Obesity and Cardiovascular disease. Results from the Netherlands Epidemiology of Obesity Study

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CHAPTER 4

Relation of overall and abdominal adiposity with electrocardiogram parameters of subclinical cardiovascular disease in individuals aged 45 to 65 years (from the Netherlands Epidemiology of Obesity study)

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ABSTRACT

Background

Overall and abdominal obesity are well-established risk factors for cardiometabolic disease. However, associations of overall and abdominal adiposity with electrocardiographic (ECG) markers of subclinical cardiovascular disease (CVD) have not yet been fully elucidated. Therefore, we investigated these associations in a population without preexisting CVD.

Methods

We performed cross-sectional analyses in the Netherlands Epidemiology of Obesity Study. Body mass index (BMI), total body fat, and waist circumference were assessed in all participants, and abdominal subcutaneous adipose tissue and visceral adipose tissue (by magnetic resonance imaging) were assessed in a random subgroup. ECG parameters were determined using 12-lead electrocardiograms. We performed linear regression analyses, adjusting for potential confounding factors and, when investigating abdominal adiposity, additionally for total body fat.

Results

After exclusion of participants with preexisting CVD (n = 654), 5939 individuals (42% men) were analyzed, with a mean (SD) age of 55 (6) years and BMI of 26.3 (4.4) kg/m^2. Measures of both overall and abdominal adiposity were associated with ECG parameters but none of these measures was more strongly associated than the others. For example, heart rate (beats/min) increased per SD higher BMI (2.2; 95% confidence interval 1.9, 2.5), total body fat (2.9; 2.4, 3.4), subcutaneous adipose tissue (2.3;1.7, 2.9), waist circumference (2.1; 1.4, 2.8), and visceral adipose tissue (1.7; 0.8, 2.5). In subgroup analyses based on gender and cardiovascular risk factors, no consistent interactions were observed.

Conclusions

In conclusion, in a middle-aged population without preexisting CVD, measures of both overall and abdominal adiposity were associated with ECG parameters. Future studies should evaluate the added value of adiposity measures in electrocardiography-based diagnoses and the prognostic value of adding adiposity measures to risk prediction tools.

INTRODUCTION

Several studies have shown that high abdominal fat, especially excess visceral adipose tissue (VAT), plays an important role in the increased cardiometabolic risk associated with excess fat mass, on top of the important role that overall adiposity plays [1-3]. Both overall and abdominal adiposity have been associated with cardiovascular end points, and more rarely with subclinical cardiovascular disease (CVD) [4-8]. Excess fat mass is often assessed by body mass index (BMI); however, this might not be the best measure because it does not distinguish fat mass from fat-free mass. Total body fat and subcutaneous adipose tissue are more accurate measures of overall adiposity, and waist circumference and VAT are more accurate measures of abdominal adiposity. Reports on associations between both measures of overall and abdominal adiposity and commonly used electrocardiographic (ECG) parameters indicative of subclinical CVD (in a population without preexisting CVD) are scarce. Electrocardiography is widely used in clinical practice for diagnostics and also has significant prognostic value for CVD and mortality [9]. We therefore focused on subtle changes in ECG parameters, which do not have immediate obvious importance, but that have previously been associated with a broad range of future cardiovascular abnormalities or mortality [10-17]. We aimed to investigate associations between measures of overall and abdominal adiposity and ECG parameters in a population without preexisting CVD.

METHODS

The Netherlands Epidemiology of Obesity (NEO) Study is a prospective, population-based cohort study with 6671 individuals, included between 2008 and 2012. Men and women aged between 45 and 65 years, living in the area of greater Leiden (in the Netherlands), and with a BMI ≥ 27 kg/m^2 were eligible to participate. In addition, all inhabitants aged between 45 and 65 years from 1 municipality (Leiderdorp) were invited to join irrespective of their BMI, allowing a reference distribution of BMI. Participants completed a questionnaire on demographic and clinical information before the visit to the NEO study center. Participants were invited to a baseline visit at the NEO study center after an overnight fast. Participants with preexisting CVD were excluded from the present analyses because we were interested in subclinical CVD. Preexisting CVD was defined as either self-reported myocardial infarction, angina, congestive heart failure, stroke or peripheral vascular disease, or as presence of Minnesota codes for atrial fibrillation, left bundle branch block, right bundle branch block or Wolff-Parkinson-White syndrome, or as presence of an artificial pacemaker [18]. Additionally, individuals with missing electrocardiograms were excluded. More information on the study design and population has been published elsewhere [19]. The Medical Ethics Committee of the Leiden University Medical Center approved the design of the study. All participants gave their written informed consent.

