of follow-up, there were 177 incident adverse CVD events. In models adjusted for traditional CVD risk factors, enlarged infrarenal abdominal aorta (hazard ratio=1.57; 95% confidence interval=1.06 to 2.32) and lower abdominal aorta (hazard ratio=1.53; 95% confidence interval=1.00 to 2.34) were associated with an increased hazard of CVD events. Enlarged ascending thoracic aorta and descending thoracic aorta were not significantly associated with CVD events.

Conclusions—Among community-dwelling adults initially free of clinical CVD, enlarged infrarenal abdominal aorta and lower abdominal aorta, on noncontrast multidetector computed tomography scans, are independent predictors of incident adverse CVD events above traditional risk factors alone. (Circ Cardiovasc Imaging. 2017;10:e006776. DOI: 10.1161/CIRCIMAGING.117.006776.)

Key Words: aorta, thoracic cardiovascular diseases coronary artery disease epidemiology multidetector computed tomography
abdominal aorta [LAA]) and sought to determine the association of these measures with incident adverse CVD events.

**Methods**

The data, analytic methods, and study materials may be available to other researchers for purposes of reproducing the results or replicating the procedure contingent on obtaining appropriate approval per the Framingham Heart Study’s Research Application Review Process & Procedures.

**Study Population**

Participants from the Framingham Offspring and Third Generation cohorts who underwent cardiac MDCT scanning from 2002 to 2005 and had complete risk factor profiles were included in this study. Men had to be ≥35 years of age and women were ≥40 years and nonpregnant to qualify for MDCT scanning. Nonpregnant status was verified by questionnaire and urine pregnancy test ≤24 hours before the MDCT study. All participants weighed <160 kg because of scanner limitations. Participants provided written informed consent, and the study was approved by the institutional review boards of the Boston University Medical Center and the Massachusetts General Hospital.

**Risk Factor and End Point Ascertainment**

The Offspring and Third Generation cohorts have been previously described. For the present study, covariates were collected during the Offspring cycle 7 (1998–2001) or Third Generation cycle 1 (2002–2005) examinations that were most adjacent in time to the MDCT substudy. Height and weight were measured with participants in light clothing. Body mass index was calculated as weight divided by the height squared (kg/m²). BSA was calculated using the Mosteller formula. A venous blood draw was obtained after a 12-hour overnight fast. An interim history, which included medications taken and smoking status, was obtained via interview and questionnaires. A physical examination was performed by a physician, which included 2 separate brachial blood pressure measurements using a mercury sphygmomanometer; the average of the 2 blood pressure measurements was used. Current cigarette smoking was defined by smoking ≥1 cigarette daily during the past year. Hypertension was defined as a systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or the use of antihypertensive medication. Diabetes mellitus was defined as a fasting plasma glucose ≥126 mg/dL or treatment with insulin or antihyperglycemic medication. Hyperlipidemia was defined as a serum cholesterol ≥240 mg/dL or use of lipid-lowering therapy.

The primary end point was a composite of incident events which included myocardial infarction, coronary insufficiency (prolonged ischemic chest pain of >15 minutes accompanied by documented transient ischemic S-T segment and T-wave abnormality without coronary artery calcium), transient ischemic attack, coronary insufficiency (prolonged ischemic chest pain of >15 minutes accompanied by documented transient ischemic S-T segment and T-wave abnormality without coronary artery calcium), transient ischemic attack, or CVD death. If a participant experienced >1 primary event, the first event was considered in our analyses. Outcomes were associated with an increased hazard of incident adverse CVD events, which is described in detail by Rogers et al. We previously reported a detailed description of absolute aortic diameter measures at the different levels and their associations with risk factors. These measurements were highly reproducible.

**Statistical Analysis**

Baseline characteristics of participants are presented as mean and SD, median and interquartile range, or as a number and percentage as appropriate. Continuous variables between men and women were compared using the 2-sample t test. Categorical variables were compared between men and women using the χ² test.

Aortic diameters vary with age, sex, and BSA. We previously described normal reference values (for age-, sex-, and BSA-specific upper 90th percentile [P90] cut points to define high aortic diameters) in this population based on a healthy referent group free of prevalent CVD, hypertension, and previous valvular or aortic surgery. For the current analyses, participants with a history of adverse CVD events and valvular or aortic surgery before MDCT scanning were excluded.

