Published in final edited form as:

Acad Radiol. 2013 November ; 20(11): . doi:10.1016/j.acra.2013.08.008.

Distribution of Abdominal Aortic Calcium by Computed Tomography: Impact of Analysis Method on Quantitative Calcium Score

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Abstract

Rationale and Objectives—Abdominal aortic calcification (AAC) can be quantified using computed tomography (CT), but imaging planes are prescribed based on bony landmarks, so that individual variation between the landmark and the aortoiliac junction can result in variable aortic coverage. In the Framingham CT substudy, we scanned a 15-cm (Z-direction) abdominal segment cranial to the S1 vertebral body. We sought to determine the range and distribution of length of aorta scanned, the distribution of AAC within the abdominal aorta, and to compare burden of AAC measured from fixed-length segments versus AAC from all slices cranial to the aortoiliac bifurcation.

Materials and Methods—AAC was quantified by modified Agatston score (AS) in 100 Framingham Heart Study participants (60±13 years, 51 men). We compared AS measured from 5-cm and 8-cm segments to AS_{ALL} (total visualized aorta).

Results—73/100 participants had AAC > 0. The total length of aorta imaged was 8 cm in 84% of participants. Qualitatively, 5-cm and 8-cm segments correctly identified 96% and 99%, respectively, of participants as having or not having AAC. Quantitatively, AS_{8cm} was within 20% of AS_{ALL} in four-fifths and within 30% of AS_{ALL} in nine-tenths of participants. AS_{5cm} more severely underestimated AS_{ALL}.

Conclusion—Using S1 as the caudal imaging landmark in a 15-cm slab yields 8 cm aortic coverage in most adults. Both 5-cm and 8-cm analysis strategies are comparable to analyzing the total visualized abdominal aorta for prevalent AAC, but only 8-cm segment analysis yields quantitatively similar measures of AAC.

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There are no conflicts of interest.

Keywords

abdominal aorta; calcium; population study; segment length; computed tomography

INTRODUCTION

Abdominal aortic calcification (AAC) is associated with increased burden of cardiovascular morbidity and mortality and may be a predictor of future adverse cardiovascular disease events (1–5). Autopsy (6) and imaging (7, 8) studies suggest that the prevalence of abdominal aortic atherosclerosis, including calcified aortic plaques, generally is greatest at the bifurcation of the abdominal aorta, with decreasing burden of atherosclerosis at a greater distance from the aortic bifurcation. Computed tomography (CT) allows quantitative measurement of AAC, an index of atherosclerosis burden, but there is no standard method for CT-based assessment of AAC. Although it clearly is desirable to scan comparable segments of abdominal aorta across individuals for purpose of comparisons, in practice this can be challenging since the aorta is not well visualized on CT scout images. CT imaging planes for the abdominal aorta are most commonly prescribed based on bony (vertebral) landmarks, but there can be individual variation between the level of the aortoiliac bifurcation and any given vertebral landmark, thus resulting in variable-length coverage of the abdominal aorta. The need to minimize radiation exposure makes an “over-coverage” strategy, i.e. imaging a longer segment of the abdomen than likely to be needed, impractical.

In the Framingham CT substudy a 15-cm extent in the Z (cranial-caudal) direction was prespecified for abdominal imaging. The slab was prescribed so that the S1 vertebral body delineated the caudal-most extent of imaging. S1 was selected as the lower end point to avoid irradiation of pelvic organs, as some study participants were women of childbearing age. This protocol provided views of the lower abdominal aorta and the upper portions of the iliac arteries. The purpose of this study was to determine the lengths of abdominal aorta imaged and to assess the effect of various analysis schemes (fixed and variable-length segments of abdominal aorta) on quantitative calcium burden. We hypothesized that AAC within the imaged portion of abdominal aorta tends to be concentrated caudally, based on autopsy and imaging literature, and that fixed and variable-length segment measurement methods may yield comparable quantitative results.

MATERIALS AND METHODS

The study was approved by the local institutional review boards. All study participants provided written informed consent.

