Eur Radiol (2016) 26:969–978
DOI 10.1007/s00330-015-3926-6

MAGNETIC RESONANCE

Thoracic and abdominal aortic diameters in a general population: MRI-based reference values and association with age and cardiovascular risk factors

Birger Mensel[1] · Lydia Heßelbarth[1] · Michael Wenzel[1] · Jens-Peter Kühn[1] · Marcus Dörr[2,5] · Henry Völzke[3,5] · Wolfgang Lieb[4] · Katrin Hegenscheid[1] · Roberto Lorbeer[6]

Received: 17 December 2014 / Revised: 5 July 2015 / Accepted: 8 July 2015 / Published online: 25 July 2015

Abstract
Objectives To generate reference values for thoracic and abdominal aortic diameters determined by magnetic resonance imaging (MRI) and analyse their association with cardiovascular risk factors in the general population.
Methods Data from participants (n=1759) of the Study of Health in Pomerania were used for analysis in this study. MRI measurement of thoracic and abdominal aortic diameters was performed. Parameters for calculation of reference values according to age and sex analysis were provided. Multivariable linear regression models were used for determination of aortic diameter-related risk factors, including smoking, blood pressure (BP), high-density lipoprotein cholesterol (HDL-C).
Results For the ascending aorta (β=−0.049, p<0.001), the aortic arch (β=−0.061, p<0.001) and the subphrenic aorta (β=−0.018, p=0.004), the body surface area (BSA)-adjusted diameters were lower in men. Multivariable-adjusted models revealed significant increases in BSA-adjusted diameters with age for all six aortic segments (p<0.001). Consistent results for all segments were observed for the positive associations of diastolic BP (β=0.001; 0.004) and HDL (β=0.035; 0.087) with BSA-adjusted aortic diameters and for an inverse association of systolic BP (β=−0.001).
Conclusions Some BSA-adjusted median aortic diameters are smaller in men than in women. All diameters increase with age, diastolic blood pressure and HDL-C and decrease as systolic BP increases.
Key Points
- *Median aortic diameter increases with age and diastolic blood pressure.*
- *Median aortic diameter is larger in men than in women.*
- *Some BSA-adjusted median aortic diameters are smaller in men than in women.*

Keywords Aortic diameter · Magnetic resonance imaging · Reference values · Risk factors · Population-based research

✉ Birger Mensel
birger.mensel@uni-greifswald.de

[1] Institute of Diagnostic Radiology and Neuroradiology, University Medicine Greifswald, Ferdinand-Sauerbruch-Straße, 17475 Greifswald, Germany

[2] Department of Internal Medicine, University Medicine Greifswald, Greifswald, Germany

[3] Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany

[4] Institute of Epidemiology, Christian Albrechts University, Kiel, Germany

[5] DZHK (German Center for Cardiovascular Research), partner site Greifswald, Greifswald, Germany

[6] Institute of Clinical Radiology, Ludwig-maximilians-University Hospital, Munich, Germany

Introduction

The aorta connects the heart with the peripheral organs and plays a central role in the cardiovascular system. Aortic conditions such as thoracic or abdominal aneurysm and dissection are common and progress over time, often becoming life-threatening with a need for elective or emergency therapy [1–3]. Because these conditions are often associated with an increase in aortic diameter, the latter is an important parameter in deciding when and how to treat these patients [1]. Moreover, there is evidence that an increased baseline diameter of the infrarenal aorta is a strong and independent risk factor for the development of abdominal aortic aneurysm [4]. Therefore,

it is crucial to have reference values for the different aortic segments.

Regardless of the imaging modality used (CT or MRI), the identification of reference values is hampered by the fact that aortic diameter depends on many physiologic factors including age, sex and body surface area (BSA) and is affected by a number of cardiovascular risk factors [5–7]. A positive correlation of aortic diameter and age is well established. In contrast, the association of other risk factors for cardiovascular disease (CVD) or morphologic pathologies of the aorta with aortic diameters and the cumulative and interactive effects of multiple risk factors on different aortic segments are not fully understood [5, 6, 8–10]. In addition, further evidence is also needed with regard to how these factors affect different aortic segments. Cross-sectional imaging using magnetic resonance imaging (MRI) allows visualization of the entire aorta and reliable measurement of diameters at different levels [11, 12]. However, studies analysing aortic diameter by MRI are sparse and have some limitations such as small number of subjects, highly selected study populations or incomplete imaging of the aorta [13–15].

The aim of this study was to provide reference values for thoracic and abdominal aortic diameters derived by MRI and to evaluate associations with age and other cardiovascular risk factors in a large general population.

Methods

Study sample

A subsample of participants of the Study of Health in Pomerania (SHIP-TREND), who underwent a whole-body magnetic resonance imaging (WBMRI) examination between 2008 and 2012 (n=1759; 872 women), were included in this study. SHIP-TREND is a cross-sectional, population-based study conducted in the northeast region of Germany. A sample of 8826 adults (20–79 years) was drawn from local population registries [16], and 4420 subjects volunteered for baseline examinations. Exclusion criteria were non-WBMRI examination (n=2373) and missing data on aortic diameters (n=35). Furthermore, subjects with self-reported stroke (n=26) and myocardial infarction (n=22) were excluded from analysis of aortic diameters. Other exclusion criteria were aortic pathologies such as thoracic (≥5 cm) or abdominal (≥3.5 cm) aneurysm and aortic dissection (n=7). A total of 1759 participants were analysed in this study. All participants provided written informed consent. The study was approved by the Ethics Committee of University of Greifswald and complies with the Declaration of Helsinki.

MRI examination and aortic diameter measurement

WBMRI was performed on a 1.5-T MRI scanner (Magnetom Avanto; Siemens Healthcare, Erlangen, Germany). Imaging was performed using integrated coil elements and phased-array surface coils. Aortic diameters were measured on plain axial 3D T1-weighted volumetric interpolated breath-hold examination (VIBE) images. Imaging parameters for the thoracic aorta (one slab) were field of view 450×360 mm, TR/TE 3.1/1.1 ms, flip angle 8°, voxel size 1.8×1.8×3.0 mm, scan time 21 s and slices per scan 96. Imaging parameters for the abdominal aorta (two slabs) were field of view 450×360 mm, TR/TE 7.5/2.4 ms, flip angle 10°, voxel size 2.4×1.6×4.0 mm, scan time 38 s and slices per scan 96. Slice thickness was always 1.5 mm with a gap of 0.3 mm.