**Primary Analyses**

Multivariable-adjusted Cox proportional hazards models were constructed to determine whether enlarged segmental aortic diameters were associated with an increased hazard of incident adverse CVD events. Model 1 adjusted for age and sex. Model 2 adjusted for CVD risk factors defined by the American Heart Association/American College of Cardiology, which included age, sex, systolic blood pressure, total and high-density lipoprotein cholesterol, diabetes mellitus, and current smoking. In an additional exploratory model (model 3), we adjusted for the above CVD risk factors plus the burden of coronary artery calcium. Each model also included an interaction-by-sex term as hypothesis-generating analyses. Our primary exposure consisted of dichotomized aortic diameters (≥P90 cut point). The secondary exposure was continuous aortic diameters (with hazard ratios [HRs] expressed in increments of 1 SD). We also constructed Kaplan–Meier survival curves for each segment, which compared event-free survival between individuals with and without enlarged (≥P90) aortic diameters.

We then sought to determine the incremental prognostic value of individual aortic diameter segments that were found to be independent predictors of CVD events in our Cox models. We used the categorical net reclassification improvement (NRI) metric to assess the effect of individually adding enlarged aortic diameters to model 2 on model performance.

**Secondary Analyses**

Although our primary analyses sought to determine whether individual, dilated segments of the aorta were predictors of incident adverse CVD events, in secondary analyses, we assessed whether the number of enlarged segments seen on MDCT scanning in an individual was also associated with an increased risk of CVD events. We constructed Cox proportional hazards models using the same covariates (model 1, model 2, and model 3) from our primary analyses. Our exposure was categorized as having 1 enlarged segment, 2 enlarged segments, or 3 to 4 enlarged segments. The referent group consisted of study participants with no enlarged segments. We constructed Kaplan–Meier models.
survival curves for each number of dilated segments. We compared event-free survival for individuals without any aortic enlargement and those with a total of 1, 2, or 3 to 4 enlarged aortic segments.

Results
Baseline characteristics of the 3318 participants are described in Table 1. Men comprised 1686 (51%) of the total participants. Women were slightly older than men. The prevalence of diabetes mellitus, hypertension, and use of lipid-lowering therapy was higher in men than women. Coronary artery calcium prevalence was greater among men (54.4%) than women (33.1%). Aortic diameter measures at each segment were larger in men than in women. Over a mean of 8.8±2.0 years, there were 177 incident adverse CVD events. Myocardial infarction (n=66) and stroke (n=60) accounted for 71% (126 of 177) of CVD events. Overall, women had fewer events than men (men=99, women=78 events, respectively).

Primary Results
Table 2 describes the association of enlarged (≥P90) aortic diameters with incident adverse CVD events. In model 2, enlarged (dichotomized) IRA (HR=1.57; 95% confidence interval [CI]=1.06 to 2.32) and LAA (HR=1.53; 95% CI=1.00 to 2.34) were both associated with an increased hazard of CVD events. In model 3, IRA and LAA remained positively associated with CVD events even after addition of coronary artery calcium to standard CVD risk factors (Table 3). Testing for interaction-by-sex for each aortic segment resulted in a significant association for LAA in model 1 but not in multivariable-adjusted models (models 2 and 3).

We conducted parallel analyses to evaluate the association of our secondary exposure of continuous (per 1 SD) aortic diameters with incident adverse CVD events (Table 3). In multivariable models 2 and 3, there was a significant association between continuous LAA and incident adverse CVD events (Table 3). There was also an interaction-by-sex for LAA in models 2 and 3 (Table 3). Continuous IRA was not associated with adverse CVD events (Table 3). This finding differs from the overall strong relationship seen between dichotomized IRA and CVD events. Although dichotomized DTA was not associated with CVD events, greater continuous DTA was in models 2 and 3.

On addition of dichotomized IRA (NRI=1.93%; 95% CI=−0.6% to 4.7%) and LAA (NRI=0.59%; 95% CI=−1.4% to 3.2%) to the traditional CVD risk factors in model 2, we found that the incremental prognostic value of these segments was not statistically significant. However, the addition of continuous LAA to model 2 (NRI=18.62%; 95% CI=12.2% to 27.2%) resulted in appropriate movement of participants to a higher risk category compared with the model that did not include continuous LAA. The addition of continuous DTA appeared to not have any incremental prognostic value (NRI=0.00%; 95% CI=−3.2% to 3.2%) above traditional CVD risk factors. In Figure 1, we illustrate via Kaplan–Meier survival curves that event-free survival is decreased for individuals with enlarged aortic diameters (≥P90).