Study Sample

Members of the Framingham Offspring (9) and Third Generation (10) cohorts were invited to participate in the CT substudy if they had attended the Offspring cycle 7 (1998–2001) or Third Generation cycle 1 (2002–2005) examinations, had complete risk factor profiles, and were 35 (men) or 40 (women) years of age. Participating women were not pregnant, verified by pregnancy testing prior to CT scanning. Persons weighing > 160 kg were not eligible for CT study, due to scanner-gantry limitations and the likely need for greater radiation exposure to maintain image quality. Clinical covariates were collected at the Offspring cycle 7 or Third Generation cycle 1 examinations, as previously described (11). Among the 3285 Offspring and Third Generation participants who underwent CT scanning (51% men, 49% women), we selected 100 Offspring (51 men, 49 women) from equal strata of age for more detailed analysis of AAC. The present study was restricted to Offspring due to the lower prevalence of AAC in the Third Generation cohort.

CT Imaging Protocol

Participants were imaged on an eight-slice multidetector CT scanner (LightSpeed Ultra, General Electric, Milwaukee, WI) with prospective ECG triggering during a single breath hold as previously described (11, 12). Scans were prospectively initiated at 50% of the RR interval (13). The top of the S1 vertebral body was prospectively selected as the most caudal extent of the abdominal volume to be imaged. Thirty contiguous 5-mm thick slices were obtained cranial to S1 for a total coverage of 15 cm in the Z-direction. Imaging parameters included: 120 kVp, 400 mA, gantry rotation time 500 ms, table feed 3:1. The effective radiation exposure was 2.7 mSv.

Image Analysis Protocol

CT data were analyzed on a commercially available workstation (Aquarius, TeraRecon, San Mateo, CA) using a previously described protocol (11). Briefly, a calcified lesion was defined as an area of at least 3 connected pixels with >130 Hounsfield units (HU) attenuation. Agatston score (AS) was calculated as described by Agatston and colleagues (14). For each participant the level of the aortoiliac bifurcation was identified. The nearest slice with $>50\%$ common lumen (between iliac branches) was labeled as the caudal extent of the abdominal aorta. Three AAC scores were calculated: first the caudal-most 5-cm segment of abdominal aorta was analyzed to determine AS_{5cm} ; second, the caudal-most 8 centimeters were analyzed for AS_{8cm} ; finally, the entire imaged portion of the abdominal aorta was analyzed, yielding AS_{ALL} . From these definitions it follows that $AS_{ALL} \geq AS_{8cm} \geq AS_{5cm}$.

Data and Statistical Analyses

The extent of abdominal aorta imaged was summarized by median and interquartile (IQR) ranges. We also report the minimal and maximal lengths visualized. The quantitative burdens of AAC for 5-cm, 8-cm and total-scanned segments are similarly reported. We tabulated the number of participants without any AAC detected ($AS_{ALL} = 0$). For each participant with $AS_{ALL} > 0$, we computed the ratio of AAC for 5 cm to total AAC (AS_{5cm}/AS_{ALL}) and compared this to the ratio of 5 cm to the total length imaged (L_{ALL}) to assess the distribution of AAC. (If AAC was distributed uniformly in the Z direction then the ratio of $5/L_{ALL}$ should exactly equal the ratio of AS_{5cm}/AS_{ALL} . However, if there was more AAC caudally than cranially in the imaged segment then AS_{5cm}/AS_{ALL} would be $> 5/L_{ALL}$ while greater burden of AAC in the cranial direction would be reflected by $AS_{5cm}/AS_{ALL} < 5/L_{ALL}$.) We then tabulated the number of participants with > 8 cm of abdominal aorta imaged in total and performed similar analysis comparing AS_{8cm} and AS_{ALL} with $8/L_{ALL}$. Finally, we repeated the above ratio analyses only for participants with $AS_{ALL} > 400$. These secondary analyses were performed to investigate whether the primary analyses might have been skewed by participants with minimal overall AAC, but large proportional differences between fixed-length and total-segment AS. The cutpoint of 400 was selected because across the Offspring and Third Generation participants with AAC, this represents the median burden of AAC among women with intermediate 10-year risk of CAD(11).

