Correlation of MRI Derived Adipose Tissue Measurements and Anthropometric Markers with Prevalent Hypertension in the Community

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Abstract

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

Methods: MRI derived fat content measures were obtained in 345 participants (143 women; aged 39 to 73) of the KORA FF4 survey 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 (BMI), waist circumference (WC), hip circumference (HC), 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%). In the overall sample, VAT and PAT had the highest AUC values for identifying individuals with prevalent hypertension (0.75; 0.73, respectively), whereas WtHR and WC were best performing anthropometric markers (0.72; 0.70, respectively). In women, a 1-standard deviation increment of PAT was associated with the highest risk for hypertension in the age-adjusted model (OR=3.69, 95%CI 1.97; 6.92, p<0.001) and in the fully adjusted model (OR=3.39, 95%CI 1.69; 6.80, p=0.001). In men, SCAT revealed the strongest associations with hypertension in the age-adjusted model (OR=3.02, 95%CI 1.84; 4.98, p<0.001) and the fully adjusted model (OR=2.60, 95%CI 1.52; 4.47, p=0.001).

Conclusion: MRI derived fat content measures perform similarly or even better in identifying prevalent hypertension compared to anthropometric markers. Especially, PAT and VAT in women and SCAT and TAT in men are highly correlated with hypertension.

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

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 cardio-metabolic disease conditions [2, 3], and hypertension is an important link between increased body fat distribution and cardiovascular outcomes [4, 5].

However, it is not well established which is the best adiposity measurement for cardiovascular risk assessment and which most strongly correlates with hypertension. Since they are easy and cost-effective to measure, anthropometric markers have been investigated in a large number of studies, and are part of commonly used risk prediction algorithms for CVD [6].

Since anthropometry provides only indirect measurements of body fat distribution, interest continues to grow regarding more accurate and direct measures of body fat. Bioelectrical impedance analysis (BIA) enables to distinguish between body fat mass and body fat free mass. However, BIA derived body fat could not be demonstrated to better predict either various metabolic abnormalities or hypertension than anthropometric markers [7].

By contrast, different imaging technologies, including 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 body and organ fat measurements with hypertension and their performance in predicting prevalent hypertension compared to established anthropometric markers. MRI measures of body and organ fat obtained in our sample include 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 measures 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, free of 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 (south Germany) and two surrounding counties between 1999 and 2001. Of all 4261 participants of the KORA S4 baseline study, 2279 subjects also participated in the 14-year follow-up FF4 study conducted between 2013 and 2014 [8]. In a FF4 MRI sub-study, a total of 400 FF4 participants free of stroke, myocardial infarction, and arterial vessel occlusion [9] were examined by MRI. Participants with missing data for total adipose tissue (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; aged 39 to 73).

The investigations were carried out in accordance with the Declaration of Helsinki, including written informed consent of all participants. All study methods were 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 further approved by the ethics committee of the Ludwig Maximilian University Hospital, Munich.

MR examination and fat measurements

MR examinations were performed at 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]. Subjects were scanned in supine position.

TAT, VAT, SCAT: Based on the volume-interpolated 3D in/opposed-phase VIBE-Dixon sequence a fat selective tomogram was calculated (slice thickness 5mm at 5mm increment). An in-house algorithm based on Matlab R2013a was used to ~~semi-~~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.

HFF: The multi-echo Dixon was based on a Volume Interpolated Body Examination (VIBE) sequence with the following parameters: TR 8.90 ms, six TEs ranging from 1.23 ms, to 7.38 ms, flip angle 4º, matrix 256×256. 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 seconds. Data was analyzed using Osirix (Vers. 4.1 64-bit, Pixmeo SARL, Bernex, GE, 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.

PFF: For quantitative assessment of pancreatic adipose 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 artifacts (e.g. phase swaps) were excluded from the analysis.

PAT: Pericardial adipose tissue was defined as the sum of epicardial and paracardial fat deposits, in which epicardial fat was defined as the fat located inside the visceral layer of the pericardial sac in close proximity to the myocardium and paracardial fat was defined as the fat compartment located 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 Markers

Body mass index (BMI) was calculated as weight divided by squared height (kg/m^2). Waist circumference (WC) and hip circumference (HC) were measured in cm to the closest 0.1 cm. HC was measured at the widest protrusion of the gluteal region between the superior border of the iliac crest and crotch. WC was measured at the smallest position between the lower rib and the upper margin of the iliac crest. WC was divided by HC to get waist-hip-ratio (WHR) and by height to get waist-hight-ratio (WHtR).

Blood pressure and hypertension

Systolic and diastolic BP measurements were obtained three times at the right arm of seated participants after a five-minute resting period. The time interval between readings was three minutes. 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 systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg [12] or use of antihypertensive medication under awareness of having hypertension. Medication intake of the last seven days was recorded during the medical interview by computer-based software, and participants were also asked to bring their medication packages with them. Anatomical Therapeutic Chemical (ATC) codes were used. Antihypertensive medication was defined according to the German Hypertension Association and included antihypertensives (C02), diuretics (C03), beta blocking agents (C07), calcium channel blockers (C08) or agents acting on the renin-angiotensin system (C09) [13]. If participants reported that they had ever been told that they have high or elevated BP they were characterized as being aware of hypertension.

