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Total atherosclerotic burden by whole body magnetic resonance angiography predicts major adverse cardiovascular events

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ABSTRACT

Objective: The purpose of the present study was to investigate the relationship between the Total Atherosclerotic Score (TAS), a measurement of the overall atherosclerotic burden of the arterial tree by whole body magnetic resonance angiography (WBMRA), and the risk of major adverse cardiovascular events (MACE), defined as cardiac death, myocardial infarction, stroke and/or coronary revascularization, assuming that TAS predicts MACE.

Methods and results: 305 randomly selected 70 year-old subjects (47% women) underwent WBMRA. Their atherosclerotic burden was evaluated and TAS > 0, that is atherosclerotic changes, were found in 68% of subjects. During follow-up (mean 4.8 years), MACE occurred in 25 subjects (8.2%). Adjusting for multiple risk factors, TAS was associated with MACE (OR 8.86 for any degree of vessel lumen abnormality, 95%CI 1.14–69.11, $p = 0.037$). In addition, TAS improved discrimination and reclassification when added to the Framingham risk score (FRS), and ROC (Receiver Operator Curve) increased from 0.681 to 0.750 ($p = 0.0421$).

Conclusion: In a population-based sample of 70 year old men and women WBMRA, with TAS, predicted MACE independently of major cardiovascular risk factors.

1. Introduction

Identifying individuals with atherosclerosis in need of preventive treatment is an important task. Numerous tests and examinations [1–5] have been suggested to improve risk stratification as an addition to scoring systems, such as the Framingham Risk Score (FRS) [6].

The ultra-fast high-performance gradient system with the bolus chase method has enabled whole body magnetic resonance angiography (WBMRA), allowing visualization of the majority of the arterial tree by means of a single contrast-injection [7]. The method is continuously improving, but so far, the atherosclerotic burden and its relation to outcome have not been investigated [8,9].

The Total Atherosclerotic Score (TAS), established with WBMRA, has been proposed to estimate systemic atherosclerosis [10].

The purpose of the present study was to investigate the relationship between TAS and the risk of major adverse cardiovascular events (MACE), assuming that TAS predicts MACE. Other markers of atherosclerosis (Ankle Brachial Index (ABI), Carotid Intima Media Thickness (CIMT), and evidence of plaques in the carotid arteries on ultrasound) were also evaluated for their ability to predict MACE.

2. Methods

2.1. Study population

After approvement by the Ethics Committee of the University of Uppsala, and written consent by the participants, WBMRA was performed on 306 subjects, aged 70, who were chosen consecutively from the population-based PIVUS (Prospective Investigation of the Vasculature in Uppsala Seniors) study [11]. They were thoroughly examined, as displayed in Table 1, and underwent the WBMRA within 3–22 months (mean 16 months) from study enrollment. 305 WBMRA-examinations were assessable: Previous studies have demonstrated this sub-population to be representative of the total epidemiological cohort [12].

2.2. Image acquisition

The WBMRA examination was performed with a 1.5 Tesla (T) scanner. The subjects were scanned in the supine position. The

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Table 1
Baseline characteristics in the WBMRA samples.

	WBMRA study cohort	Units
n	306	Subjects
Females	47	%
Height	169 ± 9.4	cm
Weight	77 ± 14	kg
BMI	27 ± 4	kg/m^2
SBP	149 ± 22	mmHg
DBP	78 ± 10	mmHg
Serum cholesterol	5.4 ± 1.0	mmol/l
LDL-cholesterol	3.3 ± 0.8	mmol/l
HDL-cholesterol	1.5 ± 0.4	mmol/l
Serum triglycerides	1.3 ± 0.6	mmol/l
Fasting blood glucose	5.3 ± 1.6	mmol/l
Currently smoking	8	%
Previous MI	7	%
Previous stroke	4	%
Previous CABG or PCI	4	%
Angina pectoris	7	%
Diabetes	12	%
FRS	11.1 ± 3.3	
hsCRP	2.3 ± 4.5	mg/l
ABI right side	1.15 ± 0.16	
ABI left side	1.14 ± 0.15	
CIMT	0.90 ± 0.17	mm
Beta blockers	19	%
Ca-antagonists	12	%
ACE-inhibitors	8	%
Statins	13	%
A2Blockers	8	%
Diuretics	12	%
Warfarin	2	%
ASA	18	%

Means ± standard deviation are given.
Abbreviations: BMI – Body Mass Index; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; HDL – high-density lipoprotein; LDL – low-density lipoproteins; MI – myocardial infarction; CABG – coronary artery bypass graft surgery; PCI – percutaneous coronary interventions; FRS – Framingham risk score; hsCRP – high sensitivity C-reactive protein; ABI – ankle brachial index; CIMT – carotid intima media thickness; ACE – angiotensin converting enzyme; A2 – angiotensin 2; ASA – acetylsalicylic acid.

