Original Article

Correlation of MRI-derived adipose tissue measurements and anthropometric markers with prevalent hypertension in the community

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Objectives: To compare the correlations of MRI-derived adipose tissue measurements and anthropometric markers, respectively, with prevalent hypertension in a community-based sample, free of clinical cardiovascular disease.

Methods: MRI-derived adipose tissue measurements were obtained in 345 participants (143 women; age 39–73 years) of the KORA FF4 survey from Southern Germany using a 3-Tesla machine and included total adipose tissue (TAT), visceral adipose tissue (VAT), subcutaneous adipose tissue (SCAT), hepatic fat fraction (HFF), pancreatic fat fraction (PFF) as well as pericardial adipose tissue (PAT). In addition, the anthropometric markers body mass index, waist circumference, hip circumference, waist–hip ratio (WHR) and waist–height ratio (WHtR) as well as blood pressure measurements were obtained.

Results: The prevalence of hypertension was 33.6% (women: 28%, men: 38%). VAT and PAT had the highest area under the curve (AUC) values for identifying individuals with prevalent hypertension (AUC: 0.75; 0.73, respectively), whereas WHtR and waist circumference were best performing anthropometric markers (AUC: 0.72; 0.70, respectively). A 1SD increment of TAT was associated with the highest odd for hypertension in the age-adjusted and sex-adjusted model (OR = 2.20, 95% CI 1.67–2.91, $P < 0.001$) and in the fully adjusted model (OR = 1.97, 95% CI 1.45–2.66, $P < 0.001$). TAT was the only MRI-derived adipose tissue measurement that was associated with hypertension independently of the best performing anthropometric marker waist circumference in the fully adjusted model (OR = 1.93, 95% CI 1.00–3.72, $P = 0.049$).

Conclusion: MRI-derived adipose tissue measurements perform similarly in identifying prevalent hypertension compared with anthropometric markers. Especially, TAT, VAT and PAT as well as WHtR and waist circumference were highly correlated with prevalent hypertension.

Keywords: adipose tissue, anthropometry, hypertension, MRI, population

Abbreviations: AUC, area under the curve; BIA, bioelectrical impedance analysis; BP, blood pressure; CVD, cardiovascular disease; HFF, hepatic fat fraction; OR, odds ratio; PAT, pericardial adipose tissue; PFF, pancreatic fat fraction; SCAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue; WHR, waist–hip ratio; WHtR, waist–height ratio

INTRODUCTION

Elevated blood pressure is a major cardiovascular risk factor that is considered a cardiovascular disease (CVD) equivalent [1]. On a parallel note, adiposity predisposes to cardiometabolic disease conditions [2,3], and hypertension is an important link between increased body fat distribution and cardiovascular outcomes [4,5].

It is not well established, however, which is the best adiposity measurement for cardiovascular risk assessment and which most strongly correlates with hypertension. As they are easy and cost-effective to measure, anthropometric markers have been investigated in a large number of studies, and are part of nonlaboratory-based prediction algorithms for CVD in primary care [6].

As anthropometry provides only indirect measurements of body fat distribution, it is of major interest to identify more accurate and direct measures of body fat and to explore their relation to CVD risk factors, including blood pressure. Bioelectrical impedance analysis (BIA) enables to distinguish between body fat mass and body fat-free mass.

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However, in a Chinese community-based sample, BIA-derived body fat displayed weaker associations with various metabolic abnormalities and hypertension as compared with anthropometric markers [7].

By contrast, different imaging technologies, including computed tomography (CT) and MRI, allow the visualization and quantification of direct measures of body and organ adipose tissue. Thus far, particularly, little is known about the association of MRI-derived adipose tissue measurements with hypertension compared with established anthropometric markers. MRI measures of body and organ fat obtained in our sample include total adipose tissue (TAT), visceral adipose tissue (VAT), subcutaneous adipose tissue (SCAT), hepatic fat fraction (HFF), pancreatic fat fraction (PFF) as well as pericardial adipose tissue (PAT). In the present analysis, we aimed to compare the associations of these MRI-derived adipose tissue measurements on the one hand and of anthropometric markers on the other hand with prevalent hypertension. Specifically, we assessed the performance of these different adiposity measures in identifying people with prevalent hypertension in a sample from the general population, without clinical CVD.

