Characterization of atherosclerotic disease in thoracic aorta: A 3D, multicontrast vessel wall imaging study

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\textbf{ABSTRACT}

\textbf{Purpose:} To investigate the characteristics of plaque in the thoracic aorta using three dimensional multi-contrast magnetic resonance imaging.

\textbf{Materials and methods:} Elderly subjects (≥60 years) were recruited in this study. Thoracic aorta was imaged on a 3.0T MR scanner by acquiring multicontrast sequences. The plaque burden was evaluated by measuring lumen area, wall area, wall thickness, and normalized wall index. The presence or absence of plaque and intraplaque hemorrhage (IPH)/mural thrombus (MT) were identified. The characteristics of atherosclerosis among different thoracic aorta segments (AAO: ascending aorta; AOA: aortic arch, and DOA: descending aorta) were determined.

\textbf{Results:} Of 66 recruited subjects (mean age 72.3 ± 6.2 years, 30 males), 55 (83.3\%) had plaques in the thoracic aorta. The prevalence of plaque in AAO, AOA, and DOA was 5.4\%, 72.7\%, and 71.2\%, respectively. In addition, 21.2\% of subjects were found to have lesions with IPH/MT in the thoracic aorta. The prevalence of IPH/MT in segment of AAO, AOA and DOA was 0\%, 13.6\% and 12.1\%, respectively. The aortic wall showed the highest NWI in DOA (34.1\% ± 4.8\%), followed by AOA (31.2\% ± 5\%), and AAO (26.8\% ± 3.3\%)\textsuperscript{(p < 0.001)}.

\textbf{Conclusion:} Three dimensional multicontrast MR imaging is capable of characterizing atherosclerotic plaques in the thoracic aorta. The findings of high prevalence of plaques and the presence of high risk plaques in the thoracic aorta suggest early screening for aortic vulnerable lesions in the elderly.

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\section{1. Introduction}

Atherosclerotic vulnerable plaque in the aortic arch is one of the major embolic sources for ischemic stroke. Previous studies have shown that the advanced atherosclerotic plaques in the thoracic aorta are prevalent in patients with ischemic cerebrovascular events [1], particularly for those with cryptogenic stroke [2]. Therefore, assessing the vulnerability of atherosclerotic plaques that occur in the thoracic aorta, especially in the aortic arch, is important for stroke prevention.

Computed tomography angiography (CTA), magnetic resonance angiography (MRA) and transesophageal echocardiography (TEE) have been widely used to characterize aortic atherosclerosis by measuring either luminal stenosis or echo intensity of the plaque [3–14]. However, these imaging modalities provide limited information on plaque compositional features, such as intraplaque hemorrhage (IPH) and lipid-rich necrotic core (LRNC), which are critical determinants for plaque vulnerability. In addition, investigators demonstrated that luminal stenosis may not be a good indicator for plaque vulnerability due to positive remodeling effect [15]. Therefore, it is desirable to directly visualize atherosclerotic lesions in vessel wall for assessment of plaque vulnerability.

Two-dimensional (2D) black-blood MR imaging (MRI) has been introduced to noninvasive evaluation of atherosclerosis in the thoracic aorta [16,17]. However, it is challenging to investigate...
the distribution of atherosclerotic plaques across all segments of the thoracic aorta using 2D MR imaging technique due to its limited longitudinal coverage and lower inter-slice resolution (3–5 mm). Recently, three-dimensional (3D) black-blood MR imaging sequences, such as 3D SNAP (simultaneous non-contrast angiography and intraplaque hemorrhage) [18] and 3D VISTA (volume isotropic turbo spin echo acquisition) [19,20], have been proposed for assessment of atherosclerotic plaques in arterial wall. Because 3D imaging techniques enable fast acquisition with high spatial resolution and large longitudinal coverage, they have the potential to noninvasively determine the characteristics of atherosclerotic diseases in the thoracic aorta. Most recently, Eikendal et al. reported that 3D T1-weighted VISTA sequence provided excellent reproducibility for quantification of aortic wall characteristics and may be able to assess early atherosclerosis in asymptomatic populations [20]. As such, to acquire both 3D SNAP and VISTA imaging sequences may enable looking at both wall dimensions and plaque vulnerability in the thoracic aorta. This study sought to characterize the vulnerable atherosclerotic plaques in the thoracic aorta in the elderly using 3D multicontrast MR vessel wall imaging techniques.