Ethnicity was self-reported in 8 categories on the questionnaire and then grouped into white and other. Education level was grouped as low (none, primary school, or lower vocational education) and high education (intermediate secondary education, middle-level vocational education, higher secondary education, higher professional education, university, or other). Tobacco smoking was categorized into current, former, or never smokers. Alcohol

consumption was reported on a food frequency questionnaire and recalculated into gram/day [20]. Participants reported their physical activity using the Short Questionnaire to Assess Health-Enhancing Physical Activity, and physical activity was expressed in hours per week of metabolic equivalents [21]. Participants were asked to bring all medications they were currently using to the study visit. Height and weight were measured without shoes and 1 kg was subtracted from the weight to correct for the weight of clothing. BMI was calculated by dividing the weight in kilograms by the height in meters squared. Waist circumference was measured with a horizontally placed flexible tape in the middle of the distance between the lowest rib and the iliac crest. With a bioimpedance device (TBF-310, Tanita International Division, Yiewsley, United Kingdom), total body fat was estimated. Abdominal subcutaneous adipose tissue and VAT were assessed by magnetic resonance imaging (1.5 T magnetic resonance imaging, Philips Medical Systems, Best, the Netherlands) using a turbo spin echo imaging protocol in a random group of 2580 participants without contraindications for magnetic resonance imaging (most notably metallic devices, claustrophobia, or a body circumference of more than 1.70 m). Three transverse images with a slice thickness of 10 mm were obtained at the level of the fifth lumbar vertebra during a breath-hold. The fat depots were converted from the number of pixels to centimeters squared. In the analyses, the average of the 3 slices was used. Brachial blood pressure was measured in a seated position on the right arm using a validated automatic oscillometric device (OMRON, Model M10-IT, Omron Health Care Inc, Lake Forest, Illinois). Blood pressure was measured 3 times with 5-minute rest between consecutive measurements. The mean systolic and diastolic blood pressure were calculated. Blood was sampled after an overnight fast of 10 hours. Fasting glucose, triglyceride, high-density lipoprotein, and low-density lipoprotein concentrations were measured with the enzymatic colorimetric method (Roche Modular Analytics P800, Roche Diagnostics Mannheim, Germany). A 12-lead electrocardiogram at rest was obtained using a Mortara Eli-350 electrocardiograph (Mortara Instrument Inc., Milwaukee, Wisconsin) after a period of rest of at least 10 minutes. ECGs were stored in a MegaCare electrocardiogram management system (Dräger, Zoetermeer, the Netherlands). Values for heart rate, P-wave duration, QRS complex duration, PR interval, corrected QT interval (corrected according to the Bazett formula), P-wave axis, T-wave axis, and QRS axis were recalculated using the GRI interpretation program, which is part of the management system, to assess subtle changes in ECG parameters, which could indicate subclinical CVD in a population without known overt CVDs [22].

We defined various subgroups to perform stratified analyses in, namely, men or women, high or normal blood pressure levels, serum triglyceride, fasting plasma glucose, serum high-density lipoprotein cholesterol, and serum low-density lipoprotein cholesterol concentrations. Cut-off points were used that were proposed by the National Cholesterol Education Program Adult Treatment Panel III to define the metabolic syndrome, with minor modifications as stated in the American Heart Association and the National Heart, Lung, and Blood Institute statement and additionally also cut-off points for low-density lipoprotein cholesterol [23]. High blood pressure was defined as blood pressure ≥ 130 systolic /≥ 85 mm Hg diastolic or on antihypertensive drug treatment in a patient with a history of hypertension; high serum triglyceride concentrations were defined as serum triglycerides ≥ 150 mg/dl or 1.7 mmol/L or use of prescription drugs to reduce serum triglyceride concentrations; low serum high-density lipoprotein cholesterol was defined as serum high-density lipoprotein

cholesterol < 40 mg/dl or 1.03 mmol/L for men and <50 mg/dl or 1.3 mmol/L for women or use of prescription drugs to elevate serum high-density lipoprotein cholesterol; high fasting plasma glucose was defined as fasting plasma glucose ≥ 100 mg/dl or 5.56 mmol/L or use of prescription drugs to lower plasma glucose concentrations; and high serum low-density lipoprotein cholesterol is defined as serum low-density lipoprotein cholesterol > 160 mg/dl or 4.1 mmol/L or use of prescription drugs to reduce serum low-density lipoprotein cholesterol concentrations.