Secondary Results
Table 4 describes the results of Cox proportional hazards models constructed to identify whether participants with multiple enlarged aortic segments are at increased risk of CVD events. Among individuals with 2 segments that were enlarged (≥P90), the model adjusted for traditional CVD risk factors (model 2) demonstrated that the risk of incident adverse CVD event was 2.3-fold higher when compared with individuals without any enlarged aortic diameter segments. Among participants with 3 or 4 enlarged segments, HRs were indicative of a positive relationship with CVD events; however, the associations did not achieve statistical significance. In Figure 2, Kaplan–Meier survival curves illustrated that event-free survival was the lowest among individuals with 3 to 4 enlarged aortic diameters.

Discussion
In this study of 3318 community-dwelling adults, high (≥P90) aortic diameters stratified by age, sex, and BSA) abdominal aortic diameters, specifically IRA and LAA, were associated with an increased hazard of incident adverse CVD events in multivariable Cox proportional hazards models adjusted for traditional CVD risk factors. In multivariable models that further adjusted for coronary artery calcium in addition to traditional CVD risk factors, coronary artery calcium did
not attenuate HRs for the association of IRA and LAA with CVD events. In parallel analyses for continuous aortic diameters, the relationship for LAA with CVD events remained significant. In our primary analysis, dichotomized, enlarged thoracic aortic diameters (AA and DTA) were not associated with an increased hazard of CVD events in multivariable-adjusted models although the HRs indicated a positive relationship. Continuous DTA was associated with an increased risk of incident adverse CVD events compared with individuals without any enlargement of the aorta.

### In the Context of the Current Literature
The distribution of aortic diameters and normal reference values measured on CT scanning have been described previously. Prior literature has also demonstrated that there is an association between CVD risk factors and aortic dilation. Abdominal aortic aneurysm as a risk factor for nonaneurysmal CVD has also been previously described. However, the data are sparse on the clinical and prognostic value of enlarged aortic diameter measurements on CT scanning in a community-dwelling population.

Thoracic aortic diameters, such as those from the AA and DTA, have been weakly associated with CVD events in previous literature. Gondrie et al found that the ascending

### Table 2. Cox Proportional Hazards Regression Models for Association of High (>90th Percentile Cut Point) Aortic Diameter With Incident Cardiovascular Disease Events

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted Model</th>
<th>Model 1*</th>
<th>Model 2†</th>
<th>Model 3‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI) P Value</td>
<td>Interaction-by-Sex P Value</td>
<td>HR (95% CI) P Value</td>
<td>Interaction-by-Sex P Value</td>
</tr>
<tr>
<td>AA</td>
<td>1.51 (1.03–2.23) 0.04</td>
<td>0.08</td>
<td>1.36 (0.92–2.00) 0.12</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTA</td>
<td>2.05 (1.44–2.93) &lt;0.001</td>
<td>0.18</td>
<td>1.45 (1.01–2.07) 0.04</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRA</td>
<td>2.22 (1.53–3.21) &lt;0.001</td>
<td>0.13</td>
<td>1.74 (1.20–2.52) 0.004</td>
<td>0.79</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAA</td>
<td>1.73 (1.15–2.60) 0.009</td>
<td>0.57</td>
<td>1.43 (0.95–2.16) 0.08</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AA indicates ascending thoracic aorta; CI, confidence interval; DTA, descending thoracic aorta; HR, hazard ratio; IRA, infrarenal abdominal aorta; and LAA, lower abdominal aorta.

*Model 1=Adjusted for age and sex.
†Model 2=Adjusted for model 1+systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, hypertension treatment, current smoking, and diabetes mellitus.
‡Model 3=Adjusted for model 2+coronary artery calcium.

### Table 3. Cox Proportional Hazards Regression Models for Association of Continuous Aortic Dilation (per 1 SD) With Incident Adverse Cardiovascular Disease Events

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted Model</th>
<th>Model 1*</th>
<th>Model 2†</th>
<th>Model 3‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI) P Value</td>
<td>Interaction-by-Sex P Value</td>
<td>HR (95% CI) P Value</td>
<td>Interaction-by-Sex P Value</td>
</tr>
<tr>
<td>AA, per SD</td>
<td>1.74 (1.53–1.99) 0.001</td>
<td>0.78</td>
<td>1.10 (0.93–1.30) 0.25</td>
<td>0.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTA, per SD</td>
<td>1.90 (1.74–2.07) &lt;0.001</td>
<td>0.02</td>
<td>1.35 (1.17–1.57) &lt;0.001</td>
<td>0.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRA, per SD</td>
<td>1.62 (1.48–1.77) &lt;0.001</td>
<td>0.82</td>
<td>1.17 (1.03–1.33) 0.01</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAA, per SD</td>
<td>1.49 (1.37–1.60) &lt;0.001</td>
<td>0.31</td>
<td>1.18 (1.06–1.32) 0.003</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AA indicates ascending thoracic aorta; CI, confidence interval; DTA, descending thoracic aorta; HR, hazard ratio; IRA, infrarenal abdominal aorta; and LAA, lower abdominal aorta.