RESULTS

The study sample comprised 51 men and 49 women with a mean age of 60 years, as shown in Table 1. Compared with the overall cohort of Offspring cycle 7 participants, the men in this study had similar body mass index (BMI) and prevalences of hypertension, dyslipidemia, diabetes and smoking. Women had slightly lower BMI (mean 26.7 versus 27.7 kg/m²) and prevalence of hypertension (35% vs. 44%), and markedly lower prevalences of dyslipidemia and diabetes as compared with all women participating in Offspring cycle 7. The median [IQR] length of abdominal aorta imaged was 9.5 [8.5, 10.5] cm. The shortest

segment scanned was 5.75 cm while the longest was 14.0 cm. Figure 1 shows the distribution of participants according to the length of abdominal aorta scanned.

Among the 100 participants, 27 had no detectable AAC ($AS_{ALL} = 0$). Among those with $AAC > 0$, median AS_{ALL} was 1312 [186, 4430] with a maximal AS_{ALL} of 17,885. Median AS_{5cm} was 1027 [127, 3449], maximum 12,582, while median AS_{8cm} was 1213 [184, 4250], maximum 16,771. Four participants (4%) had no AAC on 5-cm analysis but detectable AAC on whole-segment analysis. In each discrepant case the absolute burden of AAC was low, with $AS_{ALL} = 2, 11, 58$ and 188. Corresponding AS_{8cm} scores for these participants were 2, 11, 2 and 0, respectively; i.e. a single participant had $AS_{8cm} = 0$ and $AS_{ALL} > 0$.

Among the 61 participants with $AS_{ALL} > 0$ and > 8 cm of abdominal aorta imaged, the ratio of AS_{8cm}/AS_{ALL} was $> 8/L_{ALL}$ in 54 (89%), indicating that AAC was not uniformly distributed over the visualized segment of aorta, but was instead caudally concentrated, with more AAC toward the aortoiliac bifurcation. This pattern persisted when comparing AS_{5cm} to AS_{ALL} where 47 (77%) of participants had proportionally more AAC in the caudal-most 5 cm of abdominal aorta versus the remainder.

An example of the effect of analyzed segment-length on quantitative AAC in a single participant is shown in Figure 2. Figure 3 shows the effect of analysis-segment length across all participants with nonzero AAC ($AS_{ALL} > 0$) and > 8 cm of abdominal aorta imaged, $n=61$. Figure 3a shows percentage of participants whose AS_{5cm} is x percent of AS_{ALL} in gray, while AS_{8cm} results are shown by black bars. For example, AS_{8cm} was 90% of AS_{ALL} in 65.6% of participants, while only 16.4% of participants had an AS_{5cm} 90% of their corresponding AS_{ALL} . In summary, approximately two-thirds of participants had an AS_{8cm} within 10% of AS_{ALL} while ninety percent of participants had AS_{8cm} within 30% of AS_{ALL} . Comparing AS_{5cm} to AS_{ALL} less than half of participants had an AS_{5cm} within 30% of AS_{ALL} . Figure 3b shows results for participants with $AS_{ALL} > 400$ ($n=41$) and indicates that among participants with greater burden of AAC AS_{8cm} is slightly closer to AS_{ALL} as compared with the overall study sample (shown in Figure 3a).

DISCUSSION

Abdominal aortic calcification, an independent measure of increased risk for incident CVD, was seen in over 70% of Framingham Offspring cohort participants who underwent MDCT scanning. Imaging planes were prescribed using the S1 vertebral body as a landmark to delineate the caudal-most extent of imaging. As expected, this resulted in variable-length coverage of the abdominal aorta due to individual differences between the level of S1 and the aortoiliac bifurcation. The minimum length of abdominal aorta scanned was 5.75 cm, but 84% of participants had ≥ 8 cm of abdominal aorta scanned. In the majority of participants AAC was preferentially distributed caudally, toward the aortoiliac junction. When quantifying AAC, analysis of a fixed 8-cm segment (proceeding cranially from the aortoiliac junction) resulted in an AAC score that was lower than but at least two-thirds of the AAC score of the total-visualized-aorta in 90% of participants. When considering only those with “notable” AAC ($AS_{ALL} > 400$), the 8-cm segment resulted in an AAC score at least four-fifths that of the total AAC score in 90% of participants.