Covariables

Besides age and sex, a broad range of health-related variables were measured in KORA FF4 by standardized interview, basic health examinations 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 and winter for ≥ 1 hour per week or as physically inactive if they did <1 hour of sports per week. Alcohol consumption was measured in grams per day and was derived from a quantity-frequency questionnaire.

Diabetes was defined according to the WHO definition as a 2-hour plasma glucose concentration measured by OGTT equal or above 200 mg/dl and/or a fasting glucose level above 125 mg/dl [14].

Laboratory measurements including triglycerides, total cholesterol, high- and low-density lipoprotein cholesterol were described elsewhere [15].

Statistical analyses

Descriptive characteristics of normotensive and hypertensive participants are provided as median and interquartile range for continuous measurements and absolute numbers and percent values for categorical measurements.

Receiver operating characteristic (ROC) curves for separating individuals with prevalent hypertension from those without were estimated separately for each MRI-derived adipose tissue measurements and for each anthropometric marker in the overall sample and stratified by sex. We ran age-adjusted, as well as multivariable-adjusted models including basic cardiovascular risk factors such as age, diabetes mellitus, physical activity, smoking status, alcohol consumption, total cholesterol and HDL-cholesterol. Likelihood-ratio tests were used to test the improvement of area under the curve (AUC) values between a) a basic prediction model including only traditional risk factors vs. the basic model with an adiposity marker added; and between b) a prediction model with only the respective adiposity trait of interest vs. a model with the adiposity trait of interest and traditional risk factors.

Associations of adiposity traits (expressed as odds ratios per 1-standard deviation increment) with hypertension were evaluated by logistic regression models with age-only adjustment (Model 1) and with multivariable adjustment using the covariates as mentioned above (Model 2), separate for men and women as well as in the overall sample. In addition, the associations of MRI derived adiposity traits with hypertension were tested upon additional adjustment for the best associated anthropometric marker (in women, WC; in men, WHtR). In the overall sample, ORs for the association of each adiposity trait with hypertension were ordered and graphically displayed.

To detect relevant combinations of MRI-based adipose tissue and anthropometric traits for identifying prevalent hypertension, interaction analysis according to chi-square automatic interaction detection (CHAID) [16] was performed and a classification tree was plotted. For this purpose all adiposity traits of interest were dichotomized at the sex-specific median. A p-value of <0.05 was considered

statistically significant. Statistical analyses were performed using Stata 14.1 (Stata Corporation, College Station, TX, U.S.A.).

RESULTS

Baseline characteristics of the study sample, stratified by hypertension status, are provided in **Table 1**. Hypertension prevalence in the overall sample was 33.6% (women: 28%, men: 38%). Hypertensive participants were older (median=62 years), more ex-smoker (50%) and less physically active (51%) compared to normotensive participants (52 years, 40% ex-smoker, 64% active). All MRI-derived adipose tissue measurements and anthropometric markers were higher in participants with hypertension compared to participants without hypertension.

Among the MRT-derived measures, VAT and PAT had the highest AUC values for identifying individuals with prevalent hypertension (0.75; 0.73, respectively), whereas WtHR and WC were the best performing anthropometric markers (0.72; 0.70, respectively, **Figure 1**). PFF and HC had lowest AUC values for hypertension (0.65; 0.63, respectively).

In women, AUC values were also highest for PAT and VAT when being added to a basic cardiovascular risk model including age, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol and HDL-cholesterol (0.79; 0.78, respectively, **Table 2**). PAT and VAT alone showed higher AUC values than the basic model, based on traditional risk factors only (AUC_{basic}=0.74; **Table 2**) and could significantly improve the model performance of the basic risk model identifying prevalent hypertension ($p<0.001$; $p=0.002$, respectively; **Table 2**). However, adding traditional risk factors to the model with only VAT (AUC=0.77; AUC=0.78 upon multivariable adjustment) as predictor for hypertension, did not increase model performance ($p=0.803$; **Table 2**). Similar observations were made for PAT models.

In men, TAT and SCAT, as the best MRI-based measurements, and WC and WHtR as the best performing anthropometric measures revealed the highest AUC values (AUC=0.82 for each model). Consistently, both imaging-based and both anthropometric traits could significantly improve the model performance when added to the basic risk factor model (AUC_{basic}=0.79; all $p<0.001$; **Table 2**).

In contrast to women, the basic prediction model, based on traditional risk factors only, did better perform than TAT and SCAT alone (AUC=0.71; AUC=0.66, respectively) and adding traditional risk factors to the models with individual adiposity traits could improve the hypertension identifying performance of each MRI-based and of each anthropometric adiposity measurement (all p<0.001, **Table 2**).