METHODS

Study sample

The KORA FF4 study is the second follow-up examination of the KORA S4 study ('Cooperative Health Research in the Region of Augsburg'), a population-based health survey conducted in the city of Augsburg (Southern Germany) and two surrounding counties between 1999 and 2001. Of all 4261 participants of the KORA S4 baseline study, 2279 participants also participated in the 14-year follow-up FF4 study conducted between 2013 and 2014. In a FF4 MRI substudy, a total of 400 FF4 participants without history of stroke, myocardial infarction and arterial vessel occlusion were examined by MRI [8]. Participants with missing data for TAT ($n=16$), HFF ($n=11$), PFF ($n=4$) and PAT ($n=24$) were excluded from the present analysis, yielding an analytical sample of 345 participants (143 women; age 39–73 years).

The investigations were carried out in accordance with the Declaration of Helsinki, and written informed consent was provided by all participants. The study was approved by the ethics committee of the Bavarian Chamber of Physicians, Munich (S4: EC No. 99186 and for genetic epidemiological questions 05004, F4 and FF4: EC No. 06068). The MRI examination protocol was approved by the ethics committee of the Ludwig Maximilian University Hospital, Munich.

Magnetic resonance examination and MRI-derived fat measurements

MR examinations were performed on a 3-Tesla Magnetom Skyra (Siemens AG, Healthcare Sector, Erlangen, Germany) using an 18-channel body array coil in combination with the table-mounted spine matrix coil [8]. Participants were scanned in a supine position.

Total adipose tissue, visceral adipose tissue and subcutaneous adipose tissue

On the basis of the volume-interpolated 3D in/opposed-phase VIBE-Dixon sequence, a fat selective tomogram was calculated (slice thickness 5 mm at 5 mm increment). An in-house algorithm based on Matlab R2013a was used to automatically quantify the TAT from the femoral head to the cardiac apex, VAT from the femoral head to the diaphragm and SCAT from the femoral head to the cardiac apex. All segmentations were manually adjusted if necessary. TAT, VAT and SCAT were indexed by squared height (m^2).

Hepatic fat fraction

The multiecho Dixon was based on a Volume Interpolated Body Examination (VIBE) sequence with the following parameters: TR 8.90 ms, six echos with an increment of 1.23–7.38 ms, flip angle 4°, matrix 256×179. Slice thickness was 4 mm. For the estimation of liver proton density fat fraction, confounding effects of T2$*$ decay and the spectral complexity of fat were taken into account [9]. Acquisition time was approximately 15 s. Data was analyzed using Osirix (Vers. 4.1 64-bit, Pixmeo SARL, Bernex, Geneva, Switzerland). A region of interest was manually drawn on one slice at the height of the portal vein including the whole liver parenchyma avoiding large vessels and surrounding extrahepatic tissue to measure HFF at the level of the portal vein. Data are given in percentage (%).

Pancreatic fat fraction

For quantitative assessment of pancreatic fat tissue content, one or two circular regions of interest (ROI) covering an area of approximately 100 mm^2 were drawn into the pancreatic head (caput), the pancreatic body (corpus) and the pancreatic tail (cauda) on different MRI layers, using a dedicated off-line workstation (Syngo Via, Siemens Healthcare, Erlangen, Germany). Images with severe image artefacts (e.g. phase swaps) were excluded from the analysis. Data are indexed in percentage (%).

Pericardial adipose tissue

Pericardial adipose tissue was defined as any mediastinal fat between the pulmonary artery bifurcation and the diaphragm, this includes fat inside the visceral layer of the pericardial sac in close proximity to the myocardium as well as outside of the pericardial sac [10]. Applying an automated procedure based on cluster analysis (Matlab R2013a) PAT was quantified between thoracic diaphragm and vascular bifurcation of the pulmonary artery and carefully avoiding inclusion of mediastinal adipose tissue.

Anthropometric measurements

Weight was measured with an electronic scale (SECA 635, SECA 877), standing height with a stadiometer (SECA 242) allowing accurate measurements up to 0.1 kg and 0.1 cm, respectively. BMI was calculated as weight divided by squared height (kg/m^2). Waist circumference and hip circumference were measured with an inelastic multicolored measuring tape (Fa Hoechstmass) in centimeters to the closest 0.1 cm. Hip circumference was measured at the widest protrusion of the gluteal region between the superior border of the iliac crest and crotch. Waist circumference was measured at the level midway between the lower rib margin and the iliac crest whereas the participants breathed out gently. Waist circumference was divided by hip circumference to get waist–hip ratio (WHR) and by height to get waist–height ratio (WHtR).