The outer diameters of six predefined aortic segments were measured: the ascending and descending aorta (level of the pulmonary trunk), the aortic arch (proximal to the origin of the left subclavian artery), the subdiaphragmatic aorta (level of the aortic hiatus), and the supra- and infrarenal aorta (1 cm above/below the right renal artery origin; Fig. 1). Diameters were measured on axial slices in coronal orientation from outer wall to outer wall using the OsiriX image viewing and processing software (version 3.6.1; Pixmeo Sarl, Bernex, Switzerland). Diameter measurements were carried out independently by two observers (LH, MW) and are based on either one reader's measurement. The readers were blinded to other individual data. The method of measurement including intra- and interobserver agreement was validated in a previous study using orthogonal contrast-enhanced magnetic resonance angiography [12]. If at least one diameter measurement was missing, the whole data set was excluded from further analysis.

Before starting diameter measurements in a data set, each observer separately rated the image quality of each segment to be measured as sufficient (clear delineation of the outer aortic wall from perivascular tissue without significant artefacts (breathing, cardiac movement) hindering diameter measurement) or insufficient (significant blurring or artefacts obscuring the aortic wall). If at least one segment of the aorta was rated as insufficient the entire data set was discarded. The criteria for sufficient image quality were very strict.

Aortic diameters were analysed unadjusted and adjusted for body surface area (BSA). BSA was calculated according to the Du Bois formula [17]: $(BSA = 0.007184 \times (\text{height in cm})^{0.725} \times (\text{weight in kg})^{0.425}$.

Risk factor measurement

Methods for measurement of baseline characteristics in SHIP-TREND have been described elsewhere [16]. Besides age and sex, other factors considered to potentially affect aortic diameter included smoking status, blood pressure (BP), HbA1c, low-density and high-density lipoprotein cholesterol (LDL-C

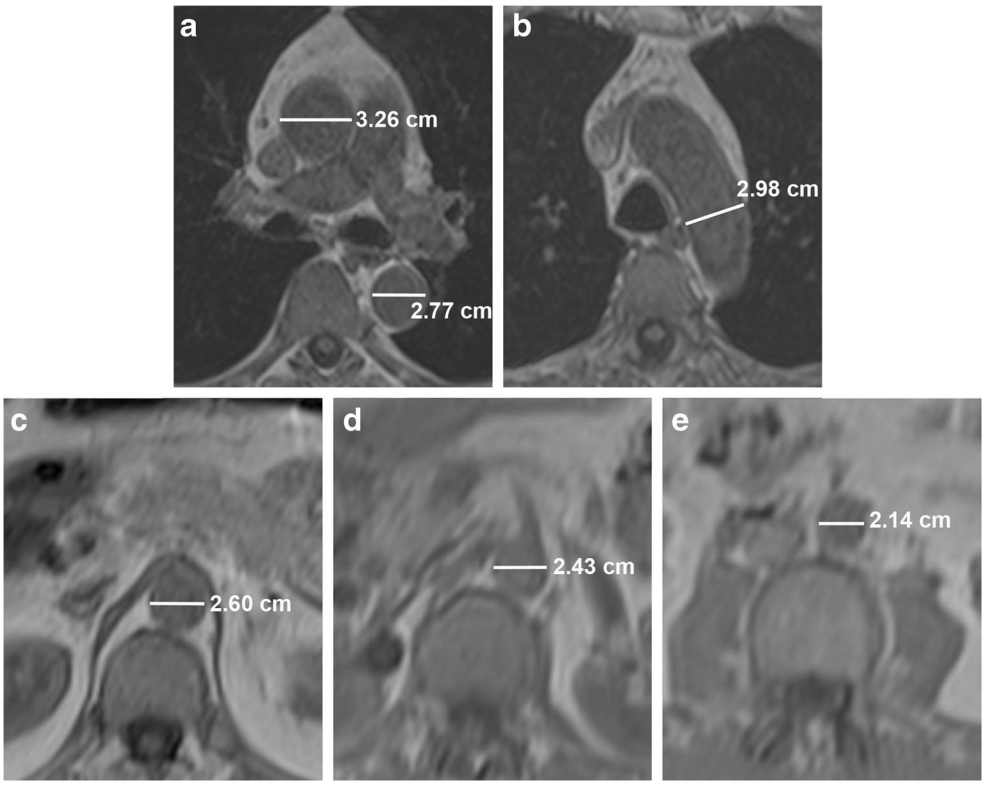

Fig. 1 T1-weighted VIBE images illustrating diameter measurement in a 73-year-old male volunteer: **a** ascending and descending aorta, **b** aortic arch, **c** subphrenic aorta, **d** suprarenal aorta, **e** infrarenal aorta

and HDL-C) and triglyceride. Interview-assessed smoking status was categorized as never, former or current smoker. Systolic and diastolic BP were measured at the right arm of seated subjects after a 5-min rest period during the core examination. The mean of the second and third measurement was used for the present analysis. Blood samples were taken from each volunteer in the supine position between 07.00 a.m. and 04.00 p.m. and were analysed immediately.

Statistical analysis

Medians (25th and 75th percentiles) and absolute numbers (percentages) were used to summarize baseline characteristics of the male and female study sample of SHIP-TREND.

Different percentiles (5th, 25th, 50th, 75th and 95th) of aortic diameters were calculated for 10-year age groups and separately for women and men. Differences in median diameter between women and men were tested for significance using quantile regression. Age- and sex-specific reference values for BSA-adjusted aortic diameters were provided by estimated intercepts and β coefficients using quantile regression for the median and for 5th and 95th percentiles. Exemplarily, reference values were calculated for a 51-year-old man (representing median age). Additionally, the 5th and 95th percentile reference limits according to age were presented graphically using fractional polynomial regression models [18, 19].