2. Materials and methods

2.1. Study subjects

The subjects were recruited from a pilot community study of Cardiovascular Risk of Older Population (CROP). The aim of CROP study was to investigate the cardiovascular disease risk of old subjects from a community using ultrasound and MR imaging. The inclusion criteria were as follows: (1) elderly subjects (≥60 years); (2) no cardiovascular symptoms within 6 months before MR imaging. Subjects who had severe consciousness disturbance (coma) and contraindications to MR imaging were excluded from this study. All subjects underwent thoracic aorta MR imaging. The clinical information including age, gender, and history of hypertension (defined as diastolic blood pressure ≥90 mmHg or systolic blood pressure ≥140 mmHg), diabetes, smoking, hyperlipidemia, statin use, coronary heart disease, and stroke was collected. The levels of lipoprotein including high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol (TC), and triglycerides (TG) were recorded. The study protocol was approved by institutional review board and the written informed consent was obtained from all subjects.

2.2. MR imaging

Thoracic aorta was imaged on a 3.0T MR scanner (Philips Achieva TX, Philips Healthcare, The Netherlands) with 32-channel cardiac coil. The 3D T2-VISTA and SNAP sequences were acquired obliquely along the orientation of the thoracic aorta with the following parameters: 3D T2-VISTA: turbo spin echo (TSE), repetition time (TR)/Echo time (TE) 800 ms/64 ms, field of view (FOV) 250 mm × 160 mm × 64 mm, spatial resolution 1.25 mm × 1.25 mm × 1.25 mm; 3D SNAP: turbo field echo (TFE), TR/TE 7.5 ms/3.7 ms, FOV 220 mm × 280 mm × 37 mm, spatial resolution 1.5 mm × 1.5 mm × 1.5 mm.

2.3. Assessment of the thoracic aorta atherosclerosis

All MR images were reviewed by two radiologists with >5 years’ experience in cardiovascular MR imaging using a custom-designed software “3D CASCADE”. The lumen and wall contours were outlined semi-automatically on the reconstructed axial images which were perpendicular to the centerline of the thoracic aorta. The morphological parameters including lumen area (LA), wall area (WA), total vessel area (TVA), maximum wall thickness (Max WT), mean wall thickness (Mean WT) and normalized wall index (NWI = WA/[LA+WA] × 100%) were measured. NWI was considered as the best parameter to evaluate the plaque burden because it normalizes the natural differences in vasculatures with different lumen size. In addition, the presence or absence of atherosclerotic plaque which was defined as eccentric thickening in aortic wall was determined. Hyperintense lesions (higher than 150% of the surrounding muscle signal [18]) on SNAP images which may reflect intraplaque hemorrhage or mural thrombus (IPH/MT) were also identified. The presence of atherosclerotic plaque or hyperintense lesion was determined per vessel segment.

2.4. Reproducibility

The inter-scan reproducibility for 3D VISTA sequence had been proved to be excellent with all intraclass correlation coefficients (ICC) >0.75 in measuring wall area and thickness in the thoracic aorta [20]. Thirty subjects were randomly selected for the inter-reader and intra-reader reproducibility studies. The presence or absence of atherosclerotic plaque, hyperintense lesion and NWI of the thoracic aorta were identified and measured twice by one radiologist with time interval of two months for minimizing the memory bias. Another radiologist conducted above image review for inter-reader reproducibility analysis blinded to the review results of previous radiologist.

2.5. Statistical analysis

Thoracic aorta was divided into three segments: aortic arch (AOA), the proportion of the thoracic aorta above the plane of sternal angle; ascending aorta (AAO), the proportion of the thoracic aorta from the outlet of left ventricle to aortic arch; and descending aorta (DAO), the proportion of the thoracic aorta from aortic arch to the plane of diaphragm. The plaque burden measurements were compared among three segments of the thoracic aorta using One-Way ANOVA analysis. The prevalence of plaque and IPH/MT in different segments of the thoracic aorta was calculated and compared using Chi-square analysis. The intra-reader and inter-reader ICCs and corresponding 95% confidence interval (CI) were calculated for NWI measurement. The Cohen’s Kappa (κ) value was analyzed to determine the intra-reader and inter-reader agreement in identification of atherosclerotic plaque and hyperintense lesion. A p value of p <0.05 was considered as statistically significant. All statistical analyses were performed using SPSS 16.0 (SSPS Inc. Chicago, IL, USA).