Comparison with the current literature

AAC is associated with excess burden of cardiovascular risk factors and appears to have predictive value for development of cardiovascular disease (1–5). AAC is of interest as it may develop earlier than coronary artery calcium, and might also be detected on abdominal imaging performed for reasons other than cardiovascular risk stratification (15). However, at

present methodology for quantitation of AAC varies between studies and institutions and there are no standard protocols for either scanning or analysis.

The Jackson Heart Study performed abdominal CT from the S1 vertebral body cranially to approximately the middle of the L3 vertebral body (16) and images containing the abdominal aorta, i.e. above the aortoiliac junction, were analyzed for AAC. As with Framingham, the Jackson protocol can yield a variable-length segment of abdominal aorta analyzed. In contrast, the Multi-Ethnic Study of Atherosclerosis (MESA) analyzed a fixed 8-cm segment out of a 15-cm thick (Z-direction) imaging slab (17).

Implications for research

The lack of a standard scanning and analysis protocol for AAC is a potential limitation for pooled analyses across cohorts and trials. If we consider the MESA fixed 8-cm segment as the reference method, a low proportion of Framingham participants were “undercovered”; 84% of the Framingham participants in the present study had at least 8 cm of abdominal aorta imaged. Another 9% differed by less than 1 cm (had 7 and <8 cm covered), and only 7% had <7 cm of aorta scanned. We show in this study that AAC tends to be concentrated caudally, suggesting that the effect of “undercoverage” on quantitative AAC may be proportionally less than the difference in analyzed-segment length. Similarly, the “over-coverage” of > 8 cm analyzed probably has less effect than might be anticipated based on comparison of the lengths of abdominal aorta scanned, again because AAC is, in general, preferentially distributed toward the aortoiliac junction.

Although the tendency of AAC to be distributed more caudally in the abdominal aorta seems on average to mitigate potential differences between the variable segment-length and fixed 8-cm analysis protocols, it does appear that quantitative AAC burden determined using a 5-cm analysis segment notably underestimates AS_{8cm} and AS_{ALL} in a sizeable proportion of participants. However, with respect to presence or absence of AAC, it is worth noting that only 4% of participants were misclassified as having/not having AAC when comparing the 5-cm to the full-segment analyses, and that quantitative AAC was very low in each of the 4 participants thus misclassified. Based on results from this substudy, across-cohort AAC measures appear amenable to pooled qualitative analyses, and may be suitable for pooled quantitative analyses despite differences in analysis protocols. Nonetheless, the length of segment analyzed clearly has an effect on quantitative measures of AAC, and potential data pooling should probably be considered on a cohort-by-cohort basis.

Clinical implications

It is difficult to determine which, if any, of the analysis schemes is superior. The fixed-segment scheme obviously results in identical-length segments of aorta across individuals, which appears to facilitate more meaningful comparisons as opposed to variable-length schemes. However, when considering the segment analyzed as a proportion of the entire abdominal aorta, the apparent consistency advantage of the fixed-segment scheme is diminished. That is, 8 cm in a tall (or long-trunked) person is proportionally less abdominal aorta than 8 cm in a short (or short-trunked) person. Critique of the variable-length scheme in the context of overall height (or trunk length) is more complicated and depends on whether there is a systematic relationship between height (trunk length) and relative positions of the S1 vertebral body and the aortoiliac junction. That said, it also appears that the variable-length scheme used in the present study is unlikely to be more consistent than the fixed length scheme. In terms of the process of quantitative AAC analysis, our variable-length scheme is conceptually more straightforward (i.e., identify aortoiliac junction and analyze all image planes in the cranial direction) than the fixed-segment method, which adds the additional complexity of determining a “stop point” after finding the aortoiliac junction.

