SUPPLEMENTAL MATERIALS

Methods (continues)

Assessment of hepatic fat content by magnetic resonance imaging (MRI)

In SHIP, a 1.5-T MRI (Magnetom Avanto; Siemens Healthcare AG, Germany) was performed by using a 12-channel phased-array coil. A three-echo confounder-corrected chemical shift-encoded MRI protocol acquired the imaging of the upper abdominal organs [1]. The following parameters were used: repetition time (msec)/echo time 1 (msec)/echo time 2 (msec)/echo time 3 (msec), 11.0/2.4/4.8/9.6; flip angle, 10°; one signal average; bandwidth, 1065 Hz/pixel; 224 × 126 × 32 matrix; field of view, 410 × 308; section thickness, 6.0 mm; and monopolar readout.

Following image acquisition, intrahepatic lipid content was estimated by proton-density fat fraction (PDFF,%) by using an offline reconstruction algorithm written in Matlab (Mathworks, Natick, Mass) [2]. PDFF maps were generated on a pixel-by-pixel basis with correction for T2* decay, T1 bias, noise bias, eddy current, multipeak spectral complexity of fat. Operator-defined selection of the entire liver excluding the central portal vein and inferior vena cava was performed in one section by using the region-of-interest tool in Osirix vesion 4.6; Pixmeo, Bernex, Switzerland). [3]

In KORA, MRI examinations were performed at a 3-T Magnetom Skyra (Siemens Healthcare AG, Germany) using an 18-channel body coil in combination with the table-mounted spine matrix coil [4]. The participants were scanned in the supine position.

Intrahepatic lipid content at the level of portal vein was estimated by PDFF measurement with a multiecho Dixon sequence with six echo times. It was based on a volume interpolated body

examination sequence with the following parameters: repetition time 8.90 ms, six echo times ranging from 1.23 to 7.38 ms, flip angle 4°, matrix 256 × 256. Slice thickness was 4 mm. For the estimation of hepatic PDFF, confounding effects of $T2^+$ decay and the spectral complexity of fat were taken into account [5]. T1 effect could be ignored due to the small flip angle used. Acquisition time was around 15 s. Data were analysed by a dedicated software package (Osirix, Ver. 4.1 64-bit; Pixmeo SARL, Bernex, GE, Switzerland). At the height of the portal vein, a region of interest was drawn on one slice including the whole liver parenchyma avoiding large vessels and surrounding extrahepatic tissue to measure hepatic fat content at the level of portal vein [6].

Assessment of aortic diameters by MRI

In SHIP, the outer diameters (cm) of the ascending and descending aorta were measured at the level of the pulmonary trunk. The infrarenal aorta diameter (cm) was measured 1 cm below the right renal artery origin. Aorta images were viewed and processed, and the diameters were measured on axial slices in coronal orientation from outer wall to outer wall with the software OsiriX (version 3.6.1; Pixmeo Sarl, Bernex, Switzerland). [7]

In KORA, the measurement of maximal aortic diameters was conducted by a gradient echo sequence, and the imaging data were further assessed by the 3D-function of a dedicated software (Syngo.via, Siemens). The maximal anterior–posterior diameter (cm) of the ascending and descending aorta at the level of right pulmonary artery was measured. Infrarenal aorta was located in a 3D coronal and sagittal view of the abdomen. The maximal anterior-posterior diameter (cm) of the infrarenal aorta was measured in the axial direction of the cross-section.

Assessment of subclinical carotid plaque

In SHIP, certified medical examiners assessed the extracranial carotid arteries for plaques and carotid intima-media thickness (cIMT) with B-mode ultrasound (vivid-I, GE Medical Systems, Waukesha,Wisconcin, WI, USA) with an operating frequency of 13 MHZ. Any plaque presence in the common carotid arteries (CCA), the bifurcations and the internal and external carotid arteries was defined.

Scans from the distal straight portion of the CCA on both sides were recorded. The mean far-wall IMT was measured semi-automatically on screen using an edge tracking software, which calculates a mean value by averaging approximately 250 measurements at an arterial segment of 1 cm in length. Mean cIMT (mm) was calculated as the following: (right mean cIMT + left mean cIMT)/2. If only one side had available information, the value of the available side was taken as the mean cIMT.

In KORA, presence and morphological composition of carotid plaque was determined on black-blood, T1-weighted, fat-suppressed sequences on both sides of the distal CCA, at the carotid bulb, and in the proximal internal carotid artery [8 9]. Boundary of the vessel lumen and the vessel wall were analyzed for all 14 consecutive slices using commercially available semiautomatic software (CASCADE; University of Washington, Seattle, the United States).