3. Results

A total of 66 subjects who completed thoracic aorta MR imaging were recruited in this study. Ten AAO segments with poor image quality were excluded from the final analysis due to motion artifacts. Of all 66 cases, 30 (45.5%) were male and the mean age was 72.3 ± 6.2 years old. The clinical characteristics were detailed in Table 1. IPH/MT in the thoracic aorta showed significant male preponderance in this population (p =0.037). Subjects with IPH/MT had higher level of triglyceride than those without IPH/MT in the thoracic aorta (1.7 mmol/L±0.9 mmol/L vs. 1.3 mmol/L±0.5 mmol/L, p =0.042). In addition, the prevalence of hypertension in subjects with IPH/MT was significantly greater than that of those without IPH/MT in the thoracic aorta (78.6% vs. 40.4%, p =0.016).
Table 1
Clinical characteristics of study population.

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD or N (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subjects with IPH/MT (N=14)</td>
<td>Subjects without IPH/MT (N=52)</td>
</tr>
<tr>
<td>Gender, male</td>
<td>10 (71.4%)</td>
<td>20 (38.5%)</td>
</tr>
<tr>
<td>Age, years</td>
<td>74.3 ± 4.4</td>
<td>71.8 ± 6.5</td>
</tr>
<tr>
<td>High-density lipoprotein, mmol/L</td>
<td>1.4 ± 0.4</td>
<td>1.5 ± 0.4</td>
</tr>
<tr>
<td>Low-density lipoprotein, mmol/L</td>
<td>2.8 ± 0.8</td>
<td>2.7 ± 1.0</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>1.7 ± 0.9</td>
<td>1.3 ± 0.5</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>4.8 ± 0.9</td>
<td>4.8 ± 1.0</td>
</tr>
<tr>
<td>Ankle-Brachial Index, kg/m²</td>
<td>1.2 ± 0.2</td>
<td>1.1 ± 0.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (78.6%)</td>
<td>21 (40.4%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>3 (21.4%)</td>
<td>5 (9.6%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 (14.3%)</td>
<td>9 (17.3%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>9 (64.3%)</td>
<td>34 (65.4%)</td>
</tr>
<tr>
<td>Statin use</td>
<td>6 (42.9%)</td>
<td>24 (46.2%)</td>
</tr>
<tr>
<td>History of coronary heart disease</td>
<td>3 (21.4%)</td>
<td>15 (28.8%)</td>
</tr>
<tr>
<td>History of Stroke</td>
<td>2 (14.3%)</td>
<td>5 (9.6%)</td>
</tr>
</tbody>
</table>

Table 2
The measurements of morphology in each segment of the thoracic aorta.

<table>
<thead>
<tr>
<th></th>
<th>AAO</th>
<th>AOA</th>
<th>DAO</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen area, mm²</td>
<td>849.0 ± 216.3</td>
<td>580.0 ± 188.6</td>
<td>376.5 ± 89.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wall area, mm²</td>
<td>3040.0 ± 55.2</td>
<td>2525.4 ± 48.7</td>
<td>1921.4 ± 40.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total vessel area, mm²</td>
<td>11529.0 ± 259.2</td>
<td>8324.2 ± 225.3</td>
<td>5686.5 ± 115.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Max wall thickness, mm</td>
<td>3.0 ± 0.5</td>
<td>3.1 ± 0.7</td>
<td>2.9 ± 0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean wall thickness, mm</td>
<td>2.7 ± 0.3</td>
<td>2.7 ± 0.4</td>
<td>2.5 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Normalized wall index, %</td>
<td>26.8 ± 3.3</td>
<td>31.2 ± 5.1</td>
<td>34.1 ± 4.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

3.1. Morphological measurements of the thoracic aorta

Table 2 presented the plaque burden measurements of the thoracic aorta. Among all three segments of the thoracic aorta, the AAO showed the largest LA, WA, and TVA, followed by AOA, and DAO (all p < 0.001). In contrast, the DAO (34.1% ± 4.8%) exhibited the highest NWI measurement, followed by AOA (31.2% ± 5%) and AAO (26.8% ± 3.3%) (all p < 0.001). The Mean WT of DAO was significant smaller than that of AAO (p < 0.001) and AOA (p < 0.001). There was no significant difference in the Mean WT between AAO and AOA (p = 1.000).