Blood pressure measurements and definition of hypertension

SBP and DBP measurements were obtained three times at the right arm of seated participants after a minimum resting period of 5 min. The time interval between readings was 3 min. An oscillometric digital BP monitor (HEM-705CP; Omron Corporation, Tokyo, Japan) was used and one of two cuff sizes was applied as appropriate for the participant's arm circumference. The mean of the second and third BP measurements was used for the present analyses [11]. Hypertension was defined as SBP at least 140 mmHg or DBP at least 90 mmHg [12] or use of antihypertensive medication under the awareness of having hypertension. Medication intake within the last 7 days was recorded during a medical interview by computer-based software, and participants were also asked to bring their medication packages with them. Antihypertensive medication was defined according to the German Hypertension Association and included antihypertensives, diuretics, beta blocking agents, calcium channel blockers or agents acting on the renin–angiotensin system [13]. If participants reported that they had ever been told by a physician to have high or elevated BP, they were characterized as being aware of hypertension.

Covariables

A broad range of health-related variables were measured in KORA FF4 by standardized interview, a comprehensive physical examination and laboratory analyses. Participants were classified as never-smoker, ex-smoker or current smoker; and as being physically active if they did regular sports in summer or winter for at least 1 h per week or as physically inactive if they did irregular 1 h or less of sports per week [14]. Alcohol intake was assessed using a validated recall method, calculating alcohol intake in grams per day from participants' self-reported intake of beer, wine, sparkling wine or distilled spirits over the previous weekend and workday [15].

Diabetes was defined according to the WHO definition as a 2-h plasma glucose concentration measured by oral glucose tolerance test equal or above 200 mg/dl and/or a fasting glucose level above 125 mg/dl [16]. Laboratory measurements including triglycerides, total cholesterol, high-density and low-density lipoprotein cholesterol were described elsewhere [17].

Statistical analyses

Descriptive characteristics of normotensive and hypertensive participants are provided as median and interquartile range for continuous measurements and absolute numbers and percentage values for categorical measurements. Differences between normotensive and hypertensive participants were tested using either Mann–Whitney *U* test (continuous data) or χ^2-test (categorical data). Power analysis revealed that the sample size of the present study ($N = 345$) provides 80% power at a significance level of $\alpha = 0.05$ to detect differences in TAT between the normotensive group ($N_1 = 229$, mean = 3.4, SD = 1.8) and the hypertensive group ($N_2 = 116$) of 0.58 l/m^2.

Receiver-operating characteristic (ROC) curves to distinguish individuals with prevalent hypertension from those without were estimated separately for each MRI-derived adipose tissue measurement and for each anthropometric marker. We performed age-adjusted and sex-adjusted, as well as multivariable-adjusted logistic regression models including age, diabetes mellitus, physical activity, smoking status, alcohol consumption, total cholesterol and HDL-cholesterol. We performed multivariable adjusted models to estimate the association of each adiposity marker with prevalent hypertension independently of potentially confounding variables (including traditional cardiovascular risk factors). In sex-stratified analysis, multivariable-models were additionally adjusted for hormone replacement therapy in women. Likelihood-ratio tests were used to test the improvement of area under the curve (AUC) values between a basic model including only traditional risk factors vs. the basic model with an adiposity marker added. Differences of AUC values between different adiposity markers were evaluated by χ^2-test.

Associations of adiposity traits (expressed as odds ratios per 1SD increment) with hypertension were evaluated by logistic regression models with age and sex-only adjustment (Model 1) and with multivariable adjustment using the covariates as mentioned above (Model 2). Odds ratios (ORs) for the association of each adiposity trait with hypertension were ordered from high to low and graphically displayed. In addition, the associations of MRI-derived adiposity traits with hypertension were tested upon additional adjustment for the most strongly associated anthropometric marker, waist circumference. In sensitivity analyses, the associations of MRI-derived adipose tissue measurements and of anthropometric traits with SBP, modeled as a continuous trait, were assessed by right censored normal regression, thereby accounting for antihypertensive treatment.

Effect modification by sex on the association between adiposity traits and hypertension was tested by including respective multiplicative interaction terms (adiposity trait∗sex) in the logistic regression model. In the analyses described above, all MRI-derived measurements were modeled as continuous traits. In an additional analysis, we evaluated how well different MRI-derived adiposity measurements and anthropometric markers can be used to differentiate between hypertensive participants and non-hypertensive participants, if the respective traits were dichotomized at the median (two groups for each marker with 50% in the group with values above the median and 50% below). For each adiposity marker, the prevalence of hypertension was compared between the two groups with values above vs. below the sex-specific median.