Traditional cardiovascular risk factors and other covariates

In SHIP, trained interviewers conducted computer-assisted personal interviews for the assessment of demographic, lifestyle and medical history. Blood samples were obtained and stored according to standardized procedures. The laboratory took part in the official German

external quality proficiency testing programs [1]. In KORA, information on the covariates was obtained from standardized interviews and questionnaires described elsewhere in detail [10].

For both studies, body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2), whereas obesity was defined as BMI more than 30 kg/m^2. Waist circumference (cm) was measured at the level midway between the lower rib margin and the iliac crest while the participants breathed out gently. According to smoking habits, participants were categorized into never smoker, ex-smoker and smoker. In SHIP, participants were classified as physically active if they regularly participated in sports for ≥ 1h/week in summer or winter, otherwise they were classified as physically inactive. In KORA, the duration of leisure time sport activity in winter and summer was assessed separately as follows: >2h/week (scored 1), 1-2 h/week (scored 2), <1 h/week (scored 3), none (scored 4). Possible scores for summer and winter were summed up to generate a total score for physical activity. Participants were classified as 'physically inactive' if they had a total score ≥ 5, and 'physically active' otherwise. Average alcohol intake per day were calculated from self-reported consumption of beer, wine and distilled spirits within the past month in SHIP, and over the previous weekend and workday in KORA. Excessive alcohol intake was defined in case of alcohol intake ≥ 20g/day for women or ≥ 30 g/day for men [11]. Alcohol intake was categorized into no intake, moderate intake and excessive intake. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or currently receiving antihypertensive treatment if participants were aware of having hypertension. Blood lipids levels included total cholesterol (mmol/L), high-density lipoprotein cholesterol (HDL-C) (mmol/L), low-density lipoprotein cholesterol (LDL-C) (mmol/L) and triglycerides (mmol/L). As markers of liver disease severity, levels of aspartate aminotransferase (AST) (µkat/l), alanine aminotransferase (ALT) (µkat/l) and gamma-glutamyl transferase (GGt) (µkat/l) were measured in the blood serum with the Dimension Vista System (Siemens

Healthcare AG, Germany). Imbedded in the whole body MRI protocols, visceral adipose tissue (VAT) in liter was measured from the diaphragm to the bladder in SHIP, and from the femoral head to the diaphragm in KORA.

Glucose tolerance status included normoglycaemia, prediabetes and diabetes. In SHIP, self-reported diabetes or antidiabetic medication intake together with the oral glucose tolerance test (OGTT) measurements (fasting glucose > 6.9 mmol/L and/or 2h glucose > 11.0 mmol/L) was considered when defining diabetes. In KORA, diabetes was defined by clinically validated diagnosis or OGTT measurement (fasting glucose > 6.9 mmol/L and/or 2h glucose > 11.0 mmol/L) for participants without validated diagnosis [4]. In both studies, prediabetes was defined by OGTT as impaired glucose tolerance (2h glucose between 7.8 and 11.0 mmol/L and normal fasting glucose) or impaired fasting glucose (fasting glucose between 6.1 and 6.9 mmol/L and normal 2h glucose) [12]. Normoglycaemia was defined if fasting glucose < 6.1mmol/L and 2h glucose < 7.8 mmol/L by OGTT.

Intake of medication in the last seven days prior to the interview was ascertained**.** Antihypertensive medication comprised antihypertensive effective compounds classified by the most recent guidelines [13]. Lipid-lowering medication included use of statins and fibrates in SHIP. In KORA, aside from statins and fibrates use, other lipid-modifying agents, such as omega-3 fatty acids, were also included among lipid-lowering medications.

References

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Supplemental tables

Supplemental table I. Study characteristics of study participants with and without fatty liver disease (FLD) in SHIP and KORA.