In the NEO study, there is an oversampling of individuals with a BMI of 27 kg/m^2 or higher. Adjustments for the oversampling of individuals with BMI ≥ 27 kg/m^2 were made to correctly represent baseline associations in the general population. This was done by weighing individuals toward the BMI distribution of participants from the Leiderdorp municipality, whose BMI distribution was similar to the BMI distribution of the general Dutch population [24]. All results are based on weighted analyses. Consequently, the results apply to a population-based study without oversampling of individuals with a BMI ≥ 27 kg/m^2. The data of the baseline characteristics were presented as mean (SD), median (interquartile range), or as percentage. We calculated Z-scores and standardized the adiposity measures to a mean of 0 and a standard deviation of 1. The associations between the measures of overall adiposity (BMI, total body fat, and subcutaneous adipose tissue) and the measures of abdominal adiposity (waist circumference and VAT) with the ECG parameters heart rate (beats/min), P-wave duration (milliseconds), QRS complex duration (milliseconds), PR interval (milliseconds), corrected QT interval (milliseconds), P-wave axis (°), T-wave axis (°), and QRS axis (°) were investigated using linear regression analyses and expressed as difference in ECG parameter with 95% confidence interval (CI). In crude models, the associations of waist circumference and VAT were adjusted for total body fat. Adjusted models were additionally adjusted for age, gender, ethnicity, smoking, alcohol intake, education level, physical activity, presence of chronic obstructive pulmonary disease, and use of several drugs that could influence the ECG parameters, namely, use of digoxin, class I/III blocking medication, β blockers, calcium channel blockers, and QT-prolonging drugs.

Analyses were repeated in the previously described subgroups. We tested for interaction between adiposity measures and subgroups by including product terms in the models. Data were analyzed using STATA version 14 (Statacorp, College Station, Texas, USA).

RESULTS

In the NEO study, 6671 participants were included. For the present analysis, we consecutively excluded participants with a self-reported history of CVD (n = 464), right bundle branch block (n = 95), left bundle branch block (n = 41), atrial fibrillation (n = 42), artificial pacemaker (n = 8), Wolff-Parkinson-White syndrome (n = 4), or missing electrocardiogram (n = 78), leaving 5939 participants for the main analysis. Measurements of visceral and subcutaneous adipose tissue were available in 2331 participants. The baseline characteristics of the study population are presented in Table 1. The mean (SD) age was 55 (6) years and 42% were men. Although women had more total body fat and more subcutaneous adipose tissue, men had higher BMI and more VAT.

Table 1. Characteristics of 5939 participants aged 45 to 65 year from the Netherlands Epidemiology of Obesity study

	Total population	Men (42%)	Women (58%)
Age (years)	55 ± 6	56 ± 6	55 ± 6
Ethnicity, white	95%	95%	95%
Education level, low*	19%	18%	20%
Smoker			
Never	39	36	42
Former	45	46	44
Current	16	18	14
Alcohol intake (grams/day)	9.8 (2.8 , 21.3)	16.4 (6.0 , 28.1)	7.7 (1.6 , 14.8)
Physical activity (MET-hour/week)	29.8 (15.3 , 49.3)	30.7 (15.0 , 50.0)	29.0 (15.8 , 48.5)
Fasting glucose (mmol/l; mg/dl)	5.4 ± 1.0; 98.1 ± 17.1	5.7 ± 1.1; 101.8 ± 20.0	5.3 ± 0.8; 95.4 ± 14.0
Use of glucose lowering therapy	2%	3%	2%
Systolic blood pressure (mmHg)	130.0 ± 17.1	134.4 ± 15.5	126.8 ± 17.5
Diastolic blood pressure (mmHg)	83.2 ± 10.3	85.0 ± 10.1	81.9 ± 10.3
Use of antihypertensive therapy	21%	20%	21%
Triglycerides (mmol/l; mg/dl)	1.0 (0.7 , 1.5); 88.6 (63.8 , 129.3)	1.2 (0.8 , 1.7); 102.7 (72.6 , 148.8)	0.9 (0.7 , 1.3); 81.5 (60.2 ,115.1)
HDL-cholesterol (mmol/l; mg/dl)	1.6 ± 0.5; 61.3 ± 17.8	1.4 ± 0.4; 52.2 ± 14.1	1.8 ± 0.4; 67.9 ± 17.0
LDL-cholesterol (mmol/l; mg/dl)	3.6 ± 1.0; 138.2 ± 37.2	3.6 ± 1.0; 138.8 ± 38.1	3.6 ± 0.9; 137.8 ± 36.5
Use of lipid lowering therapy	8%	11%	6%
Waist circumference (cm)	91.8 ± 13.2	98.0 ± 11.3	87.2 ± 12.5
BMI (kg/m^2)	26.3 ± 4.4	26.8 ± 3.8	25.9 ± 4.7
Total body fat (%)	31.8 ± 8.7	24.8 ± 6.0	36.9 ± 6.4
VAT (cm^2) (n=2331)	88.3 ± 55.2	113.5 ± 60.4	66.4 ± 40.3
SAT (cm^2) (n=2331)	234.6 ± 96.5	207.1 ± 84.2	258.4 ± 98.3