*Model 1=Adjusted for age and sex.
†Model 2=Adjusted for model 1+systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, hypertension treatment, current smoking, and diabetes mellitus.
‡Model 3=Adjusted for model 2+coronary artery calcium.
Qazi et al  Aortic Diameters are Predictors of CVD Events

Aorta conferred a borderline risk of CVD with every millimeter of diameter squared increase (HR=1.002; 95% CI=1.00 to 1.004), and the descending aorta was associated with a risk of CVD for every millimeter increase in diameter (HR=1.04; 95% CI=1.03 to 1.07). However, their study could not adjust for additional potential confounders because covariate data were limited to information available on radiology referral forms.18 Our study extends the findings of Gondrie et al18 by adjusting for confounders including systolic blood pressure, total and high-density lipoprotein cholesterol, diabetes mellitus, and current smoking. Within our study cohort, thoracic aortic dilation has been previously associated with CVD risk factors, including age, male sex, and hypertension.6 After adjusting for traditional CVD risk factors, high thoracic aortic diameters were not associated with CVD events, but HRs did demonstrate a positive relationship, and continuous DTA was associated with CVD events.

The abdominal aorta (IRA and LAA) was strongly associated with CVD events. This is consistent with findings from the Tromsø Study, which included 6640 participants, aged 25 to 84 years, who had maximal infrarenal aortic diameters measured on abdominal ultrasound. Over a 10-year follow-up, diameters ranging from 27 to 29 mm increased the risk of CVD mortality (mortality rate ratio=1.92; 95% CI=1.16 to 3.19) in age- and sex-adjusted models when compared with referent diameters from 21 to 23 mm. Diameters ≥30 mm were associated with a significantly higher risk of CVD mortality (mortality rate ratio=9.24; 95% CI=4.07 to 20.97). Interaction-by-sex testing yielded an association with total mortality that was stronger in men versus women, but this was not apparent for the outcome of CVD mortality.19 Our data demonstrate an association of abdominal aortic dilation at 2 different levels with CVD events including CVD death, non-fatal myocardial infarction, stroke, heart failure, and coronary insufficiency. Our findings are generally concordant with the notion that adverse remodeling, resulting in aortic dilation, leads to adverse events, and there may be sex-related differences in risk of adverse events.

Although the Tromsø study provides important insights into the prognostic value of aortic dilation, there was a paucity of mortality events, and this may have influenced its results.19 Norman et al20 included a larger cohort of men (n=12203) in their study who were aged 65 to 83 years and underwent abdominal aortic aneurysm screening via infrarenal abdominal ultrasound. Diameters of 23 to 26 mm (HR=1.26; 95% CI=1.09 to 1.44) and 27 to 30 mm (HR=1.35; 95% CI=1.09 to 1.67) were associated with higher all-cause mortality in multivariable models.20 Although the sample size in the Tromsø study was robust, it excluded women. The present study investigates the prognostic value of aortic diameters at different levels of the abdominal aorta in a population consisting of community-dwelling men and women.

In the Cardiovascular Health Study, among 4734 participants aged ≥65 years, ultrasound-measured abdominal aortic diameters ranging from 20 to 30 mm were associated with a 17% increased hazard of total mortality (HR=1.17; 95% CI=1.02 to 1.35) when compared with a referent group of participants with aortic diameters <20 mm.21 The mean age of the population analyzed within the Cardiovascular Health Study was substantially greater (men=75.2 years; women=74.6 years) than in our Framingham MDCT cohort (men=48.9 years; women=51.7 years). The present study

Figure 1. Kaplan–Meier curves showing increased event-free survival for participants with and without enlarged (A) ascending (AA), (B) descending thoracic (DTA), (C) infrarenal (IRA), and (D) lower abdominal (LAA) aortic segments.
extends the age range examined in prior studies while still showing an association between enlarged aortic diameters and CVD events.