	SHIP			KORA		
	No FLD (N=872) (65%)	FLD (N=469) (35%)	*p* value	No FLD (N=220) (57%)	FLD (N=166) (43%)	*p* value
Age(years)	47.7 (13.9)	55.5 (11.7)	**< 0.001**	54.5 (9.2)	58.3 (8.6)	**< 0.001**
Women	521 (59.7%)	208 (44.3%)	**< 0.001**	117 (53.2%)	46 (27.7%)	**< 0.001**
BMI (kg/m^2)	25.8 (3.7)	30.5 (3.9)	**< 0.001**	26.0 (4.0)	30.8 (4.7)	**< 0.001**
Waist Circumference(cm)	83.6 (11.0)	98.5 (10.4)	**< 0.001**	91.5 (11.7)	107.9 (11.9)	**< 0.001**
Physically active	639 (73.3%)	321 (68.4%)	0.061	147 (66.8%)	83 (50.0%)	**< 0.001**
Smoking			**0.007**			**< 0.001**
smoker	206 (23.6%)	83 (17.7%)		56 (25.5%)	21 (12.7%)	
ex-smoker	293 (33.6%)	193 (41.2%)		78 (35.5%)	91 (54.8%)	
never smoker	373 (42.8%)	193 (41.2%)		86 (39.1%)	54 (32.5%)	
Alcohol consumption			**0.005**			0.201
no intake	106 (12.2%)	58 (12.4%)		55 (25.0%)	37 (22.3%)	
moderate intake	724 (83.0%)	367 (78.3%)		114 (51.8%)	77 (46.4%)	
excessive intake	42 (4.8%)	44 (9.4%)		51 (23.2%)	52 (31.3%)	
Systolic blood pressure (mmHg)	121.3 (16.0)	132.3 (15.8)	**< 0.001**	115.7 (15.1)	127.2 (16.8)	**< 0.001**
Diastolic blood pressure (mmHg)	74.5 (9.1)	80.5 (9.7)	**< 0.001**	73.0 (9.0)	78.3 (10.4)	**< 0.001**
Hypertension	253 (29.0%)	286 (61.0%)	**< 0.001**	47 (21.4%)	85 (51.2%)	**< 0.001**
Total cholesterol (mmol/l)	5.4 (1.1)	5.7 (1.0)	**< 0.001**	5.6 (0.9)	5.7 (1.0)	0.430
HDL-C (mmol/l)	1.6 (0.4)	1.3 (0.3)	**< 0.001**	1.7 (0.5)	1.5 (0.4)	**< 0.001**
LDL-C (mmol/l)	3.3 (0.9)	3.6 (0.9)	**< 0.001**	3.6 (0.8)	3.7 (0.9)	0.129
Triglyceride s(mmol/l)	1.0 (0.8, 1.4)	1.6 (1.2, 2.2)	**< 0.001**	1.0 (0.8, 1.4)	1.6 (1.2, 2.2)	**< 0.001**
ALT (µkat/l)	0.3 (0.2, 0.4)	0.5 (0.4, 0.7)	**< 0.001**	0.4 (0.3, 0.5)	0.6 (0.5, 0.8)	**< 0.001**
AST (µkat/l)	0.3 (0.2, 0.3)	0.3 (0.3, 0.4)	**< 0.001**	0.3 (0.3, 0.4)	0.4 (0.4, 0.6)	**< 0.001**
GGT (µkat/l)	0.4 (0.4, 0.6)	0.6 (0.5, 0.9)	**< 0.001**	0.4 (0.2, 0.5)	0.7 (0.4, 1.1)	**< 0.001**
Glucose tolerance status			**< 0.001**			**< 0.001**
normoglycaemic	713 (81.8%)	219 (46.7%)		178 (80.9%)	61 (36.7%)	
prediabetes	123 (14.1%)	158 (33.7%)		30 (13.6%)	65 (39.2%)	
diabetes	36 (4.1%)	92 (19.6%)		12 (5.5%)	40 (24.1%)	
Antihypertensive medication	179 (20.5%)	190 (40.5%)	**< 0.001**	35 (15.9%)	63 (38.0%)	**< 0.001**
Antithrombotic medication	48 (5.5%)	54 (11.5%)	**< 0.001**	7 (3.2%)	14 (8.4%)	**0.024**
Lipid lowering medication	60 (6.9%)	49 (10.4%)	**0.023**	16 (7.3%)	25 (15.1%)	**0.014**
History of CVD	50 (5.7%)	43 (9.2%)	**0.018**	NA		

Values are expressed as the mean (SD) for normally distributed continuous variables or median (interquartile range) for non-normally distributed continuous variables, or n (%) for categorical variables.

Hepatic fat content was quantified on the level of portal vein by MRI proton density fat fraction (PDFF). FLD (PDFF >5.6%) was defined according to the EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease.
Results with *p* value <0.05 are shown in bold.

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; GGT, Gamma-Glutamyl Transferase; CVD, cardiovascular disease, including myocardial infarction, stroke and angina pectoris; SD, standard deviation; NA, not applicable.

Supplemental table II. Differences in subclinical vascular disease parameters between participants with and without fatty liver disease (FLD) in SHIP and KORA.