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent of task; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.
Results were based on analyses weighted towards the BMI distribution of the general population (n=5939).
Results are presented as mean ± SD, median (IQR) or percentage.
* lower education: none, primary school, lower vocational education

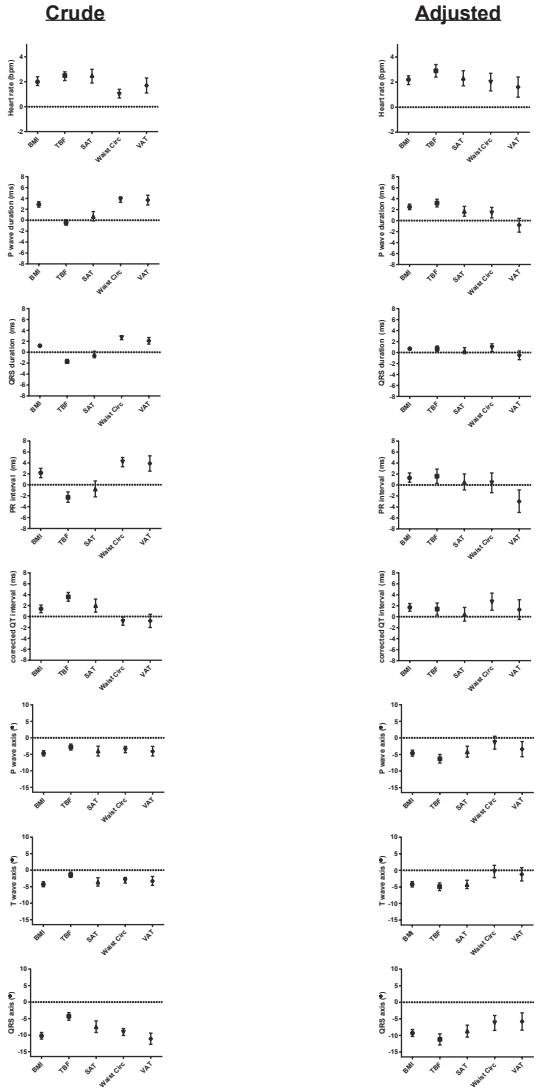

Figure 1. Associations of standardized obesity measures with electrocardiographic (ECG) parameters in 5939 participants aged 45 to 65 years from the Netherlands Epidemiology of Obesity Study (2331 with VAT and SAT). Results were based on linear regression analyses weighed toward the BMI distribution of the general population (n = 5939), and expressed as difference in the ECG parameter (with 95% confidence interval) per standard deviation of adiposity measure. Crude: Associations with waist circumference or VAT are adjusted for TBF. Adjusted: Adjusted for age, gender, ethnicity, smoking, alcohol intake, education level, physical activity, presence of chronic obstructive pulmonary disease, and use of digoxin, class I/III blocking medication, β blockers, calcium channel blockers, and QT-prolonging drugs. Associations with waist circumference or VAT are additionally adjusted for TBF. Standard deviations: BMI 4.4 kg/m^2 ; TBF 8.7%; SAT 96.6 cm^2 ; Waist circ 13.2 cm; VAT 55.2 cm^2 . BMI = body mass index; SAT = subcutaneous adipose tissue; TBF = total body fat; VAT = visceral adipose tissue; Waist Circ = waist circumference.