Table 1 Baseline characteristics of the study sample

Parameter	Women *n*=872	Men *n*=887
Age (years)	53 (42; 62)	51 (41; 62)
Smoking status		
Never smoker	420 (48 %)	282 (32 %)
Former smoker	263 (30 %)	379 (43 %)
Current smoker	188 (22 %)	223 (25 %)
Body mass index (kg/m^2)	26.4 (23.3; 30.2)	27.7 (25.3; 30.3)
Waist circumference (cm)	82 (75; 92)	95 (88; 103)
Body surface area (m^2)	1.78 (1.68; 1.88)	2.04 (1.94; 2.15)
Systolic blood pressure (mmHg)	119 (108; 131)	132 (123; 143)
Diastolic blood pressure (mmHg)	75 (69; 81)	80 (74; 86)
Hypertension	328 (38 %)	435 (49 %)
Use of antihypertensive medication	271 (31 %)	256 (29 %)
Diabetes	71 (8 %)	72 (8 %)
HbA1c (%)	5.2 (4.8; 5.6)	5.3 (4.9; 5.6)
HDL-C (mmol/l)	1.59 (1.36; 1.84)	1.25 (1.08; 1.48)
LDL-C (mmol/l)	3.37 (2.80; 4.04)	3.45 (2.83; 4.01)
Total cholesterol (mmol/l)	5.6 (4.9; 6.3)	5.4 (4.6; 6.1)
Triglycerides (mmol/l)	1.22 (0.88; 1.68)	1.41 (0.99; 2.13)

Data are given as number (percentage) or median (25th and 75th percentile)

HbA1c hemoglobin A1c, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

Associations between BSA-adjusted aortic diameter and risk factors were assessed using multivariable linear regression models, and β coefficients were provided. Sex, age, smoking status, systolic and diastolic BP, HbA1c, HDL-C, LDL-C and triglycerides were considered as potential risk factors. Adjusted R^2 and partial R^2 were calculated to evaluate the fit of the model and the contribution of each risk factor. The assumption of linearity of the association between risk factors and BSA-adjusted aortic diameter was checked visually by comparing residual distributions with the normal distribution and additionally using multivariable regression spline models [20]. Interaction effects between all analysed risk factors were additionally tested. A value of $p<0.05$ was considered statistically significant.

Statistical analysis was performed using Stata 12.1 (Stata Corporation, College Station, TX, USA).

Results

In the study sample, women ($n=872$; 50 %) had a median age of 53 years, 22 % of them were current smokers, 8 % had diabetes and 38 % a history of hypertension. Men ($n=887$) had a similar median age of 51 years, included 25 % smokers and 8 % diabetics, but had a much higher prevalence of hypertension of 49 % compared to women. Further baseline characteristics of the study sample are summarized in Table 1.

A total of 198 participants were excluded because of insufficient image quality.

Reference values for aortic diameters

The unadjusted median diameters of the different aortic segments were as follows: ascending aorta (3.20 cm for women, 3.49 cm for men), aortic arch (2.73 cm, 2.93 cm), descending aorta (2.34 cm, 2.63 cm), subphrenic aorta (2.22 cm, 2.46 cm), suprarenal aorta (2.07 cm, 2.34 cm) and infrarenal aorta (1.75 cm, 1.97 cm) with a relative reduction of 45 % for women and 44 % for men (from ascending to infrarenal aorta). Each median aortic diameter was lower in women compared to men ($p<0.001$ for all aortic segments) with the relative reduction ranging between 7 % (aortic arch) and 12 % (suprarenal) (Tables 2 and 3).

Values for 5th percentile, median and 95th percentile increase with the 10-year age group.

Table 2 Age- and sex-specific percentiles of thoracic aortic diameter (cm) in the study sample

		Women						Men					
	Age (years)	Percentiles						Percentiles					
Aorta		*n*	5th	25th	50th	75th	95th	*n*	5th	25th	50th	75th	95th
Ascending		872	2.5	2.9	3.2	3.47	3.9	887	2.75	3.18	3.49	3.79	4.2
	20–29	43	2.31	2.49	2.71	2.91	3.28	76	2.38	2.68	2.915	3.08	3.55
	30–39	113	2.34	2.61	2.82	3.01	3.37	123	2.66	2.94	3.09	3.25	3.7
	40–49	219	2.5	2.78	3.03	3.27	3.7	219	2.84	3.18	3.37	3.61	4.11
	50–59	233	2.68	3.06	3.25	3.45	3.97	214	3.09	3.37	3.61	3.87	4.22
	60–69	179	2.96	3.26	3.49	3.74	3.97	153	3.27	3.52	3.7	3.96	4.43
	70+	85	3.02	3.23	3.41	3.76	3.98	102	3.27	3.54	3.78	3.96	4.32
Arch		872	2.25	2.51	2.73	2.93	3.27	887	2.41	2.71	2.93	3.18	3.54
	20–29	43	2.02	2.22	2.38	2.63	2.83	76	2.1	2.41	2.51	2.655	2.91
	30–39	113	2.15	2.35	2.49	2.65	2.96	123	2.35	2.55	2.7	2.85	3.16
	40–49	219	2.25	2.45	2.66	2.82	3.16	219	2.48	2.67	2.87	3.09	3.39
	50–59	233	2.38	2.59	2.74	2.96	3.27	214	2.59	2.84	3.005	3.21	3.53
	60–69	179	2.48	2.72	2.88	3.09	3.32	153	2.72	2.98	3.14	3.39	3.68
	70+	85	2.54	2.72	2.87	3.05	3.45	102	2.76	2.93	3.15	3.33	3.68
Descending		872	1.86	2.11	2.34	2.53	2.83	887	2.08	2.37	2.63	2.86	3.16
	20–29	43	1.67	1.81	1.91	2	2.21	76	1.82	2.01	2.17	2.285	2.4
	30–39	113	1.77	1.9	2.04	2.12	2.41	123	2.01	2.2	2.32	2.45	2.75
	40–49	219	1.86	2.08	2.21	2.36	2.58	219	2.16	2.39	2.53	2.67	2.9
	50–59	233	2.06	2.24	2.41	2.52	2.82	214	2.33	2.55	2.71	2.88	3.07
	60–69	179	2.25	2.41	2.53	2.67	2.93	153	2.51	2.73	2.89	3.04	3.26
	70+	85	2.23	2.51	2.64	2.79	3.02	102	2.56	2.77	2.925	3.15	3.48

Table 3 Age- and sex-specific percentiles of abdominal aortic diameter (cm) in the study sample