A *P* value of less than 0.05 was considered statistically significant. Statistical analyses were performed using Stata 14.1 (Stata Corporation, College Station, Texas, USA).

RESULTS

Baseline characteristics of the study sample, stratified by hypertension status, are provided in Table 1. Hypertension

TABLE 1. Characteristics of the study sample ($N = 345$)

	Without hypertension $N = 229$	Hypertension $N = 116$	P value[a]
Covariates			
Age (years)	52 (46; 61)	62 (56; 67)	<0.001
Males	126 (55.0%)	76 (65.5%)	0.062
Smoking status			0.130
Never-smoker	86 (37.6%)	41 (35.3%)	
Ex-smoker	92 (40.2%)	58 (50.0%)	
Current smoker	51 (22.3%)	17 (14.7%)	
Alcohol consumption (g/day)	8.6 (0.9; 24.6)	11.9 (0.0; 38.6)	0.191
Physically active	146 (63.8%)	59 (50.9%)	0.021
Diabetes mellitus	12 (5.2%)	33 (28.5%)	<0.001
HDL-C (mmol/l)	1.58 (1.29; 1.91)	1.51 (1.21; 1.805)	0.048
LDL-C (mmol/l)	3.57 (2.97; 4.16)	3.46 (3.01; 4.105)	0.960
Total cholesterol (mmol/l)	5.61 (4.99; 6.25)	5.48 (4.91; 6.18)	0.763
Triglycerides (mmol/l)	1.17 (0.83; 1.63)	1.36 (1.05; 2.055)	<0.001
Weight (kg)	78.4 (68.7; 90.4)	85.1 (76.9; 95.7)	<0.001
Height (m)	1.73 (1.64; 1.80)	1.72 (1.64; 1.78)	0.359
Anthropometric markers			
BMI (kg/m^2)	26.6 (23.9; 29.2)	29.0 (26.5; 32.1)	<0.001
Waist circumference (cm)	95.7 (84.6; 103.5)	104.3 (98.2; 111.3)	<0.001
Hip circumference (cm)	104.6 (99.9; 109.1)	108.4 (102.4; 113.8)	<0.001
Waist–hip ratio, WHR	0.91 (0.85; 0.96)	0.97 (0.90; 1.02)	<0.001
Waist–height ratio, WHtR	0.55 (0.50; 0.60)	0.61 (0.56; 0.66)	<0.001
Adipose tissue (MRI)			
Total adipose tissue, TAT (l/m^2)	3.36 (2.55; 4.83)	5.03 (3.75; 6.49)	<0.001
Visceral adipose tissue, VAT (l/m^2)	1.08 (0.67; 1.62)	1.96 (1.37; 2.45)	<0.001
Subcutaneous adipose tissue, SCAT (l/m^2)	2.16 (1.70; 3.10)	2.88 (2.10; 4.23)	<0.001
Hepatic fat fraction, HFF (%)	3.84 (2.24; 6.97)	9.56 (4.10; 20.38)	<0.001
Pancreatic fat fraction, PFF (%)	4.73 (3.1; 7.33)	6.95 (4.03; 14.77)	<0.001
Pericardial adipose tissue, PAT (ml)	92.0 (61.5; 135.6)	145.8 (111.1; 206.0)	<0.001
Blood pressure			
SBP (mmHg)	116 (107; 124)	133 (120; 143)	<0.001
DBP (mmHg)	73 (68; 79)	80 (73; 89)	<0.001
Use of antihypertensive medication	–	84 (72.4%)	–

Data are given as number (percentage) or median (25th and 75th percentile). HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
[a]P values are from Mann–Whitney U test (continuous data) or chi-square test (categorical data).

prevalence in the overall sample was 33.6% (women: 28%, men: 38%). Hypertensive participants were older, more often ex-smokers and less physically active in leisure time compared with normotensive participants. All median values of MRI-derived adipose tissue measurements and anthropometric markers were higher in participants with hypertension compared with participants without hypertension.

Among the MRI-derived measures, VAT and PAT had the highest AUC values for identifying individuals with prevalent hypertension (AUC: 0.75; 0.73, respectively), whereas WHtR and waist circumference were the best performing anthropometric markers (0.72; 0.70, respectively, Table 2 and Supplemental Figure 1, http://links.lww.com/HJH/A923). PFF and hip circumference had lowest AUC values for hypertension (0.65; 0.63, respectively).