Figure 1 is a graphical representation of the associations of the standardized measures of overall and abdominal adiposity with all ECG parameters. The crude model shows associations of all adiposity measures with heart rate, P-wave axis, T-wave axis, and QRS axis, and less consistent associations for P-wave duration, QRS duration, PR interval, and corrected QT interval. The adjusted model showed that both measures of abdominal and overall adiposity were associated with higher heart rate. For example, 1 SD higher total body fat was associated with 2.9 beats/min higher heart rate (95% CI 2.4, 3.4) and 1 SD higher VAT with 1.7 beats/min (0.8, 2.5) higher heart rate. All measures of adiposity were associated with P-wave duration except for VAT adjusted for total body fat (β −0.8 millisecond; 95% CI −2.1, 0.4). BMI, total body fat, and waist circumference were positively associated with QRS duration, whereas no associations were found for subcutaneous adipose tissue (0.4 millisecond; −0.2, 1.0) and VAT (−0.5 millisecond; −1.3, 0.4). BMI (1.3 milliseconds; 0.4, 2.1) and total body fat (1.5 milliseconds; 0.2, 2.8) were positively associated with PR interval, whereas no associations were found for subcutaneous adipose tissue and waist circumference, and the association of VAT was, if anything, in the opposite direction (−2.9 milliseconds; −5.0, −0.9). All measures of adiposity were associated with longer corrected QT interval, except for subcutaneous adipose tissue (0.6 millisecond; −0.7, 1.9). All measures of overall adiposity were associated with P-wave axis, T-wave axis, and QRS axis. Furthermore, waist circumference was negatively associated with QRS axis (−6.2°; −8.4, −4.0), but not with P-wave axis (−1.3°; −3.3, 0.6) or T-wave axis (−0.3°; −2.1, 1.5). VAT was negatively associated with P-wave axis (−3.4°; −5.7, −1.1) and QRS axis (−6.0°; −8.5, −3.4), but not with T-wave axis (−1.3°; −3.3, 0.7). Including participants with preexisting CVD in the analyses did not materially change the results.

In Figure 2, associations between measures of overall and abdominal adiposity with ECG parameters are shown in men and women in adjusted models. In summary, no major or consistent differences were found between men and women in the association between overall and abdominal adiposity and any of the ECG parameters. Measures of both overall and abdominal adiposity were associated with a higher heart rate in both men and women. In both men and women, BMI, total body fat, subcutaneous adipose tissue, and waist circumference were associated with a longer P-wave duration, but VAT adjusted for total body fat was not associated with P-wave duration (per SD VAT in men: β −0.6 millisecond; 95%CI: −2.2, 1.1 and in women: −0.6 millisecond; −2.4, 1.3). Measures of both overall and abdominal adiposity showed associations with a longer QRS duration in men, except for VAT (−0.3 millisecond; −1.2, 0.5). In women, only BMI (0.5 millisecond; 0.1, 1.0) was associated with longer QRS duration. For PR interval, only in women associations were found with BMI and total body fat. Associations of total body fat were stronger in women than in men. In women, 1 SD higher TBF was associated with a 2.9 millisecond (95% CI 1.3, 4.5) longer PR interval, whereas in men, this was −0.9 millisecond (−3.0, 1.2; p-value interaction 0.002). All measures of adiposity showed an association with longer corrected QT interval in both men and women, except for subcutaneous adipose tissue in women (−0.2 millisecond; −1.8, 1.4) and a weak association of VAT in men (1.0 millisecond; −1.2, 3.1). Furthermore, the association of BMI was somewhat stronger in men (3.3 milliseconds; 2.0, 4.6) than in women (1.1 milliseconds; 0.2, 1.9; p-value interaction 0.007). In both men and women, measures of overall and abdominal adiposity were associated with a more leftward shifted P-wave axis, T-wave axis, and QRS axis. Only waist circumference was not associated with P-wave axis in

men (0.5°; −2.65, 3.6), and waist circumference (2.3°; −0.7, 5.2) and VAT (−0.3°; −2.6, 2.1) were not associated with T-wave axis in men.