3.2. Plaque characteristics of the thoracic aorta

Atherosclerotic plaque in the thoracic aorta was found in 83.3% (55/66) subjects. The prevalence of atherosclerotic plaque was 5.4% (3/56), 72.7% (48/66) and 71.2% (47/66) in AAO, AOA, and DAO, respectively (Fig. 1). Compared to AAO, AOA and DAO showed significantly greater prevalence of atherosclerotic disease (all p < 0.001). Of all 66 cases, 41 (62.1%) and 3 (4.5%) were found to have atherosclerotic plaques in both AOA and DAO segments and all three segments, respectively.

Atherosclerotic lesions with IPH/MT in the thoracic aorta on SNAP images were found in 21.2% (14/66) of subjects (Fig. 2 and Fig. 3). The prevalence of atherosclerotic lesions with IPH/MT was 0% (0/56), 13.6% (9/66), and 12.1% (8/66) in segment of AAO, AOA, and DAO, respectively (Fig. 1). The Max WT for atherosclerotic lesions with IPH/MT was 4.55 mm ± 1.0 mm. Of 14 plaques with IPH/MT, 8 (57.1%) were found to exhibit Max WT <4 mm.

3.3. Reproducibility

The intra-reader and inter-reader ICC for NWI was 0.84 (95% CI: 0.771–0.888) and 0.749 (95% CI: 0.641–0.825) for AAO, 0.785 (95% CI: 0.742–0.821) and 0.708 (95% CI: 0.649–0.756) for AOA, and 0.73 (95% CI: 0.681–0.771) and 0.79 (95% CI: 0.752–0.822) for DAO, respectively (all p < 0.001). For agreement in identification of atherosclerotic plaque, the kappa value of intra-reader and inter-reader was κ = 0.848 and κ = 0.806 for AAO, κ = 0.921 and κ = 0.905 for AOA, and κ = 0.96 and κ = 0.938 for DAO, respectively (all p < 0.001). All the kappa values of intra-reader and inter-reader agreement for identification of presence of hyperintense lesion were κ = 1.000 for each segment (all p < 0.001).

4. Discussion

This study investigated the characteristics of lesion distribution, components and burden of aortic atherosclerotic plaque in asymptomatic elderly subjects using 3D multicontrast MR vessel wall imaging techniques. Our study showed that atherosclerotic disease was prevalent in the vessel wall of the thoracic aorta, particularly in the aortic arch and descending aorta, in the elderly. More importantly, we found that more than 1/5 subjects had high risk lesions in the aortic arch or descending aorta in this study population. Our findings indicate that atherosclerosis in the thoracic aorta is prevalent and a substantial number of aortic vulnerable plaques can be seen in the elderly.

We found high prevalence of atherosclerotic disease in the aortic arch and descending aorta. This finding is consistent with previous studies. Previous TEE studies reported that the plaque incidence in the aortic arch and descending aorta is 62.2%–65.5% and 54.9%–60.9%, respectively [21,22]. The prevalence of aortic atherosclerotic plaque in our study is a little higher than literature reports. One of the reasons might be that our subjects are older than those in previous studies (mean age: 72.3 years vs. 61.8–67.0 years) because atherosclerotic disease is associated with age [23]. Compared to aortic arch and descending aorta, we found that atherosclerosis was less prevalent in the ascending aorta. This may be due to differences in hemodynamic characteristics among different segments of the thoracic aorta and different length anatomically between the ascending and descending aorta. Critical flow parameters such as low wall shear stress (WSS) and high oscillatory shear index (OSI) were considered to play an important role in flow mediated atherosclerosis in the thoracic aorta [24]. The presence of increased OSI at the inner curvature of aortic arch and proximal descending aorta corresponded to regions
which were frequently affected by aortic plaque [25]. The finding of high prevalence of plaque in the thoracic aorta in the elderly indicates that more attention needs to be paid to the vasculature of the thoracic aorta, particularly aortic arch, when screening for arterial atherosclerosis in individuals at high risk of cardiovascular disease.