In age- and sex-adjusted and in multivariable-adjusted models TAT demonstrated the strongest associations with hypertension in the overall sample (**Figure 2**). In women, a standard deviation increment of PAT was associated with the highest risk for hypertension in the age- and sex-adjusted model (OR=3.69, 95%CI 1.97; 6.92, p<0.001) and after full adjustment (OR=3.39, 95%CI 1.69; 6.80, p=0.001; **Table 3**). In men, SCAT showed the strongest association with hypertension in the age- and sex-adjusted model (OR=3.02, 95%CI 1.84; 4.98, p<0.001) and in the fully adjusted model (OR=2.60, 95%CI 1.52; 4.47, p=0.001). Only in women, the MRI derived adiposity marker PAT (OR=3.39, 95%CI 1.44; 8.00, p=0.005) as well as TAT and VAT were associated with hypertension independently of best associated anthropometric marker WC (from the fully adjusted model) and other risk factors (**Table 4**).

Sex-specific median dichotomized PAT showed the best hypertension discrimination of female subjects between low PAT (hypertension prevalence: 11.1%) and high PAT (hypertension prevalence: 45.1%). Median dichotomized VAT could best discriminate between low hypertension prevalence group (16.8%) and high hypertension prevalence group (58.4%) in men (**Figure 3**). Interaction analysis revealed no further relevant adiposity marker that could significantly identify more individual hypertension risk in these subgroups.

DISCUSSION

This is the first community-based study to investigate simultaneously the associations of prevalent hypertension with MRI derived body and organ fat content measures on the one hand and with established anthropometric markers on the other hand. We conducted our analyses in a population-based sample free of clinical cardiovascular disease. The main observations were summarized as follows. First, in general, MRI-derived fat content measures and anthropometric markers were both

associated with hypertension in a relatively similar fashion, although some criteria for evaluating the associations with hypertension (OR, AUC) were slightly higher for MRI measurements as compared to the anthropometric markers. Second, while in women, PAT and VAT were most strongly associated with hypertension, the parameters TAT, SCAT, WHR and WHtR were most relevant for predicting prevalent hypertension in men. Third, combination of measurements revealed two MRI measures (PAT, VAT) with best hypertension identification performance.

Anthropometric markers and hypertension

In the overall sample, WC and WHtR revealed the strongest fully adjusted associations with hypertension among anthropometric markers whereas in women WC and BMI and in men WHtR and WHR were the top anthropometric markers. These findings are supported by the literature. Several studies demonstrated that central obesity markers like WC, WHtR and WHR predict cardiovascular risk and hypertension better than BMI [17-20]. A stronger role of BMI in predicting risk for hypertension in women as compared to men has been reported in the study of Sakurai et al. [21] but not in the study of Zhang et al. [7].

Anthropometric markers are usually used as simple surrogate markers of body fat distribution and obesity and therefore as predictors for cardiovascular diseases [17, 22]. However, the present study focused also on the association of imaging-based direct measurements of body fat distribution determined by imaging of the fat areas and proportions.

Body and organ fat measurements and hypertension

Evidence regarding the associations of different fat depots, including pericardial fat, intrathoracic fat as well as VAT determined by CT with cardiovascular disease risk factors was obtained in a sub-sample of the Framingham Offspring cohort (n=1155 participants). One main finding of the analyses was, that VAT was more strongly associated with systolic blood pressure, diastolic blood pressure and hypertension than pericardial and intrathoracic fat [23]; and that intrathoracic fat was more strongly associated with blood pressure and hypertension than pericardial fat. In our MRI study, PAT (as the sum of epicardial and paracardial fat) was a stronger predictor for hypertension than VAT in women

(OR=3.39 for PAT; OR=2.69 for VAT, respectively) but not in men (OR=1.36 for PAT; OR=1.62 for VAT, respectively). Similarly, a MESA study with same PAT definition demonstrated a significant correlation of pericardial fat with systolic and diastolic blood pressure only in women [24].

Comparison between fat measurements and anthropometric markers

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 were investigated in a sample from the Chinese general population and revealed female WHtR and male BMI as the best predictors for hypertension. Participants within the highest quartile of adiposity measure were compared to the lowest quartile regarding hypertension with a twofold multivariable adjusted OR for male BMI (4.90; 95%CI 3.36, 7.17) than male percentage body fat (2.42; 95%CI 1.53, 3.81), whereas this definite difference was not present in women (3.92; 95%CI 2.94, 5.23 vs. 3.60; 95%CI 2.94, 5.23, respectively). In contrast, in our study ORs (per standard deviation increment) for TAT were slightly higher than for BMI with similar differences in both sexes (1.88 vs. 1.66 in women; 2.16 vs 1.98 in men). However, similarly, we detected sex differences with respect to WHtR with stronger associations with hypertension in men (OR=2.28) as compared to women (OR=1.63) and with respect to VAT with stronger association in women (OR=2.69) than in men (OR=1.62).