In multivariable-adjusted models, AUC values were highest for TAT and SCAT (AUC: 0.80, respectively, Table 2), even though all adiposity traits improved the AUC beyond the basic model (AUC: 0.767), which included only the traditional risk factors (all $P \leq 0.016$ for improvement in AUC when added to a model with only traditional risk factor). Only AUC values of single adiposity traits differed among each other ($P < 0.001$) whereas AUC values upon age and sex as well as multivariable adjustment did not ($P = 0.871$ for MRI-derived adipose tissue measurements; $P = 0.219$ for anthropometric markers). Furthermore, formal statistical comparisons revealed that there were no statistically significant differences between any of the MRI-derived adipose tissue measurements and any of the anthropometric adiposity measures (comparing the respective AUCs) in identifying prevalent hypertension (Supplemental Table 1, http://links.lww.com/HJH/A923).

A 1SD increment of TAT was associated with the highest odd for hypertension in the age-adjusted and sex-adjusted model (OR = 2.20, 95% CI 1.67–2.91, $P < 0.001$) and in the fully adjusted model (OR = 1.97, 95% CI 1.45–2.66, $P < 0.001$; Fig. 1 and Supplemental Table 2, http://links.lww.com/HJH/A923). Also SCAT and VAT were highly associated with hypertension in both models (all $P < 0.001$). Among the different anthropometric marker, waist circumference displayed the highest odd for hypertension in the age-adjusted and sex-adjusted model (OR = 2.19, 95% CI 1.63–2.93, $P < 0.001$) and in the fully adjusted model (OR = 1.92, 95% CI 1.39–2.67, $P < 0.001$). Similarly, TAT and waist circumference were the most strongly associated marker of their respective groups (MRI markers and anthropometric markers, respectively) in relation to continuously modeled SBP (Supplemental Table 3, http://links.lww.com/HJH/A923). In a secondary analysis, when the best performing anthropometric marker waist circumference was added to the

TABLE 2. Area under the curve values for different statistical models investigating the presence of prevalent hypertension

N = 345	Hypertension AUC (95% CI) of single factor	Hypertension AUC (95% CI) of single factor with age and sex	Hypertension AUC (95% CI) single factor with basic model[a]	*P* value[b]
			AUC_{basic} = 0.7665	
TAT	0.72 (0.67;0.78)	0.79 (0.73;0.84)	0.80 (0.75;0.85)	<0.001
VAT	0.75 (0.70;0.81)	0.78 (0.73;0.83)	0.79 (0.75;0.84)	<0.001
SCAT	0.66 (0.60;0.72)	0.77 (0.72;0.83)	0.80 (0.75;0.84)	<0.001
HFF	0.72 (0.67;0.78)	0.76 (0.71;0.82)	0.79 (0.74;0.84)	0.002
PFF	0.65 (0.59;0.72)	0.74 (0.68;0.79)	0.78 (0.73;0.83)	0.016
PAT	0.73 (0.67;0.78)	0.76 (0.70;0.81)	0.79 (0.74;0.84)	0.001
	P < 0.001	*P* = 0.152	*P* = 0.871	
BMI	0.68 (0.62;0.74)	0.77 (0.72;0.82)	0.79 (0.74;0.84)	<0.001
Waist circumference	0.70 (0.65;0.76)	0.78 (0.72;0.83)	0.79 (0.75;0.84)	<0.001
Hip circumference	0.63 (0.57;0.69)	0.75 (0.70;0.81)	0.79 (0.74;0.84)	<0.001
WHR	0.70 (0.64;0.76)	0.76 (0.71;0.82)	0.78 (0.73;0.83)	0.003
WHtR	0.72 (0.66;0.78)	0.78 (0.72;0.83)	0.79 (0.75;0.84)	<0.001
	P < 0.001	*P* = 0.110	*P* = 0.219	

Models either included only traditional risk factors (AUC_{basic}), only individual adiposity traits of interest, only individual adiposity traits of interest combined with age and sex, or each adiposity trait of interest combined with traditional risk factors. HFF, hepatic fat fraction; PAT, pericardial adipose tissue; PFF, pancreatic fat fraction; SCAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue; WHtR, waist–height ratio; WHR, waist–hip ratio.
[a]Basic risk factor model for hypertension includes: age, sex, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol, HDL-cholesterol.
[b]Likelihood-ratio test (comparison: basic model vs. basic risk factor model with adiposity risk factor).

multivariable-adjusted model with the different MRI-derived adiposity measures, only TAT was associated independently with prevalent hypertension (OR = 1.93, 95% CI 1.00–3.72, *P* = 0.049, Table 3). In order to further explore the association between total adipose tissue and hypertension, we provide different multivariable-adjusted models with an increasing number of potential confounders (Supplemental Table 4, http://links.lww.com/HJH/A923). In essence, the strength of association decreased slightly from the unadjusted model (OR = 2.18 [1.70; 2.81]) to the fully adjusted model including waist circumference (OR = 1.93 [1.00; 3.72]).