		Women						Men					
	Age (years)	Percentiles						Percentiles					
Aorta		*n*	5th	25th	50th	75th	95th	*n*	5th	25th	50th	75th	95th
Subphrenic		872	1.75	2.03	2.22	2.41	2.67	887	1.89	2.2	2.46	2.67	2.97
	20–29	43	1.59	1.7	1.76	1.85	1.94	76	1.64	1.82	1.945	2.06	2.16
	30–39	113	1.67	1.82	1.93	2.03	2.23	123	1.83	1.97	2.1	2.22	2.47
	40–49	219	1.76	1.98	2.1	2.24	2.49	219	2.02	2.2	2.34	2.48	2.64
	50–59	233	1.98	2.15	2.28	2.42	2.64	214	2.24	2.41	2.55	2.68	2.89
	60–69	179	2.11	2.26	2.41	2.55	2.75	153	2.32	2.59	2.73	2.88	3.07
	70+	85	2.09	2.34	2.45	2.61	2.84	102	2.39	2.62	2.765	2.91	3.23
Suprarenal		872	1.68	1.9	2.07	2.24	2.44	887	1.83	2.13	2.34	2.51	2.72
	20–29	43	1.49	1.59	1.69	1.8	1.91	76	1.61	1.75	1.855	1.995	2.14
	30–39	113	1.57	1.77	1.88	1.96	2.13	123	1.82	1.95	2.08	2.2	2.32
	40–49	219	1.71	1.87	1.98	2.14	2.31	219	1.93	2.15	2.26	2.38	2.6
	50–59	233	1.84	2.01	2.12	2.26	2.48	214	2.09	2.27	2.42	2.56	2.71
	60–69	179	1.86	2.09	2.2	2.29	2.45	153	2.18	2.41	2.53	2.64	2.83
	70+	85	1.95	2.13	2.24	2.35	2.6	102	2.24	2.41	2.535	2.64	2.86
Infrarenal		872	1.44	1.62	1.75	1.88	2.04	887	1.62	1.84	1.97	2.12	2.36
	20–29	43	1.29	1.41	1.49	1.58	1.77	76	1.47	1.595	1.67	1.76	1.92
	30–39	113	1.35	1.5	1.59	1.68	1.85	123	1.55	1.69	1.79	1.89	2.01
	40–49	219	1.46	1.6	1.71	1.83	1.95	219	1.68	1.84	1.93	2.04	2.18
	50–59	233	1.54	1.69	1.79	1.89	2.04	214	1.8	1.94	2.03	2.14	2.32
	60–69	179	1.58	1.72	1.84	1.92	2.12	153	1.84	1.99	2.12	2.21	2.43
	70+	85	1.66	1.76	1.86	1.98	2.18	102	1.88	2.01	2.12	2.26	2.47

Reference values for BSA-adjusted aortic diameters

Parameters for calculation of reference values for BSA-adjusted aortic diameters are presented in Table 4. The significant increase in diameter ($p<0.001$) with each single year of age is similar for women and men for the median, 5th percentile and 95th percentile and varies between the lowest for the female infrarenal aorta ($\beta_{p50}=0.005$, $\beta_{p5}=0.004$, $\beta_{p95}=0.006$) and the highest for the female ascending aorta ($\beta_{p50}=0.011$, $\beta_{p5}=0.008$, $\beta_{p95}=0.014$), whereas the increase at the 95th percentile is always higher than at the 5th percentile (Table 4, Figs. 2 and 3).

Cardiovascular risk factors and BSA-adjusted aortic diameters

For the ascending aorta ($\beta=-0.049$, $p<0.001$), the aortic arch ($\beta=-0.061$, $p<0.001$) and the subphrenic aorta ($\beta=-0.018$, $p=0.004$), the BSA-adjusted diameters were lower in men than in women. There were no sex differences for the descending and the suprarenal aorta, while for the infrarenal aorta the diameter was higher in men than in women ($\beta=0.013$, $p=0.013$; Table 5).

As with unadjusted association, multivariable-adjusted association revealed significant increases in BSA-adjusted diameters of all six investigated aortic segments with age ($p<0.001$ for each aortic segment). Current smoking was positively associated with the diameter of the descending, subphrenic, suprarenal and infrarenal aorta but not with the diameter of the ascending aorta and the aortic arch (Table 5). Consistent results for all aortic segments were observed for the positive associations of diastolic BP and HDL-C with BSA-adjusted aortic diameters and for the inverse association of systolic BP with aortic diameters. HbA1c and LDL-C were not associated with aortic diameters except for the subphrenic aorta (HbA1c: $\beta=-0.008$, $p=0.041$) and the infrarenal aorta (LDL-C: $\beta=-0.005$, $p=0.042$) with borderline significance. In sensitivity analysis, further adjustment for lipid-lowering medication did not substantially alter the results regarding HDL-C and LDL-C.

Furthermore, a higher triglyceride level was identified to be a potential risk factor for smaller aortic diameter, e.g. of the descending aorta ($\beta=-0.011$, $p<0.001$; Table 5).

The diameters of the descending aorta (adjusted $R^2=0.56$) and the subphrenic aorta ($R^2=0.59$) were most strongly affected by the cardiovascular risk factors investigated, while the

Table 4 Association of age with body surface area-adjusted thoracic and abdominal aortic diameters and parameters for calculation of reference values based on the study sample

Aortic diameter/BSA			Women			Men		
			Intercept	β (age)	p	Intercept	β (age)	p
Thoracic	Ascending	Median	1.230	0.011	<0.001	1.170	0.010	<0.001
		5th Percentile	1.053	0.008	<0.001	1.048	0.008	<0.001
		95th Percentile	1.401	0.014	<0.001	1.449	0.011	<0.001
	Arch	Median	1.209	0.006	<0.001	1.073	0.007	<0.001
		5th Percentile	0.993	0.006	<0.001	0.913	0.006	<0.001
		95th Percentile	1.363	0.009	<0.001	1.212	0.009	<0.001
	Descending	Median	0.852	0.009	<0.001	0.831	0.009	<0.001
		5th Percentile	0.732	0.008	<0.001	0.729	0.008	<0.001
		95th Percentile	0.922	0.012	<0.001	0.929	0.011	<0.001
Abdominal	Subphrenic	Median	0.797	0.009	<0.001	0.704	0.010	<0.001
		5th Percentile	0.669	0.007	<0.001	0.619	0.008	<0.001
		95th Percentile	0.896	0.010	<0.001	0.820	0.011	<0.001
	Suprarenal	Median	0.837	0.006	<0.001	0.766	0.007	<0.001
		5th Percentile	0.738	0.005	<0.001	0.620	0.007	<0.001
		95th Percentile	0.899	0.009	<0.001	0.866	0.008	<0.001
	Infrarenal	Median	0.746	0.005	<0.001	0.708	0.005	<0.001
		5th Percentile	0.638	0.004	<0.001	0.603	0.005	<0.001
		95th Percentile	0.840	0.006	<0.001	0.798	0.006	<0.001

Parameters are from quantile regression

aortic arch (R^2=0.35) and infrarenal aorta (R^2=0.38) were least affected by these factors.