Furthermore, the impact of adding traditional risk factors to individual fat measures was different between men and women in models predicting prevalent hypertension. In women, the addition of traditional risk factors (age, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol and HDL-cholesterol) to the prediction models with the individual adiposity measure did not improve the AUC values for any of the adiposity and anthropometric traits. Of note in women, AUC values of VAT alone (0.77) and of PAT alone (0.78) for predicting hypertension were even larger compared to the basic risk model, including only traditional risk factors (AUC_{basic}=0.74).

By contrast, in men, the AUC value of the basic risk factor model (AUC_{basic}=0.79) was greater than the AUC of every individual fat marker alone (AUCs between 0.65 and 0.72 for the individual fat parameter) and the addition of traditional risk factors to the individual fat markers could improve the AUC values of the prediction models for hypertension (all $p<0.001$).

Sex-differences of stronger associations between cardiovascular risk factors and cardiovascular diseases in men compared to women have been explained hypothetically by cardio-protective estrogen [25]. However, evidence for sex-differences in associations between fat distribution markers and hypertension is limited so far [7].

The study of Rosito et al. investigated if intrathoracic or pericardial fat have an impact on explaining blood pressure and hypertension in addition to BMI and WC as well as to VAT and found that a) only intrathoracic fat had a borderline significant effect on hypertension when added to a model including to BMI and WC in women but not in men and b) VAT and not intrathoracic or pericardial fat was independently and statistically significantly associated with systolic blood pressure and hypertension only in women in multivariable models including both measurements, respectively [23]. In our analyses, we detected that in women TAT, VAT and PAT were associated with hypertension independently of basic cardiovascular risk factors including the strongest associated anthropometric marker WC. However in men, no MRI derived fat marker was associated with hypertension independently of WHtR and other risk factors.

Clinical impact of associations between body and organ fat parameters and hypertension

MRI-derived fat distribution markers are discussed as emerging candidate biomarker for a more individualized cardiovascular medicine [26]. The aim of individualized medicine is to better characterize smaller groups of patients and to adjust therapies accordingly [27]. To find combined parameters that can divide the study population by their median and to identify smaller groups with low and high hypertension prevalences in our study, interaction analysis of the different adiposity measures was conducted. Within the study population characterized by a hypertension prevalence of 34% we could identify a female subgroup (low PAT) and a male subgroup (low VAT) with low hypertension prevalences (11% and 17%, respectively). On the other hand, prevalences for high PAT in women (45%) and high VAT in men (58%) were relatively high compared to the overall prevalence. This finding suggests that MR derived PAT and VAT improve the prediction of hypertension and the associated cardiovascular risk and demonstrate the chance for additional therapy in subjects with high

PAT and high VAT. Although a MRI examination is time-consuming and cost-intensive a PAT and VAT measurement could be worthwhile in patients with indicated MRI.

Strengths and limitations

Strengths of our study are the well characterized sub-sample 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. The representativeness of the study sample for the initial cohort sample and the population of the study region is also limited. Reasons for non-response included contraindications for MRI examinations and refusal of informed consent and refusal of telephone invitation. A comparison of the MRI sub-study with the KORA FF4 cohort revealed that participants of the MRI sub-study were a bit younger and more often men compared to the entire KORA FF4 cohort.

Conclusion

MRI derived fat content measures perform similarly or even better in identifying hypertension compared to anthropometric markers. Especially, PAT and VAT in women and TAT and SCAT in men were highly correlated with hypertension. The use of PAT and VAT measurements seems to improve the individual characterisation of hypertensive subjects. However, the established anthropometric markers WC and WHtR could be also confirmed as significant independent associates of hypertension, especially in men. 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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Table 1. Characteristics of the study sample (N=345).