WBMRA examination was attained from 4 overlapping combined stations giving a maximum covering length of 171 cm, starting at the Circle of Willis. Breath-holding was performed in the abdominal station: Thigh compression was not applied. A 3D RF-spoiled, T1-weighted gradient echo acquisition was performed prior to and after injection of 40 ml of Gadodiamide. The stations were scanned sequentially from head to feet; each scan took 87 s to perform. This has been described elsewhere [13].

2.3. Image analysis

As reported previously [10] a scoring system, TAS, was developed prospectively by dividing the arterial tree into 26 vessel segments, categorized into five territories: 1. The carotids; 2. The aorta; 3. The renal arteries; 4. The pelvic and upper legs; and, 5. The lower legs.

Each segment of vessel lumen was evaluated, in the original coronal images, by a radiologist (TH), with 5 years experience in MRI; only the most severe stenosis was scored. A normal vessel segment scored null points; stenosis less than 50% scored one point, even the slightest irregularity of the vessel wall acknowledged; and, luminal reduction of 50% or more, including occlusions, scored two points (Fig. 1). The obtained score was divided by the maximum possible score. This quotient was multiplied by 100, generating a maximum score per territory of 100. TAS was calculated as the sum of all five territories, giving a maximum total score of 500, and a lowest possible score, in case of abnormality, of 5.

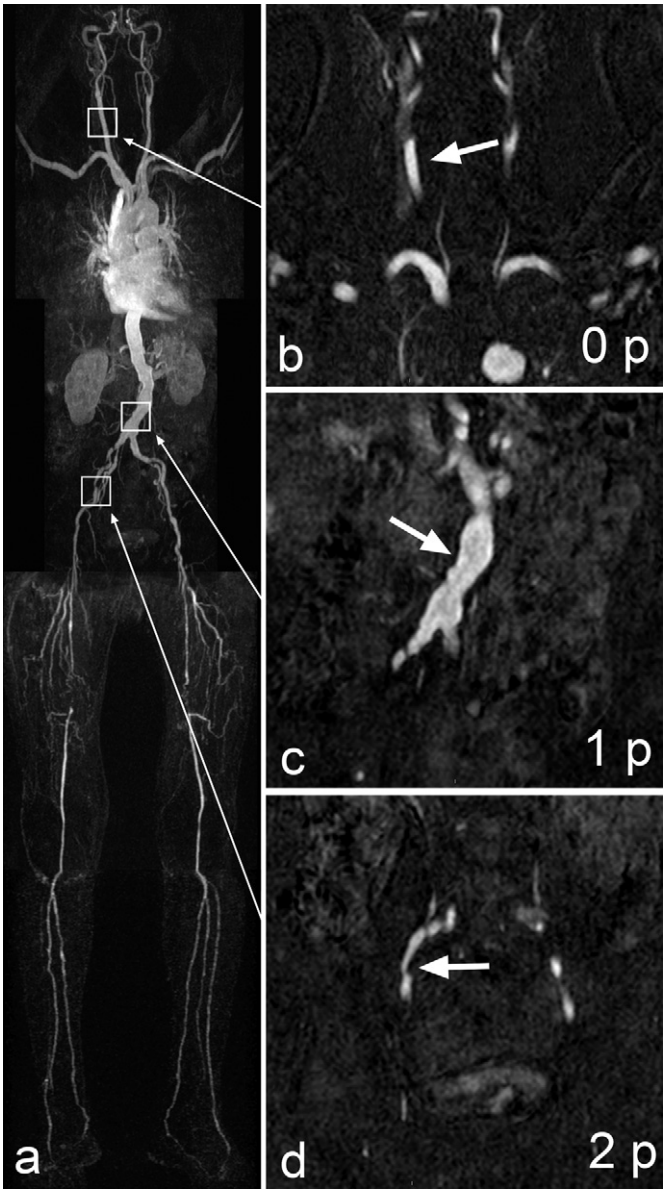

Fig. 1. Illustration of WBMRA with scoring examples. Whole body magnetic resonance angiography (WBMRA) illustrated by Maximum Intensity Projection Images of the four stations (a) on a subject scoring 102.5 points in the total atherosclerotic score. The enhanced areas exemplify given scores in the original coronary images: (b) Arrow points to a normal right common carotid artery. (c) Arrow points to abdominal aorta with irregular vessel wall scoring 1 point, and (d) arrow points to severe stenosis (>50% of the diameter) in the left external iliac artery (2 points).

Reproducibility and reliability of the scoring system have previously been rated good to excellent [12].

2.4. Other parameters

The data needed to determine multiple risk factors was obtained at study enrollment [11]. These data were: sex; waist circumference; body-mass index; fasting blood glucose; systolic blood pressure; HDL and LDL-cholesterol; total cholesterol; serum triglycerides; smoking; and, hsC-reactive protein. FRS was calculated [6]. Diabetes was defined as the use of antidiabetic drugs or fasting blood glucose >6.2 mmol/l.

Calculation of ABI, analysis of CIMT, and assessment of carotid plaques were done by standardized methods that have been described previously [14,15].