Interactions

A multivariable-adjusted model revealed a statistically significant interaction between sex and age with respect to the diameter of the ascending aorta. Age was more strongly associated with aortic diameter in women compared to men (women: β=0.012, 95 % CI 0.011–0.013, p<0.001; men: β=0.010, 95 % CI 0.009–0.011, p<0.001 for interaction) HbA1c was inversely associated with the subphrenic aortic diameter in women (β=−0.016, 95 % CI −0.029 to −0.002, p=0.022) but not in men. Interactions between HDL-C or LDL-C with lipid-lowering medication were not significant.

Discussion

This is the first study presenting MRI-based age- and sex-specific reference diameters for the thoracic and abdominal aorta derived in an unselected European population. Additionally, the BSA-adjusted aortic diameters of women and men were compared and their associations with cardiovascular risk factors were evaluated. Our results suggest that the median aortic diameter decreases from ascending to infrarenal aorta for women and men and that the median diameters of all aortic segments are lower in women than men, supporting the findings of earlier studies [5, 6, 8, 14, 21]. However, most studies used CT [5, 6, 8], analysed only the thoracic aorta [5, 8, 15] or investigated a small or highly selected study sample [14, 15]. In contrast, our study assessed the whole aorta using MRI in a large unselected population.

Moreover, the median aortic diameters of all six segments as well as the 5th and 95th percentiles increased with age group. The increase in aortic diameter with age for both sexes is a well-known fact [7, 8, 21, 22]. In a study of a North-American population, Rogers et al. found an annual increase in the diameter of the ascending aorta of 0.016 cm in women and 0.02 cm in men. The results for the descending and infrarenal aorta were 0.016 cm/0.019 cm and 0.009 cm/0.013 cm, respectively [6]. Kälsch et al. presented a similar analysis for a European population, demonstrating an increase in diameter for women and men of 0.015 cm/0.015 cm per year (ascending aorta) and 0.016 cm/0.017 cm (descending aorta) [5]. We analysed the association of age with median aortic diameter for both the thoracic and abdominal aorta after adjustment for BSA. The significant increase in aortic diameter with each single year of age was similar for women and men for the median, 5th percentile and 95th percentile. The associations between age and unadjusted diameters varied

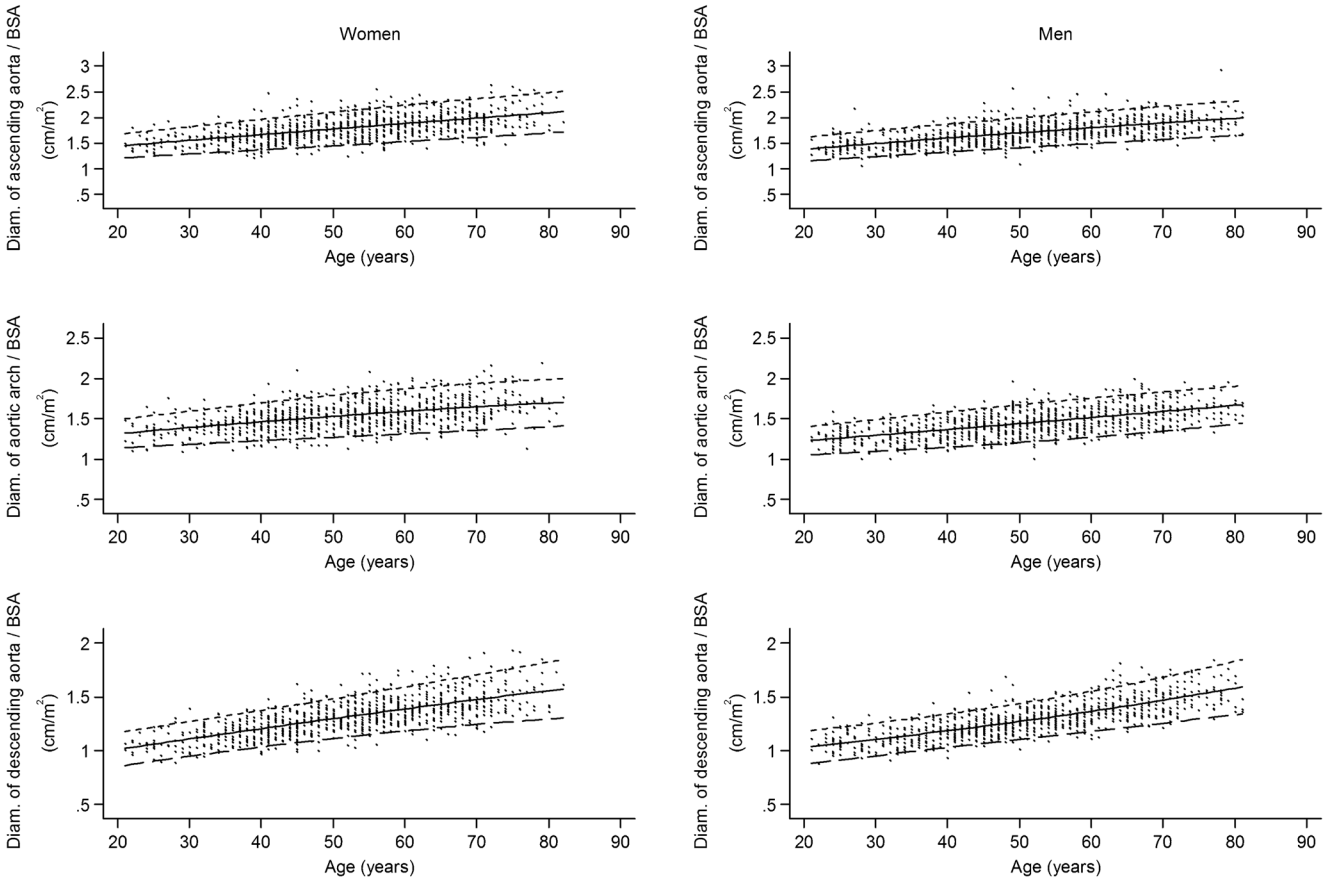

Fig. 2 Age-specific distributions of BSA-adjusted diameters of the thoracic ascending, the aortic arch and the descending aorta. The diameters are given as mean values with 5th and 95th percentiles for women and men. The values were calculated using fractional polynomial regression models