	Without Hypertension N=229	Hypertension N=116
Covariates		
Age (years)	52 (46; 61)	62 (56; 67)
Males	126 (55.0%)	76 (65.5%)
Smoking status		
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)
Physically active	146 (63.8%)	59 (50.9%)
Diabetes mellitus	12 (5.2%)	33 (28.5%)
HDL-C (mg/dl)	61 (50; 74)	58 (47; 70)
LDL-C (mg/dl)	138 (115; 161)	134 (117; 159)
Total cholesterol (mg/dl)	217 (193; 242)	212 (190; 239)
TG (mg/dl)	102 (73; 143)	119 (92; 180)
Weight (kg)	78.4 (68.7; 90.4)	85.1 (76.9; 95.7)
Height (m)	1.73 (1.64; 1.80)	1.72 (1.64; 1.78)
Anthropometric markers		
Body mass index, BMI (kg/m²)	26.6 (23.9; 29.2)	29.0 (26.5; 32.1)
Waist circumference, WC (cm)	95.7 (84.6; 103.5)	104.3 (98.2; 111.3)
Hip circumference, HC (cm)	104.6 (99.9; 109.1)	108.4 (102.4; 113.8)
Waist-hip-ratio, WHR	0.91 (0.85; 0.96)	0.97 (0.90; 1.02)
Waist-height-ratio, WHtR	0.55 (0.50; 0.60)	0.61 (0.56; 0.66)
Adipose tissue (MRI)		
Total adipose tissue, TAT (l/m^2)	3.36 (2.55; 4.83)	5.03 (3.75; 6.49)
Visceral adipose tissue, VAT (l/m^2)	1.08 (0.67; 1.62)	1.96 (1.37; 2.45)
Subcutaneous adipose tissue, SCAT (l/m^2)	2.16 (1.70; 3.10)	2.88 (2.10; 4.23)
Hepatic fat fraction, HFF (%)	3.84 (2.24; 6.97)	9.56 (4.10; 20.38)
Pancreatic fat fraction, PFF (%)	4.73 (3.1; 7.33)	6.95 (4.03; 14.77)
Pericardial adipose tissue, PAT (ml)	92.0 (61.5; 135.6)	145.8 (111.1; 206.0)
Blood pressure		
Systolic blood pressure (mmHg)	116 (107; 124)	133 (120; 143)
Diastolic blood pressure (mmHg)	73 (68; 79)	80 (73; 89)
Use of antihypertensive medication	-	84 (72.4%)

Data are given as number (percentage) or median (25^{th} and 75^{th} percentile).
HbA1c, hemoglobin A1c; HDL-C, high-density-lipoprotein cholesterol; LDL-C, low-density-lipoprotein cholesterol; TG, triglycerides

Table 2. Area under the curve values for different statistical models predicting the presence of prevalent hypertension, stratified by sex. Models either included only traditional risk factors (AUC_{basic}), only individual adiposity traits of interest, or each adiposity trait of interest combined with traditional risk factors.

N=345	Hypertension AUC (95%CI) of single factor	Hypertension AUC (95%CI) single factor + basic model*	p-value**	p-value[#]
Women (N=143)	*28% Hypertension*	AUC_{basic}=0.7362		
TAT	0.73 (0.64;0.82)	0.77 (0.68;0.85)	0.007	0.341
VAT	**0.77 (0.68;0.85)**	**0.78 (0.70;0.86)**	0.002	0.803
SCAT	0.70 (0.61;0.79)	0.76 (0.67;0.84)	0.024	0.098
HFF	0.71 (0.61;0.81)	0.77 (0.69;0.85)	0.044	0.344
PFF	0.63 (0.53;0.74)	0.76 (0.67;0.84)	0.013	0.152
PAT	**0.78 (0.69;0.86)**	**0.79 (0.72;0.87)**	<0.001	0.811
BMI	0.71 (0.62;0.81)	0.77 (0.68;0.85)	0.010	0.102
WC	0.71 (0.61;0.80)	0.76 (0.68;0.84)	0.030	0.264
HC	0.68 (0.58;0.77)	0.76 (0.68;0.85)	0.024	0.058
WHR	0.66 (0.55;0.76)	0.75 (0.66;0.83)	0.236	0.151
WHtR	0.71 (0.61;0.80)	0.76 (0.68;0.84)	0.019	0.278
Men (N=202)	*38% Hypertension*	AUC_{basic}=0.7885		
TAT	0.71 (0.64;0.78)	**0.82 (0.76;0.88)**	<0.001	<0.001
VAT	**0.72 (0.65;0.79)**	0.80 (0.74;0.86)	0.026	<0.001
SCAT	0.66 (0.59;0.74)	**0.82 (0.76;0.88)**	<0.001	<0.001
HFF	0.71 (0.64;0.78)	0.80 (0.74;0.87)	0.011	<0.001
PFF	0.65 (0.57;0.73)	0.80 (0.74;0.86)	0.164	<0.001
PAT	0.69 (0.62;0.77)	0.80 (0.74;0.86)	0.090	<0.001
BMI	0.65 (0.57;0.73)	0.81 (0.75;0.87)	0.001	<0.001
WC	0.69 (0.61;0.77)	**0.82 (0.76;0.88)**	<0.001	<0.001
HC	0.59 (0.51;0.68)	0.81 (0.74;0.87)	0.011	<0.001
WHR	**0.72 (0.65;0.80)**	0.81 (0.75;0.87)	0.002	<0.001
WHtR	**0.72 (0.65;0.80)**	**0.82 (0.76;0.88)**	<0.001	<0.001

Bold: Highest AUC values among adiposity risk factors

* Basic risk factor model for hypertension includes: age, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol, HDL-cholesterol

** Likelihood-ratio test (comparison: basic model vs. basic risk factor model + adiposity risk factor)

[#] Likelihood-ratio test (comparison: adiposity risk factor vs. adiposity risk factor + basic risk factor model)

Table 3. Association of each MRI-derived and of each anthropometric adiposity measurement with the presence of hypertension in women and men.

