

## ONLINE APPENDIX

### VASCULAR RISK FACTORS

Baseline smoking habits and alcohol intake were assessed with questionnaires. Packyears of smoking was calculated and alcohol intake was categorized as 'no or <1 U per week', '1–10 U per week', and '≥11 U per week'. Height and weight were measured, and the body mass index (BMI) was calculated ( $\text{kg}/\text{m}^2$ ). Systolic blood pressure (SBP) (mm Hg) and diastolic blood pressure (DBP) (mm Hg) were measured three times with a sphygmomanometer, and the average of these measures was calculated. Hypertension was defined as a mean SBP of >140 mm Hg, a mean DBP of >90 mm Hg or self-reported use of antihypertensive drugs. An overnight fasting venous blood sample was taken to determine glucose, lipids, total homocysteine and apolipoprotein-B levels. Diabetes mellitus was defined as fasting serum glucose levels of  $\geq 7.0$  mmol/l, and/or use of glucose-lowering medication, and/or a known history of diabetes. Hyperlipidemia

was considered if the serum cholesterol was  $\geq 5.0$  mmol/l, a low-density lipoprotein cholesterol of  $>3.2$  mmol/l, or if the patient was by using lipid lowering medication. History of stroke was based on a composite scoring made of neurologist-verified self-reported symptoms of previous stroke, previous history of carotid artery operation, or a physician diagnosis at study inclusion of the following conditions: transient ischemic attack, brain infarct, ischemic stroke, cerebral ischemia, amaurosis fugax or retinal infarction. Mean carotid intima-media thickness (in mm) was calculated for the left and right common carotid arteries based on six far-wall measurements on sonography. Ankle brachial index measurements were made by using a Vasoguard Doppler probe (8 MHz) and measurement techniques have been described in detail elsewhere.<sup>1</sup> Metabolic syndrome was determined by the National Cholesterol Education Program Adult Treatment Panel III criteria.<sup>2</sup> Genotyping for apolipoprotein-E

(Apo-E) was performed on coded DNA specimens and has been described in detail elsewhere.<sup>3</sup>

### MR IMAGING PROTOCOL

High-field imaging of the brain was performed on a whole-body 7T MR system (Philips Health care, Cleveland, OH, USA) with a volume transmit and 32-channel receive head coil (Nova Medical, Wilmington, MA, USA). The standardized scan protocol is described in detail in previous publications.<sup>4,5</sup>

Conventional MR imaging of the brain was performed on a 1.5T whole-body system (Gyrosan ACS-NT, Philips Medical Systems, Best, the Netherlands) by using a standardized scan protocol described in detail in previous work.<sup>6,7</sup>

### ASSESSMENT OF COGNITIVE FUNCTIONING

Memory was assessed with the 15 Word Learning Test by using a composite score of the immediate and delayed recall based on five trials, and the Rey-Osterrieth Complex figure test.<sup>8,9</sup> Executive functioning was assessed with the Verbal Fluency test by using animals as categories (2 minutes) and the letter A (1 minute); the Visual Elevator test (10 trials), and the Brixton Spatial Anticipation test.<sup>10–12</sup> Working memory was assessed with the combined longest span scores and total span scores