In the present study, the atherosclerotic lesions with IPH/MT were found in more than one fifth of subjects. A previous MRI study by Bitar et al. [26] reported that 13% of patients with cerebrovascular disease had IPH/MT in the thoracic aorta, in which 10.9% involved in the upper thoracic aorta. IPH/MT was believed to be an indicator for high risk atherosclerotic plaques [27]. In carotid and intracranial arteries, IPH has been demonstrated to be associated with ischemic events [28,29]. One study showed that IPH in carotid arteries could accelerate the progression of atherosclerosis and fibrous cap rupture which could offset the effect of statins in the treatment of atherosclerotic plaque [30]. In this study, the presence of high risk plaques in the descending aorta may also suggest the risk of developing future ischemic stroke. This is because that there is retrograde blood flow in the proximal descending aorta which is susceptible to the formation of plaque and thrombus leading to ischemic stroke. Wehrum et al. [31] revealed that retrograde blood flow in the descending aorta was a common phenomenon, particularly in stroke patients. Retrograde blood flow connecting plaque was in 60.6% of stroke patients [32]. The descending aortic plaques had been postulated as a potential embolic source in cryptogenic stroke patients through retrograde aortic blood flow [33].

In this study, more than half of the aortic atherosclerotic lesions with IPH/MT were found to have Max WT < 4 mm. Previously, the plaque thickness ≥4 mm in the thoracic aorta was considered as vulnerable plaque, which has been shown to be a significant predictor for recurrent cerebral infarction [34]. This thickness-based definition of vulnerable plaque is indirect since the vulnerability of plaque is dependent on the compositional changes in arterial wall histologically. The finding of Max WT for 57.1% of high risk plaques is less than 4 mm in this study indicates that it may underestimate the risk of atherosclerotic plaques in the thoracic aorta to only measure wall thickness. This suggests the necessity of direct viewing the compositional features in arterial wall.
Three dimensional multicontrast MR vessel wall imaging techniques were applied to this study. The advantages of 3D vessel wall imaging include fast acquisition, high spatial isotropic resolution, long longitudinal coverage, and superior blood suppression. Benefitting from 3D vessel wall imaging techniques, the arterial wall of aortic arch with irregular geometry was well delineated and the measurements of plaque burden and identification of plaque were found to be highly reproducible in this study. In addition, this 3D imaging technique can provide large longitudinal coverage which makes it possible to determine the distribution of atherosclerotic disease among different segments of the thoracic aorta. The multicontrast imaging sequences include 3D T2-VISTA and 3D SNAP in our study. Previous study proved that the 3D VISTA imaging sequences had excellent performance in measuring plaque burden [19,20]. The T2-weighted images derived from 3D VISTA sequence may allow the identification of LRNC [19]. However, in general, both LRNC and calcification show relatively low signal intensity. It is difficult to differentiate them on T2-weighted images alone in some cases. Therefore, comprehensive characterization of aortic plaque compositional features including LRNC and calcification by acquiring T1-VISTA and T2-VISTA sequences in future studies is suggested. Wang et al. [18] illustrated that 3D SNAP sequence utilized a phase sensitive acquisition, and was designed to provide positive signals corresponding to intraplaque hemorrhage and negative signals corresponding to lumen. The high signal on 3D SNAP images represented IPH/MT validated by histology [18]. Therefore, the use of 3D multicontrast imaging sequences has the potential to characterize the compositional features, such as LRNC and IPH.

There are some limitations in this study. First, ten AAO segments were excluded from the final analysis due to poor image quality. Elimination of respiratory and motion artifacts by using more robust motion correction techniques is needed in future studies. Second, calcification and LRNC were not evaluated in this study. Future studies with adding more imaging sequences, such as T1-weighted 3D sequence, are suggested to comprehensively characterize plaque compositions. Third, this study only targeted the asymptomatic subjects. It might be more interesting to investigate the significance of characteristics of atherosclerotic disease in the thoracic aorta, particularly IPH/MT, by 3D multicontrast MRI in predicting future ischemic cerebrovascular events.

5. Conclusions

Three dimensional multicontrast MR vessel wall imaging is capable of characterizing atherosclerotic plaques in the thoracic aorta. The findings of high prevalence of atherosclerotic plaques and the presence of high risk plaques in the thoracic aorta, particularly in the aortic arch, suggest early screening for aortic vulnerable lesions in the elderly.

Conflict of interest

All authors declare that there is no conflict of interest form.

Relationship with industry

There are no relationships with industry.

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