N=345	Hypertension OR (95%CI) Age-adjusted model	p-value	Hypertension OR (95%CI) Fully adjusted model*	p-value
Women (N=143)	*28% Hypertension*			
TAT	2.00 (1.37;2.93)	<0.001	1.88 (1.22;2.90)	0.004
VAT	2.91 (1.67;5.05)	<0.001	2.69 (1.45;4.98)	0.002
SCAT	1.75 (1.22;2.51)	0.002	1.67 (1.11;2.51)	0.014
HFF	1.96 (1.22;3.14)	0.005	1.70 (1.00;2.88)	0.050
PFF	2.10 (1.22;3.60)	0.007	1.99 (1.12;3.52)	0.018
PAT	**3.69 (1.97;6.92)**	**<0.001**	**3.39 (1.69;6.80)**	**0.001**
BMI	1.77 (1.24;2.53)	0.002	1.66 (1.12;2.45)	0.011
WC	1.94 (1.28;2.94)	0.002	1.66 (1.04;2.63)	0.033
HC	1.64 (1.17;2.31)	0.004	1.53 (1.05;2.22)	0.027
WHR	1.71 (1.06;2.75)	0.027	1.38 (0.81;2.35)	0.239
WHtR	1.81 (1.24;2.64)	0.002	1.63 (1.07;2.47)	0.022
Men (N=202)	*38% Hypertension*			
TAT	2.49 (1.66;3.73)	<0.001	2.16 (1.37;3.39)	0.001
VAT	1.96 (1.36;2.81)	<0.001	1.62 (1.07;2.47)	0.023
SCAT	**3.02 (1.84;4.98)**	**<0.001**	**2.60 (1.52;4.47)**	**0.001**
HFF	1.91 (1.38;2.65)	<0.001	1.59 (1.11;2.30)	0.012
PFF	1.32 (0.99;1.76)	0.061	1.24 (0.91;1.67)	0.168
PAT	1.51 (1.08;2.10)	0.016	1.36 (0.95;1.93)	0.093
BMI	2.24 (1.52;3.29)	<0.001	1.98 (1.29;3.05)	0.002
WC	2.53 (1.67;3.83)	<0.001	2.23 (1.39;3.58)	0.001
HC	1.89 (1.28;2.77)	0.001	1.68 (1.11;2.52)	0.013
WHR	2.66 (1.66;4.28)	<0.001	2.24 (1.32;3.83)	0.003
WHtR	2.56 (1.7;3.85)	<0.001	2.28 (1.44;3.61)	<0.001

Data are odds ratios for *standard deviation (whole sample) increment* adiposity measurements from logistic regression
Bold: Highest ORs values among adiposity risk factors
* Fully adjusted model adjusted for: age, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol, HDL-cholesterol

Table 4. Association of MRI derived adiposity measurements with the presence of hypertension independent of cardiovascular risk factors and independent of the best performing anthropometric marker (WC for women and WHtR for men, respectively).

N=345	Hypertension OR (95%CI)	p-value*
Women (N=143)	*28% Hypertension*	
TAT	3.14 (1.16;8.46)	0.024
VAT	3.17 (1.23;8.18)	0.017
SCAT	1.71 (0.74;3.95)	0.208
HFF	1.41 (0.81;2.47)	0.228
PFF	1.74 (0.97;3.12)	0.062
PAT	3.39 (1.44;8.00)	0.005
Men (N=202)	*38% Hypertension*	
TAT	1.24 (0.45;3.41)	0.682
VAT	0.83 (0.44;1.55)	0.556
SCAT	1.90 (0.65;5.53)	0.239
HFF	1.28 (0.86;1.91)	0.229
PFF	1.05 (0.77;1.45)	0.742
PAT	0.96 (0.63;1.46)	0.853

Data are odds ratios for *standard deviation (whole sample) increment* adiposity measurements from logistic regression
*Adjusted for: age, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol, HDL-cholesterol (and WC in women; WHtR in men)

Figure Legends

Figure 1 Receiver operating characteristic (ROC) curves and area under the curve (AUC) values with 95% confidence intervals for explaining hypertension based on MRI-derived adipose tissue measurements only (panel A) and based on anthropometric markers only (panel B).

Figure 2 Association of MRI and anthropometric adiposity measurements (*standard deviation increment*) with presence of hypertension in the overall sample adjusted for age and sex only (panel A) and adjusted for age, sex, diabetes, physical activity, smoking status, alcohol consumption, total cholesterol and HDL-cholesterol (panel B) expressed by odds ratios and 95% confidence intervals.

Figure 3 Classification tree of interaction analysis including all MRI and anthropometric adiposity measurements (*sex-specific median-dichotomized*) for identifying hypertension according to chi-square automatic interaction detection (CHAID) adjusted for age, *$p<0.05$, ***$p<0.001$.