between different aortic segments. The ascending aorta showed a stronger association between age and diameter for women (0.011 cm/year) compared to men (0.010 cm/year), while the association between age and the diameter of the infrarenal aorta was the same for both sexes (0.005 cm/year). This result is not surprising in view of the different functions of the aortic segments. The ascending aorta is a conduit but also has a cushion function, ensuring continuous blood perfusion of the peripheral organs [23]. The mechanical stress with rapidly alternating wall tension during the cardiac cycle, which contributes significantly to the aortic enlargement, is therefore much higher for the ascending aorta compared to the infrarenal segment. The increase in diameter with age for each segment was always higher at the 95th percentile than at the 5th percentile for both sexes, indicating that the diameter of the aorta is increasing faster with larger diameters. The Norwegian population-based Tromsø Study, which focussed on the infrarenal aorta, found similar results [24]. The faster increase of larger aortic diameters can be explained by Laplace's law, predicting that an increasing vessel diameter leads to an increase in wall tension, resulting in a further increase in aortic diameter [25].

Our multivariable model for the assessment of cardiovascular risk factors and BSA-adjusted aortic diameters identified an inverse association with male sex for the ascending aorta, the aortic arch and the subphrenic aorta, whereas only the infrarenal aorta (p=0.0013) revealed a positive association. In line with our results, Kälsch et al. found a significantly greater diameter for the ascending and descending thoracic aorta after BSA adjustment for women [5]. Furthermore, diastolic BP was positively and systolic BP was slightly inversely associated with diameters for all aortic segments investigated in our study. Kälsch et al. found a greater positive association for diastolic BP (β=0.05–0.08 for women and men, per 10 mmHg) compared to systolic BP (β=0.03–0.04) with the thoracic aortic diameter [5]. Rogers et al. showed a slightly weaker positive correlation for abdominal aortic diameter with systolic BP compared to diastolic BP [6]. However, the studied populations were probably older and both results refer to absolute diameter measurements in contrast to our BSA-adjusted results.

In a sensitivity analysis of a subgroup comparable to the populations investigated in the latter studies (aged 45–74 years, using absolute diameters), we observed similar results for systolic and diastolic BP in univariate models and for

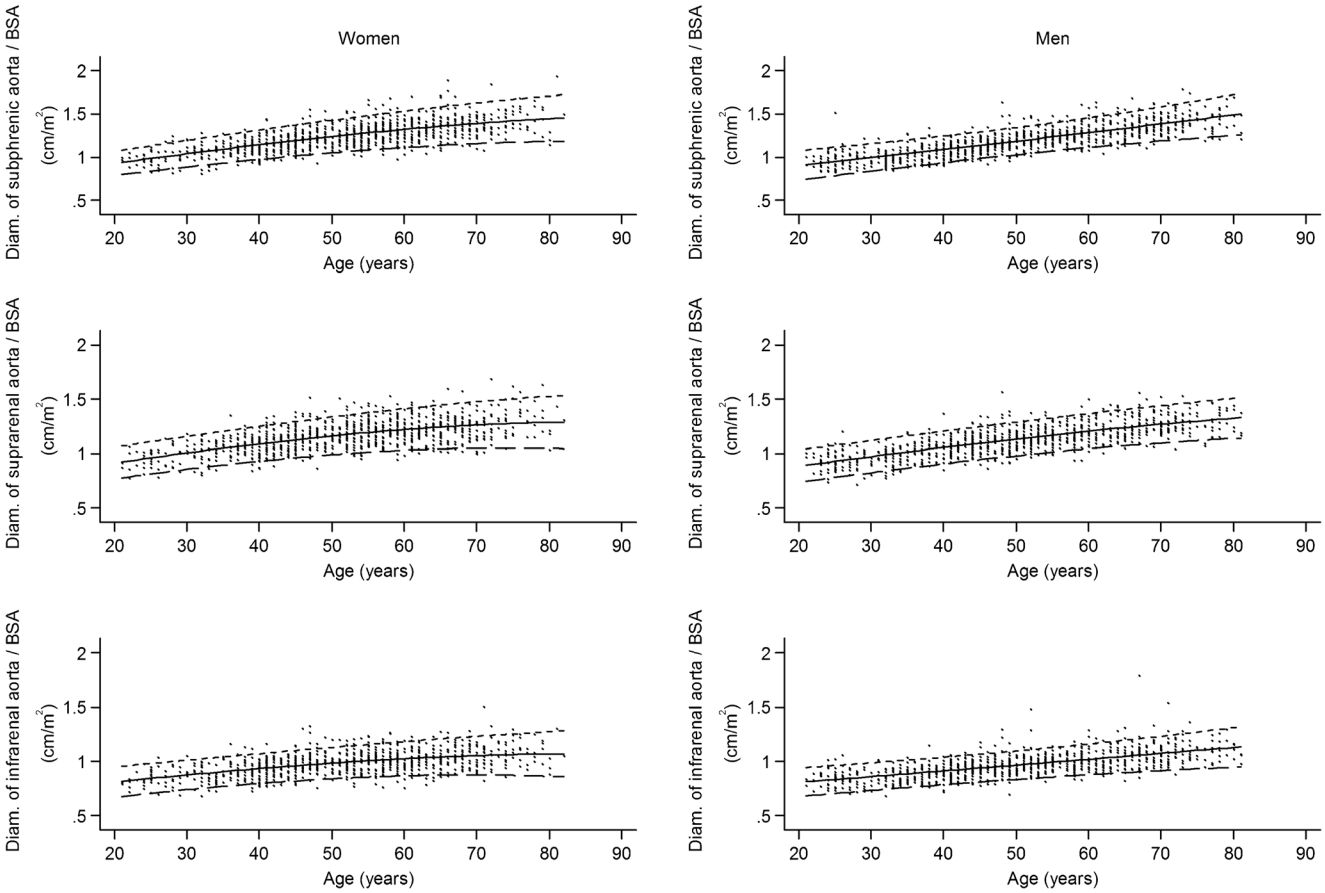

Fig. 3 Age-specific distributions of BSA-adjusted diameters of the abdominal subphrenic, suprarenal and infrarenal aorta. The diameters are given as mean values with 5th and 95th percentiles for women and men. The values were calculated using fractional polynomial regression models

diastolic BP in multivariable-adjusted models. However, the inverse association between systolic BP and aortic diameters revealed by the multivariable-adjusted models (including diastolic BP) was consistent in these subanalyses.