Interaction analysis revealed an effect modification by sex regarding the association of PAT with hypertension (*P* = 0.035). The association per 1SD increment in PAT with hypertension was stronger in women (OR = 3.53, 95% CI 1.74–7.17, *P* < 0.001) compared with men (OR = 1.36, 95% CI 0.95–1.93, *P* = 0.093) in fully adjusted models (Fig. 2).

Whenever the different adiposity traits were dichotomized at the sex-specific median, the biggest difference in hypertension prevalence was observed between women with high PAT (45% hypertension prevalence) and low PAT (11% hypertension prevalence). In men, the biggest difference in hypertension prevalence was observed between men with high VAT (58%) and low VAT (17%) (Fig. 3). Interaction analysis revealed no further relevant adiposity marker that could significantly identify more individual hypertension risk in these subgroups.

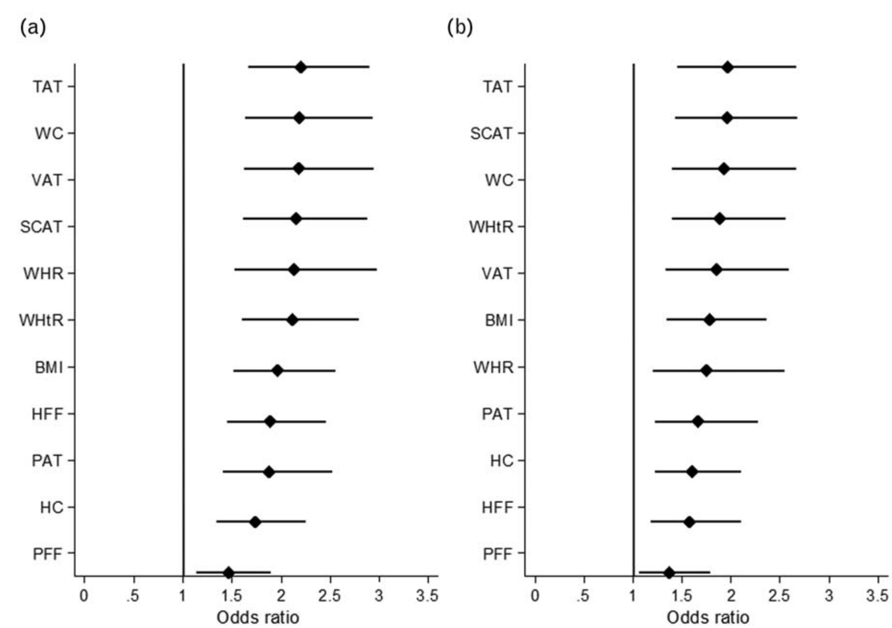

FIGURE 1 Association of MRI and anthropometric markers (SD increment) with presence of hypertension in the overall sample adjusted for age and sex only (a) and adjusted for age, sex, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol and HDL-cholesterol (b) expressed by odds ratios and 95% confidence intervals.

TABLE 3. Association of MRI-derived adiposity measurements with the presence of hypertension independent of cardiovascular risk factors and independent of the strongest associated anthropometric marker waist circumference

$N = 345$	Hypertension OR (95% CI)	*P* value[a]
TAT	1.93 (1.00–3.72)	0.049
VAT	1.29 (0.80–2.08)	0.302
SCAT	1.68 (0.92–3.06)	0.090
HFF	1.28 (0.94–1.76)	0.120
PFF	1.17 (0.89–1.55)	0.250
PAT	1.27 (0.88–1.83)	0.193

Data are odds ratios per SD increment of the respective adiposity measurements from logistic regression. HFF, hepatic fat fraction; PAT, pericardial adipose tissue; PFF, pancreatic fat fraction; SCAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue.
[a]Adjusted for age, sex, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol, HDL-cholesterol, and waist circumference.