	SHIP				KORA			
	No FLD (N=872)	FLD (N=469)	N missing	*p* value	No FLD (N=220)	FLD (N=166)	N missing	*p* value
Ascending aorta diameter (cm)	3.23 (0.45)	3.50 (0.42)	131	**< 0.001**	2.88 (0.40)	3.07 (0.40)	19	**< 0.001**
Descending aorta diameter (cm)	2.37 (0.33)	2.63 (0.31)	130	**< 0.001**	2.04 (0.30)	2.18 (0.30)	19	**< 0.001**
Infrarenal aorta diameter (cm)	1.80 (0.22)	1.93 (0.22)	105	**< 0.001**	1.46 (0.21)	1.57 (0.20)	19	**< 0.001**
Plaque presence	239 (27.4%)	228 (48.7%)	2	**< 0.001**	31 (20.3%)	23 (21.1%)	124	0.868
Type of plaque	NA	NA					124	0.910
AHA type I					122 (79.7%)	86 (78.9%)		
AHA type III					23 (15.0%)	15 (13.8%)		
AHA type V					5 (3.3%)	5 (4.6%)		
AHA type VI or VII					3 (2.0%)	3 (2.8%)		
Carotid intima-Media thickness (mm)	0.57 (0.13)	0.65 (0.14)	2	**< 0.001**	NA	NA		
Wall thickness, LCA (mm)	NA				0.71 (0.68, 0.76)	0.75 (0.70, 0.82)	135	**0.003**
Wall thickness, RCA (mm)	NA				0.72 (0.68, 0.80)	0.75 (0.71, 0.82)	129	**0.003**
Lumen area, LCA (mm^2)	NA				16.37 (13.59, 20.54)	18.35 (15.36, 22.34)	131	0.093
Lumen area, RCA(mm^2)	NA				14.98 (11.79, 20.28)	17.08 (14.34, 21.34)	124	**0.038**
Wall area, LCA(mm^2)	NA				11.82 (10.15, 13.51)	12.84 (11.67, 14.39)	135	**0.003**
Wall area, RCA(mm^2)	NA				11.14 (10.02, 13.69)	12.81 (11.57, 14.36)	129	**0.003**
NWI,LCA	NA				0.44 (0.04)	0.44 (0.05)	135	0.774
NWI,RCA	NA				0.45 (0.05)	0.45 (0.05)	129	0.719

Values are expressed as the mean (SD) for continuous variables, or n (%) for categorical variables. Results with p value < 0.05 are shown in bold.

Hepatic fat content was quantified on the level of portal vein by MRI proton density fat fraction (PDFF). FLD (PDFF >5.6%) was defined according to the EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease.

Results with *p* value <0.05 are shown in bold.

Abbreviations: AHA, American Heart Association; LCA, left carotid artery; RCA, right carotid artery; NWI, normalized wall index, calculated as (wall area/(lumen area + wall area); NA, not applicable.

Supplemental table III. Associations of hepatic fat content and subclinical disease parameters according to glucose tolerance status (normoglycaemia vs altered glucose metabolism) in the KORA study.