Recently, Duncan et al.22 demonstrated that among men screened for abdominal aortic aneurysm (n=8146) who were aged 65 to 74 years and were followed for a median of 7.4 years, after adjusting for potential confounders, a significant relationship between nonaneurysmal dilation and CVD death was not seen. Diameters of ≥25 mm conferred an increased risk of first hospital admission because of hypertensive disease (HR=1.29; 95% CI=1.08 to 1.54), ischemic heart disease (HR=1.55; 95% CI=1.29 to 1.87), and heart failure (HR=2.55; 95% CI=1.93 to 3.37) when compared with referent diameters of ≤24 mm. Our findings in the Framingham cohort are compatible with those of Duncan et al.22 because we previously found enlarged aortic diameters were associated with hypertension, and in the present study, we identified an association with CVD events inclusive of heart failure, myocardial infarction, and coronary insufficiency. The study by Duncan et al.22 was limited by exclusion of women (on the assumption that aortic dilation is more common among men).

Our study extends the literature by investigating the association of increased aortic diameters on noncontrast MDCT scanning with CVD events. Although ultrasound is readily available, CT scanning is routinely obtained for countless indications in the clinical setting from which the aorta is visualized and aortic diameters can be easily measured at multiple segments. Unlike ultrasound, CT imaging is less affected by obesity and body habitus, overlaying rib and lung tissue in the thorax, and bowel gas in the abdomen.2

Table 4. Cox Proportional Hazards Models for Association Number of Enlarged (>90th Percentile Cut Point for Age, Sex, and Body Surface Area) Segments of the Aorta With Incident Adverse Cardiovascular Disease Events

<table>
<thead>
<tr>
<th>No. of Enlarged Aortic Diameter Segments</th>
<th>0 (n=2345)</th>
<th>1 (n=596)</th>
<th>P Value</th>
<th>2 (n=217)</th>
<th>P Value</th>
<th>3–4 (n=138)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No events</td>
<td>105</td>
<td>31</td>
<td></td>
<td>25</td>
<td></td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Event rate</td>
<td>4.5%</td>
<td>5.2%</td>
<td></td>
<td>11.5%</td>
<td></td>
<td>11.6%</td>
<td></td>
</tr>
<tr>
<td>Unadjusted model</td>
<td></td>
<td></td>
<td>1.16 (0.77–1.73)</td>
<td>0.48</td>
<td>2.67 (1.73–4.13)</td>
<td>&lt;0.001</td>
<td>2.73 (1.61–4.61)</td>
</tr>
<tr>
<td>Model 1†</td>
<td></td>
<td></td>
<td>1.03 (0.69–1.54)</td>
<td>0.88</td>
<td>2.28 (1.47–3.53)</td>
<td>&lt;0.001</td>
<td>1.63 (0.96–2.78)</td>
</tr>
<tr>
<td>Model 2‡</td>
<td></td>
<td></td>
<td>0.93 (0.62–1.41)</td>
<td>0.74</td>
<td>2.22 (1.42–3.47)</td>
<td>&lt;0.001</td>
<td>1.62 (0.93–2.83)</td>
</tr>
<tr>
<td>Model 3‡</td>
<td></td>
<td></td>
<td>0.97 (0.64–1.46)</td>
<td>0.88</td>
<td>2.32 (1.48–3.63)</td>
<td>&lt;0.001</td>
<td>1.65 (0.94–2.88)</td>
</tr>
</tbody>
</table>

*Model 1=Adjusted for age and sex.
†Model 2=Adjusted for model 1+systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, hypertension treatment, current smoking, and diabetes mellitus.
‡Model 3=Adjusted for model 2+coronary artery calcium.

Figure 2. Kaplan–Meier curves showing increased event-free survival for participants with and without multiple (ie, 0, 1, 2, 3–4) enlarged aortic segments.
Our data do not allow us to directly extrapolate our findings to aortic diameters measured on ultrasound. Furthermore, although prior studies have demonstrated an association of aortic diameters with adverse events, literature on the incremental prognostic value of individual, enlarged aortic segments is limited. Similarly, our secondary analyses add another dimension to the current literature by demonstrating that multiple, enlarged segments identified on CT scanning of an individual may independently predict the risk of CVD events.

Potential Mechanisms
As demonstrated previously, aortic dilation is associated with traditional CVD risk factors. These include hypertension, age, male sex, and smoking.