DISCUSSION

This is the first community-based study to investigate simultaneously the associations of MRI-derived adipose tissue measurements on the one hand and of established anthropometric markers on the other hand with prevalent hypertension. We conducted our analyses in a population-based sample free of clinical cardiovascular diseases. The main observations can be summarized as follows. First, in general, MRI-derived adipose tissue measurements and anthropometric markers were both associated with hypertension in a relatively similar fashion. Second, whereas TAT, VAT and PAT were the best MRI-derived adipose tissue measurements to distinguish those with from those without hypertension, waist circumference and WHtR were the best performing anthropometric markers for identifying prevalent hypertension. Third, in women, the association between PAT and hypertension was stronger than in men.

Association of anthropometric markers with hypertension

Anthropometric markers are commonly used as surrogate markers of body fat distribution and obesity in prediction models for CVD and hypertension as they are relatively easy to measure [18,19]. In our sample, waist circumference and WHtR displayed the strongest associations with hypertension of all anthropometric markers in the multivariable-adjusted model. This observation is supported by the published literature, where several studies reported that markers of central adiposity including waist circumference, WHtR and WHR predict cardiovascular disease risk and hypertension better than BMI [19–22]. However, the present study also evaluated the associations of imaging-based direct measurements of body fat distribution with prevalent hypertension.

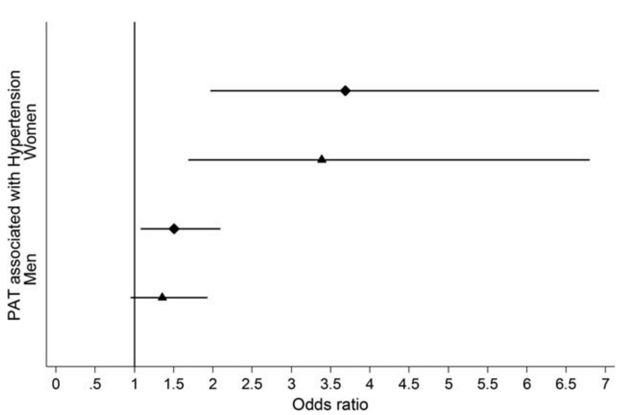

FIGURE 2 Association between pericardial adipose tissue and hypertension in men and women providing age-adjusted odds ratios (diamond) and fully adjusted odds ratios (triangle) with 95% confidence intervals.

Body and organ fat measurements and hypertension

The associations of different CT-based fat measurements, including pericardial fat, intrathoracic fat and VAT with cardiovascular disease risk factors were evaluated in a sub-sample of the Framingham Offspring cohort ($n = 1155$ participants). One main result was, that VAT was more strongly associated with SBP, DBP and hypertension than pericardial (defined as adipose tissue located within the pericardium) and intrathoracic fat [23]; and that intrathoracic fat was more strongly associated with BP and hypertension than pericardial fat. Similarly, in our MRI study, VAT was more strongly associated with prevalent hypertension than PAT (as the sum of epicardial and paracardial fat; OR = 1.85 for VAT; OR = 1.66 for PAT, respectively). However, MR-derived measurements of TAT and SCAT displayed even higher ORs for hypertension as compared with VAT and PAT. Recently, we have investigated in detail the association between liver fat and blood pressure in the present sample and observed that three different HFF measurements (measured at three different locations within the liver) displayed consistent associations with BP and hypertension [24]; independently of the measurement location.

Comparison between MRI-derived fat measurements and anthropometric markers with respect to their association with hypertension

A comprehensive comparison of anthropometric markers and more direct fat measures determined by BIA, including total body fat, percentage body fat, trunk fat mass and percentage trunk fat, with respect to their association with hypertension was conducted in a sample from the Chinese general population and revealed female WHtR and male

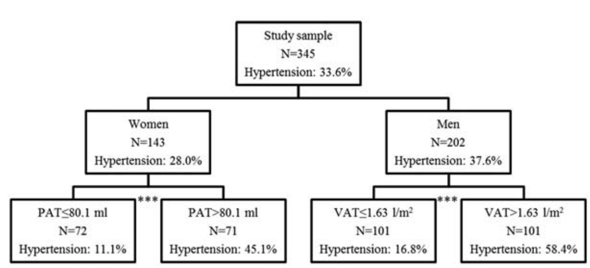

FIGURE 3 Classification tree of interaction analysis including all MRI and anthropometric markers (sex-specific median-dichotomized) for identifying hypertension according to chi-square automatic interaction detection adjusted for age, $^{*}P < 0.05$, $^{***}P < 0.001$. CHAID, chi-square automatic interaction detection.