	N	Model 1	*p* value	Model 2	*p* value	Model 3	*p* value
Altered glucose metabolism (prediabetes and diabetes)							
		OR, 95% CI		**OR, 95% CI**		**OR, 95% CI**	
Plaque Presence (n case = 24)	91	0.62 (0.37, 1.03)	0.067	**0.52 (0.29, 0.94)**	**0.030**	**0.44 (0.21, 0.91)**	**0.027**
Plaque type	91	**0.60 (0.36, 0.99)**	**0.047**	**0.47 (0.26, 0.85)**	**0.014**	**0.39 (0.19, 0.79)**	**0.009**
		ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**	
Wall thickness, LCA (mm)	87	-0.01 (-0.05, 0.02)	0.426	-0.02 (-0.06, 0.01)	0.219	-0.02 (-0.06, 0.03)	0.430
Wall thickness, RCA (mm)	90	-0.01 (-0.04, 0.02)	0.561	-0.02 (-0.05, 0.01)	0.275	-0.02 (-0.06, 0.01)	0.199
Lumen area, LCA (mm^2)	89	0.02 (-0.07, 0.10)	0.666	0.0002 (-0.09, 0.09)	0.997	-0.01 (-0.12, 0.10)	0.886
Lumen area, RCA (mm^2)	91	0.05 (-0.03, 0.14)	0.205	0.03 (-0.06, 0.12)	0.480	0.04 (-0.07, 0.14)	0.507
Wall area, LCA (mm^2)	87	-0.004 (-0.07, 0.06)	0.910	-0.02 (-0.09, 0.04)	0.490	-0.01 (-0.09, 0.06)	0.730
Wall area, RCA (mm^2)	90	0.02 (-0.04, 0.08)	0.550	-0.001 (-0.07, 0.06)	0.966	-0.01 (-0.08, 0.07)	0.848
NWI, LCA	87	-0.01 (-0.02, 0.01)	0.379	-0.01 (-0.02, 0.01)	0.342	-0.01 (-0.02, 0.01)	0.447
NWI, RCA	90	-0.01 (-0.02, -0.001)	0.042	-0.01 (-0.02, 0.0002)	0.059	-0.01 (-0.03, 0.0002)	0.058
Ascending aorta (cm)	135	0.06 (-0.004, 0.12)	0.068	0.01 (-0.06, 0.08)	0.812	0.01 (-0.07, 0.08)	0.886
Descending aorta (cm)	135	0.03 (-0.01, 0.08)	0.141	-0.01 (-0.05, 0.04)	0.822	-0.01 (-0.06, 0.04)	0.692
Infrarenal aorta (cm)	135	0.01 (-0.02, 0.04)	0.553	-0.01 (-0.04, 0.02)	0.570	-0.02 (-0.05, 0.02)	0.371
Normoglycaemia							
		OR, 95% CI		**OR, 95% CI**		**OR, 95% CI**	
Plaque Presence (n case = 30)	171	1.10 (0.69, 1.76)	0.697	1.13 (0.67, 1.90)	0.641	1.21 (0.69, 2.11)	0.507
Plaque type	171	1.11 (0.70, 1.76)	0.666	1.12 (0.67, 1.86)	0.679	1.13 (0.65, 1.95)	0.664
		ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**	
Wall thickness, LCA (mm)	164	0.01 (-0.02, 0.03)	0.615	-0.01 (-0.03, 0.01)	0.257	-0.01 (-0.03, 0.01)	0.280
Wall thickness, RCA (mm)	167	0.01 (-0.01, 0.03)	0.342	-0.01 (-0.03, 0.02)	0.572	-0.002 (-0.03, 0.02)	0.845
Lumen area, LCA (mm^2)	166	0.004 (-0.05, 0.05)	0.871	-0.01 (-0.06, 0.05)	0.822	-0.001 (-0.06, 0.06)	0.960
Lumen area, RCA (mm^2)	171	0.03 (-0.03, 0.09)	0.330	0.01 (-0.06, 0.07)	0.825	0.02 (-0.05, 0.08)	0.646
Wall area, LCA (mm^2)	164	0.01 (-0.03, 0.04)	0.803	-0.02 (-0.06, 0.02)	0.302	-0.02 (-0.06, 0.03)	0.464
Wall area, RCA (mm^2)	167	0.03 (-0.01, 0.06)	0.194	-0.004 (-0.05, 0.04)	0.861	0.01 (-0.03, 0.05)	0.715
NWI, LCA	164	0.003 (-0.004, 0.01)	0.435	-0.0002 (-0.01, 0.01)	0.961	-0.001 (-0.01, 0.01)	0.790
NWI, RCA	167	0.001 (-0.01, 0.01)	0.910	-0.001 (-0.01, 0.01)	0.841	-0.002 (-0.01, 0.01)	0.665
Ascending aorta (cm)	232	-0.002 (-0.05, 0.05)	0.921	-0.03 (-0.09, 0.02)	0.229	-0.05 (-0.11, 0.004)	0.073
Descending aorta (cm)	232	-0.01 (-0.04, 0.03)	0.794	-0.03 (-0.07, 0.01)	0.136	-0.03 (-0.07, 0.01)	0.118
Infrarenal aorta (cm)	232	0.01 (-0.02, 0.03)	0.547	-0.004 (-0.03, 0.02)	0.762	-0.003 (-0.03, 0.02)	0.829

Model 1: adjusted for age, sex

Model 2: Model 1 + BMI

Model 3: Model 2 + smoking, physical activity, alcohol intake, systolic blood pressure, HDL-C, LDL-C, triglycerides, antihypertensive medication, lipid lowering medication

Results with *p* value <0.05 are shown in bold. The coefficient estimates represent the change in subclinical disease parameters with a standard deviation increment of hepatic fat content.

Abbreviations: LCA, left carotid artery; RCA, right carotid artery; NWI, normalized wall index, calculated as wall area/(lumen area + wall area); BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; ß, ß-estimates from linear regression; CI, confidence interval.