The positive association of HDL-C with the diameters of all aortic segments in our study appeared paradoxical. Rogers et al. showed a predominantly inverse correlation of thoracic and abdominal aortic diameters with HDL-C [6]. When considering that an increase in aortic diameter is part of a vascular aging process with consecutive atherosclerosis and vascular dilatation and that HDL-C protects against this sequel, it would be more reasonable to find an inverse association [26]. On the other hand, LDL-C and triglycerides show more of an inverse association with aortic diameter, which points to the pathophysiologic role of HDL-C as an antagonist. However, recent data suggest that not only the amount of HDL-C in blood is critical but also its function [27].

The major strength of this study is its population-based setting including a large number of participants and the additional recording of comprehensive clinical and laboratory data. Another advantage is that the diameters of the thoracic as well as the abdominal aorta were assessed using a previously validated technique of aortic diameter measurement including radiation-free image acquisition. A limitation is that only a subgroup of the whole SHIP study population was examined by MRI. Another drawback is that comparability of our results with findings reported by other groups is limited. Aortic diameter measurement in volunteers using MRI is less widespread than the use of CT/electron beam computed tomography. Finally, information on diseases which might influence aortic diameter (large vessel arteritis, bicuspid aortic valve or connective tissue diseases) was not available for our study participants. All subjects included in our study were of European descent. Results for other ethnicities and possible ethnic variations remain to be established.

In conclusion, our study presents MRI-based reference values for the diameter of the thoracic and abdominal aorta in a general population. The median aortic diameter shows a positive association with male sex and age, though the association with sex is partially reversed after BSA adjustment. In addition, our results demonstrate that some cardiovascular risk factors such as systolic and diastolic BP, smoking and HDL-C are associated with thoracic and abdominal aortic diameters.

Table 5 Cardiovascular risk factor model for body surface area-adjusted thoracic and abdominal aortic diameters

	Thoracic aorta diameter/BSA				Abdominal aorta diameter/BSA	
Risk factors	Ascending β (95 % CI)	Arch β (95 % CI)	Descending β (95 % CI)	Subphrenic β (95 % CI)	Suprarenal β (95 % CI)	Infrarenal β (95 % CI)
Men	−0.049 (−0.070; −0.027)***	−0.061 (−0.078; −0.045)***	−0.005 (−0.018; 0.007)	−0.018 (−0.031; −0.006)**	−0.001 (−0.012; 0.010)	0.013 (0.003; 0.023)*
Age	0.011 (0.010; 0.012)***	0.007 (0.007; 0.008)***	0.010 (0.009; 0.010)***	0.010 (0.010; 0.011)***	0.008 (0.007; 0.008)***	0.006 (0.005; 0.006)***
Former smoker	−0.008 (−0.029; 0.013)	−0.003 (−0.019; 0.013)	0.011 (−0.002; 0.023)	0.014 (0.002; 0.026)*	0.005 (−0.006; 0.016)	0.001 (−0.009; 0.011)
Current smoker	0.006 (−0.018; 0.030)	0.007 (−0.012; 0.025)	0.031 (0.017; 0.046)***	0.039 (0.025; 0.053)***	0.030 (0.017; 0.043)***	0.026 (0.015; 0.038)***
Systolic BP	−0.001 (−0.002; −0.001)**	−0.001 (−0.001; 0.000)*	−0.001 (−0.001; 0.000)*	−0.001 (−0.001; −0.001)***	−0.001 (−0.002; −0.001)***	−0.001 (−0.001; 0.000)***
Diastolic BP	0.004 (0.003; 0.005)***	0.002 (0.001; 0.003)***	0.002 (0.001; 0.002)***	0.002 (0.001; 0.003)***	0.002 (0.002; 0.003)***	0.001 (0.000; 0.002)**
HbA1c	−0.005 (−0.018; 0.008)	0.000 (−0.010; 0.010)	−0.001 (−0.008; 0.007)	−0.008 (−0.016; 0.000)*	−0.004 (−0.011; 0.003)	−0.005 (−0.011; 0.002)
HDL-C	0.087 (0.057; 0.116)***	0.053 (0.031; 0.076)***	0.035 (0.017; 0.052)***	0.053 (0.036; 0.070)***	0.052 (0.036; 0.068)***	0.044 (0.030; 0.058)***
LDL-C	−0.004 (−0.014; 0.007)	0.002 (−0.006; 0.010)	−0.002 (−0.008; 0.004)	−0.005 (−0.011; 0.001)	−0.005 (−0.010; 0.001)	−0.005 (−0.010; 0.000)*
Triglycerides	−0.007 (−0.017; 0.003)	−0.012 (−0.020; −0.005)**	−0.011 (−0.017; −0.005)***	−0.011 (−0.017; −0.005)***	−0.010 (−0.015; −0.004)**	−0.008 (−0.013; −0.003)**
Adj. R^2	0.3983	0.3511	0.5607	0.5864	0.4908	0.3828

β parameters are from linear regression

CI confidence interval, *HbA1c* hemoglobin A1c, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

*$p<0.05$, **$p<0.01$, ***$p<0.001$

Acknowledgments The scientific guarantor of this publication is Jens-Peter Kühn. The authors of this manuscript declare relationships with the following companies: German Center for Cardiovascular Research. Roberto Lorbeer kindly provided statistical advice for this manuscript. Institutional review board approval was obtained. Written informed consent was obtained from all subjects (patients) in this study. Methodology: prospective, cross-sectional study, performed at one institution. SHIP is part of the Community Medicine Research Net of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research (01ZZ9603, 01ZZ0103, 01ZZ0403, 01ZZ0701, 03ZIK012), the Ministry of Cultural Affairs as well as the Social Ministry of the Federal State of Mecklenburg-West Pomerania. Whole-body MR imaging was supported by a joint grant from Siemens Healthcare, Erlangen, Germany, and the Federal State of Mecklenburg-West Pomerania. The University of Greifswald is a member of the 'Center of Knowledge Interchange' program of Siemens AG. Contrast-enhanced MRI research is part of the entire whole-body MRI study and was supported by Bayer Healthcare. Furthermore, this work is part of the Greifswald Approach to Individualized Medicine (GANI_MED) research project. The GANI_MED consortium is funded by the German Federal Ministry of Education and Research and by the Ministry of Cultural Affairs of the German Federal State of Mecklenburg–West Pomerania (03IS2061A). This study was further supported by the DZHK (German Center for Cardiovascular Research).