Figure 1

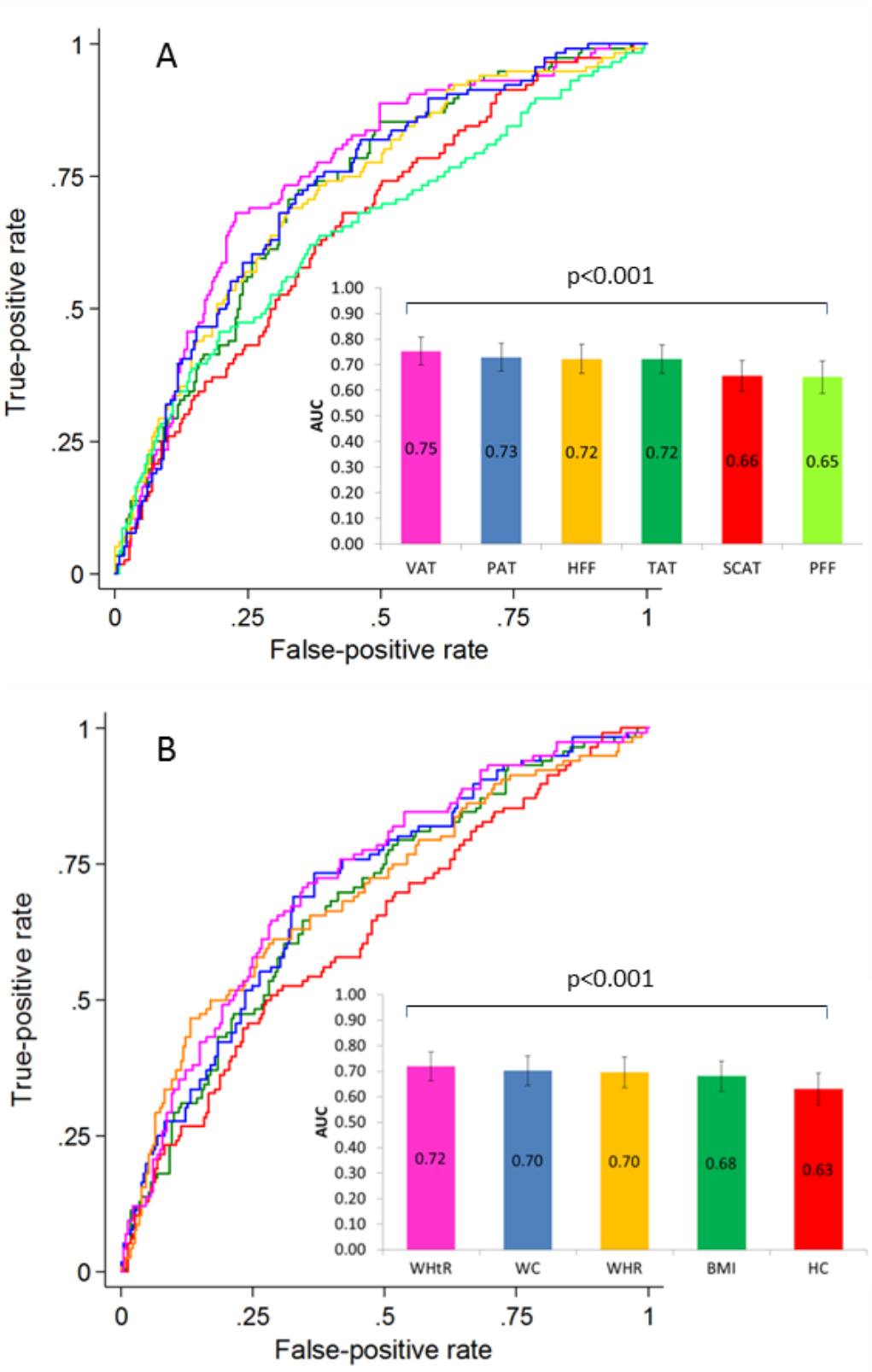
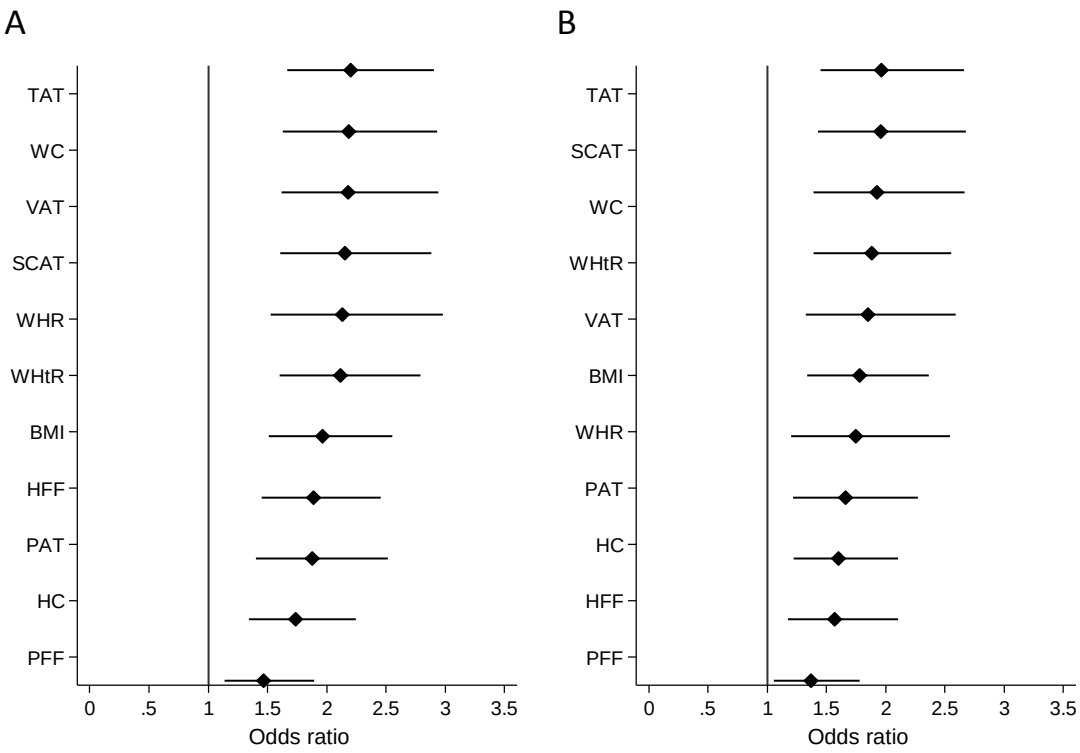