Alternate variable-length analysis schemes, such as the AAC-8 or AAC-24 scores, which measure burden of AAC in aortic segments whose length is defined by proximity to specific vertebral bodies, have been reported, but principally in the context of AAC from lumbar roentgenograms [5]. The Jackson Heart Study however used a similar vertebrally-defined segment length for CT data [16]. Another possibility is to measure a fixed proportion of the abdominal aorta between two anatomic landmarks, e.g. the caudal 50% of the distance between the renal artery origins and the aortoiliac bifurcation. Although such variable-length schemes have the theoretical advantage of being in some way scaled for body size, they add considerable complexity to analysis.

Ideally, an optimal analysis scheme might be identified by applying each candidate method to a single large dataset, then comparing the association of AAC scores by each scheme with outcomes of interest, such as myocardial infarction, cerebrovascular accident, or CVD death. However, we suspect that most “reasonable” analysis methods, such as those used in the MESA and Framingham AAC studies for example, will have similar predictive value, as it may be that above a certain burden of AAC incremental differences will add relatively little additional prognostic value, regardless of the exact length of abdominal aorta analyzed. Further, the cost of identifying an optimal analysis method via a comparative study might be prohibitive in terms both of number of subjects needed to show differences in outcome and in analytical effort. If quantification of AAC were to be used clinically, its uptake would most likely be facilitated by adoption of an analysis standard that is straightforward both conceptually and in terms of implementation, such as the fixed 8-cm analysis scheme used in the MESA study.

Limitations

The Framingham Heart Study consists principally of white participants. In this substudy we analyzed only Offspring cohort members, who were mostly middle aged or older, due to the low prevalence of AAC in the Third Generation cohort. Generalization to other ethnicities or age groups may be limited.

Conclusions

Abdominal aortic calcium is widely prevalent among community-dwelling adults of middle age or greater. The distribution of AAC is not uniform throughout the abdominal aorta, but tends to be concentrated caudally toward the aortoiliac junction. Comparison of three analysis schemes gave qualitatively similar results regarding presence or absence of AAC, but a 5-cm analysis segment underestimates quantitative burden of AAC relative to total AAC burden in the entire visualized segment.

Acknowledgments

Source 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). Dr. O’Donnell is supported by the NHLBI Division of Intramural Research.

ABBREVIATIONS

AAC	abdominal aortic calcification
AS	Agatston score
BMI	body mass index
CT	computed tomography

CVD	cardiovascular disease
ECG	electrocardiogram
HU	Hounsfield Unit
IQR	interquartile range
MDCT	multidetector computed tomography

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Figure 1.
Distribution of study participants by length of abdominal aorta scanned.

Figure 2.

Effect of analyzed-segment length on AAC in a single study participant. A total of 9.75 cm was scanned in this 81-year old man. The arrow in panel A points to the abdominal aorta, and the square shows the crop used for panel B. Panel B shows the imaged abdominal aorta slice-by-slice with the most cranial slice at top left, proceeding to the most caudal slice at bottom right. The bottom four rows (dashed line at right) show the slices analyzed under the AS_{5cm} protocol ($AS_{5cm}=937$), and the solid line the 32 slices analyzed under the AS_{8cm} protocol ($AS_{8cm}=1189$). All of the slices shown were analyzed to obtain $AS_{ALL}=1448$.

AAC Analyzed by Fixed-Length vs. Total Scanned (Maximal) Segment for Participants with AAC > 0

AAC Analyzed by Fixed Length vs. Total Scanned (Maximal) Segment: Participants with AAC > 400

Figure 3.

Comparison of quantitative AAC score by fixed-length segments versus entire visualized portion of abdominal aorta in (A) the overall study group with AAC>0 (N=61) and (B) among study participants with AAC > 400 Agatston units (N=41). AAC = abdominal aortic calcification.

Table 1

Baseline characteristics of the study sample.

	Men	Women	Men (ALL)	Women (ALL)
N	51	49	1625	1914
Age, years	60±13	61±13	62±10	61±10
Body mass index, kg/m ²	28.7±4.3	26.7± 4.7	28.8±4.6	27.7±5.9
Hypertension	42%	35%	49%	44%
Dyslipidemia	22%	8.3%	25%	18%
Current Smoking	12%	12.5%	13%	14%
Diabetes Mellitus	16%	4.2%	14%	9%

ALL refers to all Framingham Offspring cohort members participating in the cycle 7 examination.