Supplemental table IV. Associations of hepatic fat content with subclinical vascular disease parameters among participants without excessive alcohol intake in SHIP and KORA studies.

	SHIP						
	N	Model 1	*p* value	Model 2	*p* value	Model 3[a]	*p* value
Aortic Diameters		**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**	
Ascending aorta (cm)	1,128	**0.06 (0.04, 0.09)**	**< 0.001**	0.02 (-0.01, 0.04)	0.219	0.01 (-0.02, 0.04)	0.533
Descending aorta (cm)	1,128	**0.06 (0.04, 0.07)**	**< 0.001**	0.01 (-0.002, 0.03)	0.092	0.01 (-0.01, 0.03)	0.294
Infrarenal aorta (cm)	1,128	**0.02 (0.01, 0.03)**	**< 0.001**	-0.01 (-0.02, 0.01)	0.416	0.0001 (-0.01, 0.01)	0.992
Carotid Plaque		**OR, 95% CI**		**OR, 95% CI**		**OR, 95% CI**	
Plaque Presence	1,253	**1.23 (1.06, 1.42)**	**0.008**	1.12 (0.94, 1.34)	0.208	1.02 (0.83, 1.24)	0.861
		ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**	
Carotid intima-media-thickness (mm)	1,253	**0.01 (0.01, 0.02)**	**0.001**	0.004 (-0.003, 0.01)	0.299	-0.001 (-0.01, 0.01)	0.740
	KORA						
	N	Model 1	*p* value	Model 2	*p* value	Model 3	*p* value
Aortic Diameters		**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**	
Ascending aorta (cm)	271	0.03 (-0.02, 0.08)	0.197	-0.03 (-0.09, 0.02)	0.245	-0.04 (-0.11, 0.02)	0.201
Descending aorta (cm)	271	0.03 (-0.01, 0.06)	0.098	-0.02 (-0.06, 0.02)	0.407	-0.004 (-0.05, 0.04)	0.865
Infrarenal aorta (cm)	271	**0.02 (0.002, 0.05)**	**0.032**	0.01 (-0.02, 0.03)	0.697	0.002 (-0.03, 0.03)	0.918
Carotid Plaque		**OR, 95% CI**		**OR, 95% CI**		**OR, 95% CI**	
Plaque Presence	201	1.02 (0.69, 1.50)	0.927	0.87 (0.56, 1.36)	0.546	0.68 (0.39, 1.19)	0.178
Plaque type	201	1.03 (0.71, 1.50)	0.870	0.83 (0.53, 1.29)	0.399	0.60 (0.34, 1.05)	0.072
		ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**	
Wall thickness, LCA (mm)	193	0.02 (-0.01, 0.04)	0.167	-0.01 (-0.03, 0.02)	0.513	-0.01 (-0.04, 0.01)	0.306
Wall thickness, RCA (mm)	197	0.01 (-0.01, 0.03)	0.211	-0.01 (-0.03, 0.02)	0.592	-0.01 (-0.03, 0.02)	0.588
Lumen area, LCA (mm^2)	195	0.03 (-0.02, 0.08)	0.195	0.02 (-0.04, 0.08)	0.497	0.04 (-0.03, 0.11)	0.239
Lumen area, RCA (mm^2)	201	0.03 (-0.02, 0.09)	0.212	0.01 (-0.05, 0.07)	0.772	0.05 (-0.02, 0.13)	0.135
Wall area, LCA (mm^2)	193	0.03 (-0.01, 0.07)	0.158	-0.01 (-0.05, 0.04)	0.734	-0.01 (-0.06, 0.05)	0.861
Wall area, RCA (mm^2)	197	0.04 (-0.003, 0.08)	0.076	0.003 (-0.04, 0.05)	0.910	0.02 (-0.03, 0.07)	0.415
NWI, LCA	193	0.002 (-0.01, 0.01)	0.528	-0.002 (-0.01, 0.01)	0.605	-0.01 (-0.02, 0.003)	0.199
NWI, RCA	197	-0.002 (-0.01, 0.01)	0.677	-0.004 (-0.01, 0.004)	0.368	**-0.01 (-0.02, -0.0004)**	**0.043**

Model 1: adjusted for age, sex

Model 2: Model 1 + BMI

Model 3: Model 2 + Smoking, physical activity, alcohol intake, systolic blood pressure, HDL-C, LDL-C, triglycerides, glucose tolerance status, antihypertensive medication, lipid lowering medication

a. Model 3 in SHIP was additionally adjusted for history of cardiovascular diseases.