The propensity for aortic dilation to occur in the abdominal aorta, specifically at the level of the IRA, on exposure to CVD risk factors has been previously described. This relationship has been attributed to smaller diameters in addition to differing connective tissue content (higher elastin and lower collagen) in the abdominal aorta compared with the thoracic aorta. Because of these unique histological characteristics in concert with a greater tendency for atherosclerosis and a strong association with risk factors that differ from those associated with the thoracic aorta, that is, smoking, the IRA may be more sensitive to multiple stressors resulting in connective tissue breakdown and remodeling that leads to aortic dilation. Although the IRA is more often described in the literature, a similar mechanism may be attributed to the LAA. The association of enlarged aortic diameters, IRA and LAA specifically, may be a marker of pre-existing subclinical CVD that may provide additional information for predicting the risk of clinically evident CVD.

Clinical Implications
Aortic diameters can be measured accurately and reproducibly on MDCT ordered for any clinical indication and may provide additional information to appropriately identify individuals at increased risk for CVD. Rogers et al reported cut points and a nomogram that may be used clinically among community-dwelling adults. That said, we do not propose CT scanning be performed solely to measure aortic diameters for CVD risk stratification, but we note that aortic diameters obtained incidentally on scans performed for other indications may have additional value for assessment of CVD risk.

Strengths and Limitations
The Framingham Heart Study cohorts comprise community-dwelling adults followed closely with meticulous collection of clinical characteristics through history and risk factor ascertainment by trained investigators rather than through self-report. Each adverse CVD event was adjudicated after extensive review of all available records by a panel of physician-investigators using standardized criteria, as opposed to based solely on participant self-report or billing codes. Previous analyses of this study population have demonstrated that aortic diameter measurements from noncontrast CT images are highly reproducible at the levels of the AA, DTA, IRA, and LAA. However, our study is not without limitations. Data on the occurrence of aorta and valve surgery are not reported in our study because these participants were excluded. Obliquity and tortuosity of the aorta may influence diameter measurements on axial CT imaging; however, in our image analyses, we attempted to mitigate these effects as described by Rogers et al. Finally, the Framingham Offspring and Third Generation cohorts are predominantly middle-aged and overwhelmingly of European ethnicity; this may limit generalization to other age groups or races.

Conclusion
Aortic diameters increase with greater age and burden of common CVD risk factors. We found that enlarged abdominal aortic diameters are associated with excess CVD events over and above both traditional CVD risk factors and may have value in augmenting CVD risk stratification of individuals who undergo routine CT evaluation for various other clinical indications without requiring additional testing.

Sources of Funding
This project was supported by the National Heart, Lung and Blood Institute’s Framingham Heart Study (contract numbers N01-HC-25195 and N01-HC-38038).

Disclosures
None.

References
9. Hoffmann U, Massaro JM, Fox CS, Manders E, O’Donnell CJ. Defining normal distributions of coronary artery calcium in women and men (from...
CLINICAL PERSPECTIVE

Adverse aortic remodeling (dilation) has been associated with traditional cardiovascular disease risk factors. The present study demonstrates that enlarged thoracic aortic diameters (≥90th percentile diameter for age, sex, and body surface area) of the infrarenal and lower aortic aortas are independent predictors of incident adverse cardiovascular disease events in community-dwelling adults. Presently, the infrarenal aortic diameter is screened for abdominal aortic aneurysm in men in routine clinical practice. However, we demonstrate that enlargement of other regions in the aorta, namely the descending thoracic, infrarenal, and lower abdominal segments, may prognosticate incident adverse cardiovascular disease events. These segmental aortic diameters can be easily and accurately ascertained from tomographic imaging of the chest and abdomen obtained for any clinical indication. Because aortic diameters are commonly measured on axial imaging and do not require additional analysis, these measures may provide valuable clinical information that can be used to identify and appropriately categorize individuals at risk of developing cardiovascular disease events. However, we do not propose obtaining computed tomographic imaging of the chest or the abdomen specifically for the measurement of aortic diameters. When imaging is available in the appropriate clinical setting, aortic diameter measurements may provide additional important information on a patient.
Increased Aortic Diameters on Multidetector Computed Tomographic Scan Are Independent Predictors of Incident Adverse Cardiovascular Events: The Framingham Heart Study
Saadia Qazi, Joseph M. Massaro, Michael L. Chuang, Ralph B. D'Agostino, Sr., Udo Hoffmann and Christopher J. O'Donnell

Circ Cardiovasc Imaging. 2017;10:
doi: 10.1161/CIRCIMAGING.117.006776
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2017 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/10/12/e006776

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Imaging can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Imaging is online at:
http://circimaging.ahajournals.org//subscriptions/