The Community Medicine Research network of the University of Greifswald, Germany, covers several research projects that share data from the population-based Study of Health in Pomerania (SHIP; http://ship.community-medicine.de). MRI examinations were funded by Siemens Healthcare and the Federal State of Mecklenburg-West Pomerania. The contributions to data collection made by field workers, technicians, interviewers and computer assistants are gratefully acknowledged.

References

1. Elefteriades JA, Farkas EA (2010) Thoracic aortic aneurysm clinically pertinent controversies and uncertainties. J Am Coll Cardiol 55:841–857
2. Hendy K, Gunnarson R, Golledge J (2014) Growth rates of small abdominal aortic aneurysms assessed by computerised tomography–a systematic literature review. Atherosclerosis 235:182–188
3. Tsai TT, Nienaber CA, Eagle KA (2005) Acute aortic syndromes. Circulation 112:3802–3813
4. Solberg S, Forsdahl SH, Singh K, Jacobsen BK (2010) Diameter of the infrarenal aorta as a risk factor for abdominal aortic aneurysm: the Tromso Study, 1994–2001. Eur J Vasc Endovasc Surg 39:280–284
5. Kälsch H, Lehmann N, Mohlenkamp S et al (2013) Body-surface adjusted aortic reference diameters for improved identification of patients with thoracic aortic aneurysms: results from the population-based Heinz Nixdorf Recall study. Int J Cardiol 163:72–78
6. Rogers IS, Massaro JM, Truong QA et al (2013) Distribution, determinants, and normal reference values of thoracic and abdominal aortic diameters by computed tomography (from the Framingham Heart Study). Am J Cardiol 111:1510–1516
7. Wolak A, Gransar H, Thomson LE et al (2008) Aortic size assessment by noncontrast cardiac computed tomography: normal limits by age, gender, and body surface area. JACC Cardiovasc Imaging 1:200–209
8. Hager A, Kaemmerer H, Rapp-Bernhardt U et al (2002) Diameters of the thoracic aorta throughout life as measured with helical computed tomography. J Thorac Cardiovasc Surg 123:1060–1066

9. Rossi A, van der Linde D, Yap SC et al (2013) Ascending aorta dilatation in patients with bicuspid aortic valve stenosis: a prospective CMR study. Eur Radiol 23:642–649
10. Shin HJ, Shin JK, Chee HK, Kim JS, Ko SM (2015) Characteristics of aortic valve dysfunction and ascending aorta dimensions according to bicuspid aortic valve morphology. Eur Radiol 25:2013–2014
11. Groth M, Henes FO, Mullerleile K, Bannas P, Adam G, Regier M (2012) Accuracy of thoracic aortic measurements assessed by contrast enhanced and unenhanced magnetic resonance imaging. Eur J Radiol 81:762–766
12. Mensel B, Hegenscheid K, Hesselbarth L, Wenzel M, Hosten N, Puls R (2012) Thoracic and abdominal aortic diameter measurement by MRI using plain axial volumetric interpolated breath-hold examination in epidemiologic research: a validation study. Acad Radiol 19:1011–1017
13. Kaiser T, Kellenberger CJ, Albisetti M, Bergstrasser E, Valsangiacomo Buechel ER (2008) Normal values for aortic diameters in children and adolescents–assessment in vivo by contrast-enhanced CMR-angiography. J Cardiovasc Magn Reson 10:56
14. Wanhainen A, Themudo R, Ahlstrom H, Lind L, Johansson L (2008) Thoracic and abdominal aortic dimension in 70-year-old men and women–a population-based whole-body magnetic resonance imaging (MRI) study. J Vasc Surg 47:504–512
15. Garcier JM, Petitcolin V, Filaire M et al (2003) Normal diameter of the thoracic aorta in adults: a magnetic resonance imaging study. Surg Radiol Anat 25:322–329
16. Volzke H, Alte D, Schmidt CO et al (2011) Cohort profile: the study of health in Pomerania. Int J Epidemiol 40:294–307
17. Du Bois D, Du Bois EF (1989) A formula to estimate the approximate surface area if height and weight be known. 1916. Nutrition 5: 303–311, **discussion 312–303**
18. Royston P, Wright EM (1998) A method for estimating age-specific reference intervals ('normal ranges') based on fractional polynomials and exponential transformation. J R Stat Soc A 161:79–101
19. Wright E, Royston P (1997) Age-specific reference intervals for normally distributed data. Stata Tech Bull 38:4–9
20. Desquilbet L, Mariotti F (2010) Dose-response analyses using restricted cubic spline functions in public health research. Stat Med 29:1037–1057
21. Horejs D, Gilbert PM, Burstein S, Vogelzang RL (1988) Normal aortoiliac diameters by CT. J Comput Assist Tomogr 12:602–603
22. Agmon Y, Khandheria BK, Meissner I et al (2003) Is aortic dilatation an atherosclerosis-related process? Clinical, laboratory, and transesophageal echocardiographic correlates of thoracic aortic dimensions in the population with implications for thoracic aortic aneurysm formation. J Am Coll Cardiol 42:1076–1083
23. Stefanadis C, Stratos C, Vlachopoulos C et al (1995) Pressure-diameter relation of the human aorta. A new method of determination by the application of a special ultrasonic dimension catheter. Circulation 92:2210–2219
24. Singh K, Bonaa KH, Jacobsen BK, Bjork L, Solberg S (2001) Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: the Tromso Study. Am J Epidemiol 154: 236–244
25. Li JK (1986) Comparative cardiac mechanics: Laplace's law. J Theor Biol 118:339–343
26. O'Rourke MF (2007) Arterial aging: pathophysiological principles. Vasc Med 12:329–341
27. Rader DJ, Hovingh GK (2014) HDL and cardiovascular disease. Lancet 384:618–625