Results with *p* value <0.05 are shown in bold. The coefficient estimates represent the change in subclinical disease parameters with a standard deviation increment of log transformed hepatic fat content.

Abbreviations: LCA, left carotid artery; RCA, right carotid artery; NWI, normalized wall index, calculated as wall area/(lumen area + wall area); BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; ß, ß-estimates from linear regression; CI, confidence interval.

Supplemental table V. Sensitivity analyses with fatty liver disease (PDFF >5.6% or PDFF >5.1%) as exposure as well as replacing BMI with either VAT or waist circumference as covariate in SHIP and KORA studies.

SHIP								
	FLD[1] (PDFF >5.6%)	*p* value	**FLD[1] (PDFF > 5.1%)**	*p* value	**VAT replacing BMI[2] (PDFF as continuous exposure)**	*p* value	**Waist circumference replacing BMI[3] (PDFF as continuous exposure)**	*p value*
Aortic Diameters	**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**	
Ascending aorta (cm)	-0.03 (-0.08, 0.02)	0.268	-0.02 (-0.07, 0.03)	0.469	0.01 (-0.02, 0.03)	0.669	-0.01 (-0.03, 0.02)	0.689
Descending aorta (cm)	0.01 (-0.02, 0.04)	0.569	0.02 (-0.01, 0.04)	0.309	0.004 (-0.01, 0.02)	0.664	0.00003 (-0.02, 0.02)	0.998
Infrarenal aorta (cm)	-0.002 (-0.03, 0.02)	0.852	-0.01 (-0.03, 0.02)	0.578	0.002 (-0.01, 0.02)	0.729	-0.004 (-0.02, 0.01)	0.494
Carotid Plaque	**OR, 95% CI**		**OR, 95% CI**		**OR, 95% CI**		**OR, 95% CI**	
Plaque Presence	1.08 (0.76, 1.55)	0.664	1.03 (0.72, 1.47)	0.888	1.07 (0.87, 1.31)	0.546	1.04 (0.85, 1.26)	0.720
	ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**	
Carotid intima-media-thickness (mm)	0.001 (-0.01, 0.01)	0.922	-0.003 (-0.02, 0.01)	0.658	-0.004 (-0.01, 0.004)	0.351	-0.01 (-0.01, 0.002)	0.187
KORA								
	FLD[1] (PDFF >5.6%)	*p* value	**FLD[1] (PDFF > 5.1%)**	*p* value	**VAT replacing BMI[2] (PDFF as continuous variable)**	*p* value	**Waist circumference replacing BMI[3] (PDFF as continuous variable)**	*p* value
Aortic Diameters	**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**	
Ascending aorta (cm)	-0.03 (-0.13, 0.06)	0.497	-0.05 (-0.14, 0.05)	0.332	-0.03 (-0.09, 0.03)	0.260	-0.05 (-0.11, 0.002)	0.060
Descending aorta (cm)	-0.03 (-0.10, 0.03)	0.324	-0.02 (-0.08, 0.05)	0.651	-0.01 (-0.06, 0.03)	0.514	-0.03 (-0.07, 0.004)	0.079
Infrarenal aorta (cm)	-0.01 (-0.05, 0.04)	0.798	-0.0003 (-0.04, 0.04)	0.991	-0.01 (-0.03, 0.02)	0.576	-0.02 (-0.04, 0.01)	0.219
Carotid Plaque	**OR, 95% CI**		**OR, 95% CI**		**OR, 95% CI**		**OR, 95% CI**	
Plaque Presence	0.72 (0.31, 1.66)	0.444	0.74 (0.32, 1.72)	0.483	0.68 (0.39, 1.18)	0.173	0.79 (0.48, 1.31)	0.364
Plaque type	0.66 (0.29, 1.52)	0.329	0.69 (0.30, 1.59)	0.383	0.60 (0.34, 1.06)	0.077	0.72 (0.43, 1.21)	0.213
	ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**		**ß, 95% CI**	
Wall thickness, LCA (mm)	0.004 (-0.04, 0.04)	0.836	0.002 (-0.04, 0.04)	0.936	-0.01 (-0.04, 0.01)	0.319	-0.02 (-0.04, 0.01)	0.205
Wall thickness, RCA (mm)	0.002 (-0.04, 0.04)	0.901	0.002 (-0.04, 0.04)	0.930	0.001 (-0.02, 0.03)	0.924	-0.01 (-0.03, 0.01)	0.339
Lumen area, LCA (mm^2)	0.02 (-0.08, 0.13)	0.679	0.05 (-0.06, 0.16)	0.356	0.03 (-0.04, 0.09)	0.391	-0.0004 (-0.06, 0.06)	0.991
Lumen area, RCA (mm^2)	0.06 (-0.05, 0.17)	0.316	0.05 (-0.06, 0.16)	0.399	0.07 (-0.001, 0.14)	0.054	0.03 (-0.03, 0.10)	0.308
Wall area, LCA (mm^2)	0.02 (-0.06, 0.09)	0.617	0.02 (-0.06, 0.09)	0.701	-0.002 (-0.05, 0.05)	0.944	-0.02 (-0.06, 0.03)	0.414
Wall area, RCA (mm^2)	0.03 (-0.05, 0.10)	0.462	0.02 (-0.05, 0.10)	0.566	0.03 (-0.01, 0.08)	0.164	0.004 (-0.04, 0.05)	0.850
NWI, LCA	-0.002 (-0.02, 0.01)	0.775	-0.003 (-0.02, 0.01)	0.644	-0.01 (-0.02, 0.002)	0.113	-0.003 (-0.01, 0.01)	0.548
NWI, RCA	-0.01 (-0.02, 0.01)	0.334	-0.01 (-0.02, 0.01)	0.412	**-0.01 (-0.02, -0.0003)**	**0.045**	-0.01 (-0.02, 0.001)	0.099