BMI (OR = 4.90; 95% CI 3.36–7.17; top vs. bottom quartile) as the strongest correlates for hypertension. In men, BMI displayed approximately a twofold OR for hypertension than percentage body fat (OR = 2.42; 95% CI 1.53–3.81). However, this difference in the strength of the association with prevalent hypertension was not apparent in women (OR_{BMI} = 3.92; 95% CI 2.94–5.23 vs. $OR_{\%BodyFat}$ = 3.60; 95% CI 2.94–5.23, respectively). By contrast, in our study, we could not detect effect modifications by sex except for PAT, and the effect measure (OR per SD increment) for TAT was similar to the effect measure for BMI for both, men and women (OR_{TAT} = 1.97; OR_{BMI} = 1.78). Although AUC values (for differentiating between individuals with vs. without hypertension) differed for individual fat measures, these differences disappeared after adding traditional risk factors (age, sex, diabetes mellitus, physical activity, smoking status, alcohol consumption, total cholesterol and HDL-cholesterol) to the statistical model.

The study of Rosito *et al.* investigated whether intrathoracic or pericardial fat were associated with blood pressure and hypertension, independent of BMI and waist circumference or of VAT and observed that only intrathoracic fat displayed a borderline significant association with hypertension whenever added to a model including BMI and waist circumference in women and VAT, but not intrathoracic or pericardial fat, was independently and statistically significantly associated with SBP and hypertension only in women in multivariable models including both measurements (VAT and intrathoracic or pericardial fat, respectively) [23]. In our analyses, we detected that only TAT was associated with hypertension independently of basic cardiovascular risk factors in a statistical model that included the most strongly associated anthropometric marker, waist circumference.

Effect modification by sex

Our analyses revealed a strong and independent positive association of PAT with hypertension only in women but not in men. Furthermore, when all adiposity traits were dichotomized at the median, the low-PAT vs. high-PAT groups displayed the greatest difference in hypertension prevalence (11 and 45%, respectively) in women. In men, the low-VAT vs. high-VAT groups had the biggest difference in hypertension prevalence (17 and 58%, respectively). Thus, based on dichotomization at the sex-specific median, MR-derived PAT and VAT could improve the prediction of hypertension and the associated cardiovascular risk in women and men, respectively.

Consistent with our observations, PAT was significantly associated with SBP and DBP only in women in the MESA (Multi-Ethnic Study of Atherosclerosis) study [25]. In contrast to our study, a stronger role of BMI in predicting risk for hypertension in women as compared with men has been reported in the study of Sakurai *et al.* [26] but not in the study of Zhang *et al.* [7].

Sex differences of associations between cardiovascular risk factors and cardiovascular diseases in women compared with men have been explained, for example, by cardioprotective effects of estrogen before and after menopause [27]. However, evidence for sex differences in the associations of fat distribution markers with hypertension is limited so far [7]. In our sample, no other associations of adiposity traits with hypertension were modified by sex.

Strengths and limitations

Strengths of our study are the well characterized subsample of the population-based KORA study, a cohort study with detailed and highly standardized cardiovascular phenotyping, and the use of advanced MR techniques to characterize body and organ fat content.

Our study is limited by its cross-sectional design so that we could not assess the association of fat distribution measures with new-onset (incident) hypertension. Although BP measurements were obtained of seated participants after a minimum resting period of 5 min, BP elevation because of the presence of the BP-measuring personnel (white-coat hypertension) cannot entirely be excluded. The representativeness of the study sample for the initial cohort sample and the population of the study region is also limited. Reasons for nonresponse included contraindications for MRI examinations and refusal of informed consent and refusal of telephone invitation. Our sample was of European descent. The applicability of our findings to other ethnicities remains to be established. A comparison of MRI participants and non-MRI participants of the KORA FF4 cohort revealed that participants of the MRI sub-study were a bit younger, more often men and less often hypertensive compared with non-MRI participants (Supplemental Table 5, http://links.lww.com/HJH/A923).

In conclusion, MRI-derived adipose tissue measurements perform similarly in identifying patients with hypertension compared with anthropometric markers. Especially, the MRI markers, TAT, VAT and PAT, were highly correlated with prevalent hypertension. Furthermore, the established anthropometric markers, waist circumference and WHtR, were also confirmed to be significantly and independently associated with hypertension. The longitudinal predictive performance of individual MRI fat measures and anthropometric markers with respect to changes in BP over time and incident hypertension needs to be investigated in future studies.

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Conflicts of interest

There are no conflicts of interest.

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