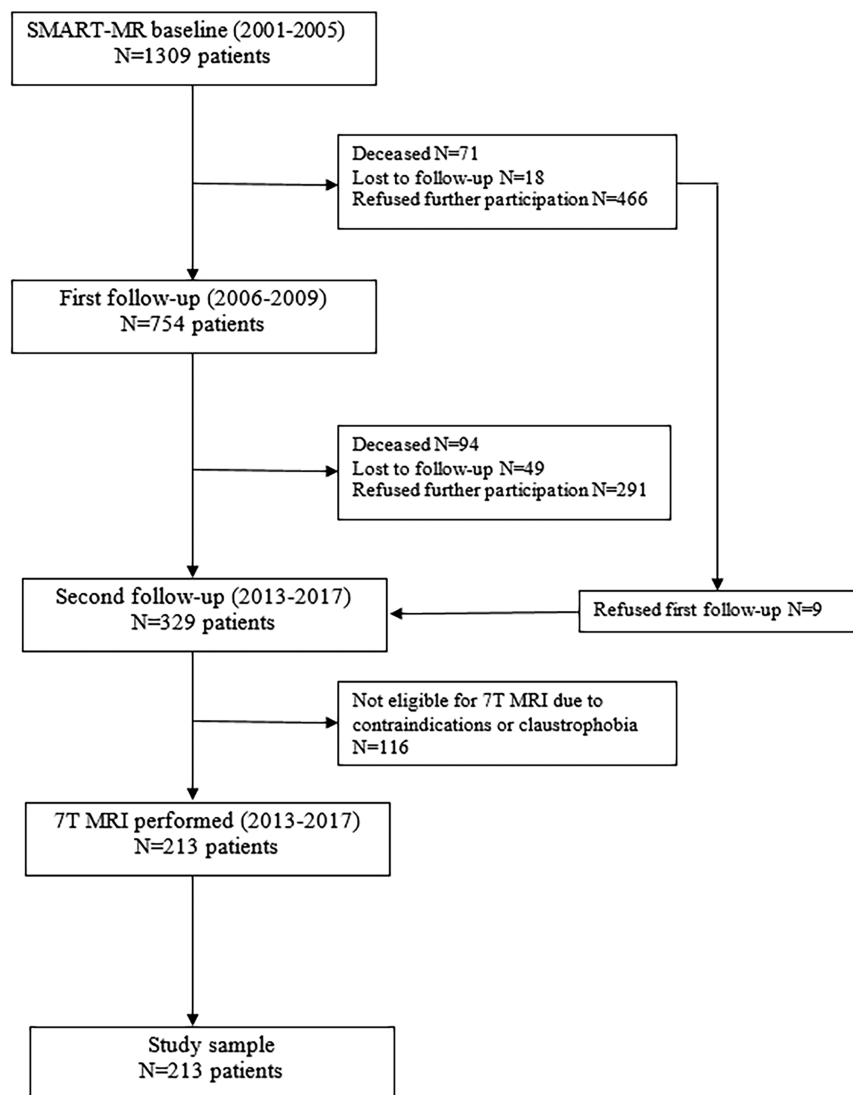


FIG 1. Participation flowchart of the SMART-MR study.

**Online Table 1: Baseline vascular risk factors of the study population (n = 1309) according to presence or absence of 7T brain MR imaging data**

	Patients with a 7T brain MR imaging scan (n = 213)	Patients without a 7T brain MR imaging scan (n = 1096)	p Value
Age (years)	55 ± 8	59 ± 10	<0.001
Sex, % men	82.6	79.1	0.242
History of stroke, %	24.4	22.8	0.611
BMI (kg/m <sup>2</sup> )	27 ± 3	27 ± 4	0.628
Smoking, pack years <sup>a</sup>	21 (0, 47)	23 (0, 52)	0.772 <sup>b</sup>
Alcohol use, % current	85	73	<0.001
Hypertension, %	51.2	52.0	0.823
Diabetes mellitus, %	11.5	22.7	<0.001
Carotid artery stenosis ≥70%, %	7.4	11.9	0.06
IMT (mm)	0.9 ± 0.2	1.0 ± 0.3	<0.001
ABI	1.2 ± 0.2	1.1 ± 0.2	<0.001

Characteristics are presented as mean ± SD or %.

BMI: body mass index; SD: standard deviation; IMT: intima-media thickness; ABI: ankle brachial index.

<sup>a</sup>Median (10th percentile, 90th percentile).

<sup>b</sup>Natural log-transformed due to a non-normal distribution in the statistical analysis.

of the Forward Digit Span and Backward Digit Span.<sup>13</sup> Processing speed was assessed with the Digit Symbol Substitution Test (120 seconds).<sup>14</sup>

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