1. Model adjustment: age, sex, BMI, Smoking status, physical activity, alcohol intake, systolic blood pressure, HDL-C, LDL-C, triglycerides, glucose tolerance status, use of antihypertensive medication, use of lipid lowering medication, CVD (only in SHIP)
In this model, FLD was defined by either PDFF > 5.6% according to the EASL-EASD-EASO Clinical Practice Guideline for the management of non-alcoholic fatty liver disease or PDFF > 5.1% according to Kühn et al.[2]
2. Model adjustment: age, sex, VAT, Smoking status, physical activity, alcohol intake, systolic blood pressure, HDL-C, LDL-C, triglycerides, glucose tolerance status, use of antihypertensive medication, use of lipid lowering medication, CVD (only in SHIP)
3. Model adjustment: age, sex, waist circumference, Smoking status, physical activity, alcohol intake, systolic blood pressure, HDL-C, LDL-C, triglycerides, glucose tolerance status, use of antihypertensive medication, use of lipid lowering medication, CVD (only in SHIP)
Results with *p* value <0.05 are shown in bold.

Abbreviations: FLD, fatty liver disease; PDFF, proton density fat fraction; LCA, left carotid artery; RCA, right carotid artery; NWI, normalized wall index, calculated as wall area/(lumen area + wall area); BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VAT, visceral adipose tissue; OR, odds ratio; ß, ß-estimates from linear regression; CI, confidence interval.

Supplemental table VI. Associations of hepatic fat content with subclinical vascular disease parameters among participants without cardiovascular disease history in SHIP study.

	N	Model 1	*p* value	Model 2	*p* value	Model 3	*p* value
		ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**	
Ascending aorta (cm)	1120	**0.06 (0.03, 0.08)**	**< 0.001**	0.004 (-0.02, 0.03)	0.754	-0.004 (-0.03, 0.02)	0.760
Descending aorta (cm)	1120	**0.05 (0.04, 0.06)**	**< 0.001**	0.01 (-0.01, 0.02)	0.400	0.002 (-0.01, 0.02)	0.853
Infrarenal aorta (cm)	1120	**0.02 (0.01, 0.03)**	**0.001**	-0.01 (-0.02, 0.003)	0.158	-0.004 (-0.02, 0.01)	0.523
		OR, 95% CI		**OR, 95% CI**		**OR, 95% CI**	
Plaque Presence	1246	**1.21 (1.04, 1.41)**	**0.014**	1.13 (0.95, 1.35)	0.177	1.06 (0.87, 1.29)	0.558
		ß, 95% CI		**ß, 95% CI**		**ß, 95% CI**	
Intima-media-thickness (mm)	1246	**0.01 (0.002, 0.01)**	**0.007**	0.001 (-0.01, 0.01)	0.873	-0.004 (-0.01, 0.003)	0.277

Model 1: adjusted for age, sex

Model 2: Model 1 + BMI

Model 3: Model 2 + smoking, physical activity, alcohol intake, systolic blood pressure, HDL-C, LDL-C, triglycerides, glucose tolerance status, antihypertensive medication, lipid lowering medication

Results with *p* value <0.05 are shown in bold. The coefficient estimates represent the change in subclinical disease parameters with a standard deviation increment of hepatic fat content.

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; ß, ß-estimates from linear regression; CI, confidence interval.