A
True-positive rate
False-positive rate
0
.25
.5
.75
1
p<0.001
AUC
0.00
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
0.90
1.00
0.75
0.73
0.72
0.72
0.66
0.65
VAT
PAT
HFF
TAT
SCAT
PFF
B
True-positive rate
False-positive rate
p<0.001
AUC
0.72
0.70
0.70
0.68
0.63
WHtR
WC
WHR
BMI
HC

Figure 2


A
TAT
WC
VAT
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BMI
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0
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Odds ratio
B
TAT
SCAT
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WHtR
VAT
BMI
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0
.5
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2
2.5
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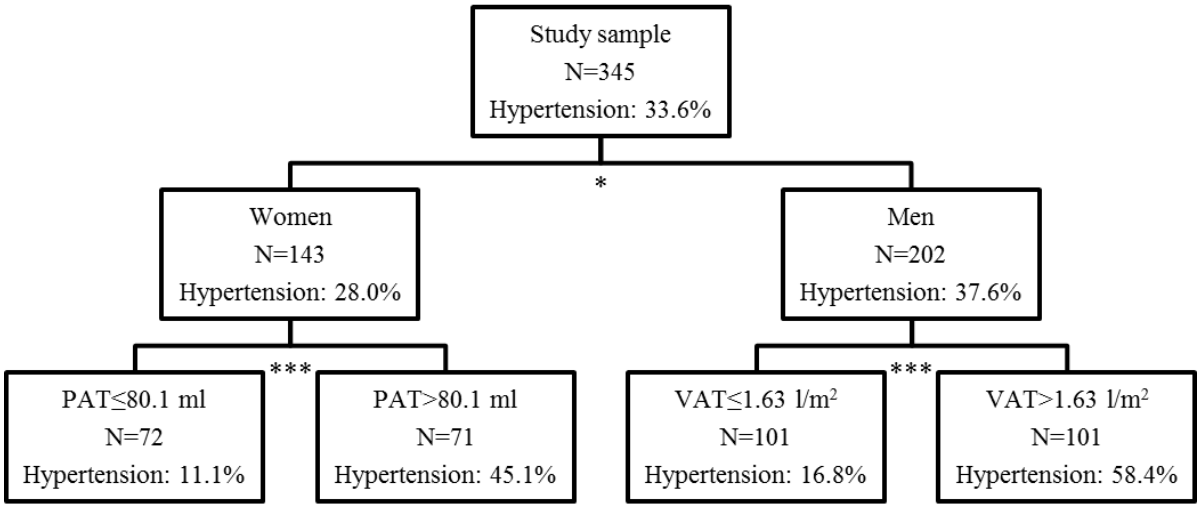
3.5
Odds ratio

Figure 3


Study sample
N=345
Hypertension: 33.6%
*
Women
N=143
Hypertension: 28.0%
Men
N=202
Hypertension: 37.6%
***
PAT≤80.1 ml
N=72
Hypertension: 11.1%
PAT>80.1 ml
N=71
Hypertension: 45.1%
***
VAT≤1.63 l/m2
N=101
Hypertension: 16.8%
VAT>1.63 l/m2
N=101
Hypertension: 58.4%