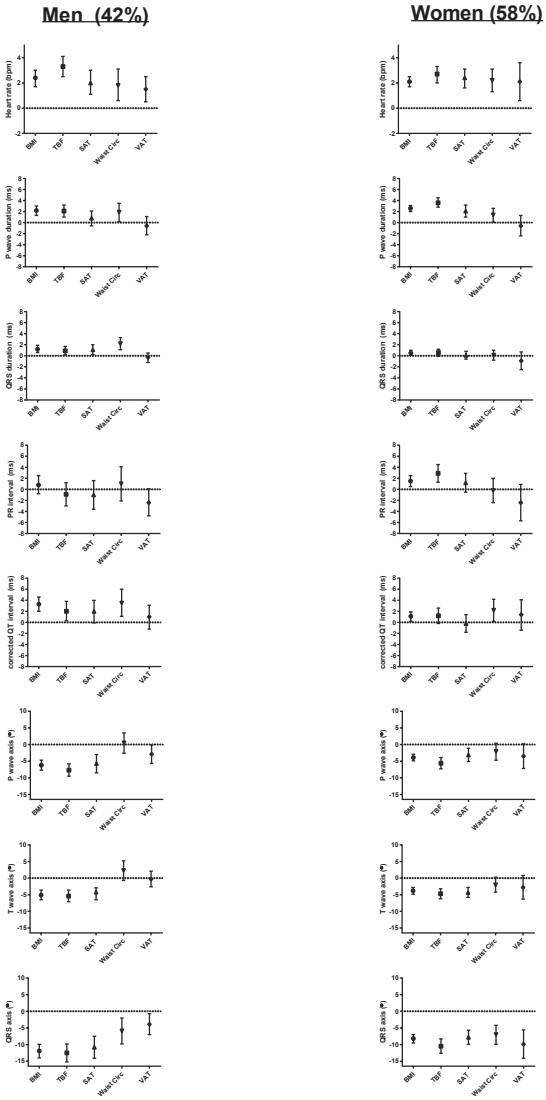

Figure 2. Associations of standardized obesity measures with electrocardiographic (ECG) parameters in men and women aged 45 to 65 years from the Netherlands Epidemiology of Obesity Study (2331 with VAT and SAT). Results were based on linear regression analyses weighed toward the BMI distribution of the general population (n = 5939), and expressed as difference in the ECG parameter (with 95% confidence interval) per standard deviation of adiposity measure. Shown results were adjusted for age, gender, ethnicity, smoking, alcohol intake, education level, physical activity, presence of chronic obstructive pulmonary disease, and use of digoxin, class I/III blocking medication, β blockers, calcium channel blockers, and QT-prolonging drugs. Associations with waist circumference or VAT are

additionally adjusted for TBF. Standard deviations: BMI 4.4 kg/m^2 ; TBF 8.7%; SAT 96.6 cm^2 ; Waist circ 13.2 cm; VAT 55.2 cm^2 . BMI = body mass index; SAT = subcutaneous adipose tissue; TBF = total body fat; VAT = visceral adipose tissue; Waist Circ = waist circumference.

As shown in Supplementary Figure 1, for the other subgroups, results were similar. We observed differences in strengths of association of some measures of overall and abdominal adiposity with ECG parameters between subgroups. However, these differences were inconsistent.

DISCUSSION

In a large cohort of individuals without overt CVD, we investigated the associations between measures of overall adiposity, BMI, total body fat, and subcutaneous adipose tissue, as well as measures of abdominal adiposity, waist circumference, and VAT, with changes in ECG parameters, indicative of subclinical CVD. We observed that measures of both overall and abdominal adiposity were associated with ECG measures associated with subclinical CVD, and that measures of abdominal adiposity were not more strongly associated with ECG measures than measures of overall adiposity. When investigating the associations of adiposity measures with ECG parameters in different subgroups, there were several interactions observed, which were neither consistent with the ECG parameters nor with the specific subgroups. Therefore, we are not able to draw any firm conclusions from these subgroup analyses.

Measures of overall and abdominal adiposity have been associated with subclinical CVD in previous literature. We expected abdominal adiposity to be most strongly associated with ECG parameters since especially VAT is known to release several cytokines, chemokines, and hormones, which can influence organ function and lead to increased progression of atherosclerosis. [1-3]

In this study, measures of abdominal adiposity were not more strongly associated with the ECG parameters than measures of overall adiposity, which could have several explanations. First, it is important to realize that associations with VAT are adjusted for total body fat to look specifically at the VAT and not general adiposity. In this study, associations of VAT were attenuated by this adjustment. Furthermore, it is important to realize which specific subclinical cardiovascular abnormalities are reflected by the different ECG parameters. Higher heart rate reflects, among others, increased sympathetic activity, which has been associated with CVD and events [10,25]. P-wave duration reflects atrial depolarization and is associated with atrial fibrillation [11]. QRS duration reflects ventricular depolarization and prolongation is associated with, among others, congestive heart failure, increased left ventricular mass, and higher cardiovascular mortality [12,26]. PR interval reflects atrial conduction, AV nodal conduction, and conduction in the heart tissue. Inconsistent associations have been reported with atrial fibrillation and cardiovascular mortality [13,27]. QT interval reflects ventricular depolarization and repolarization, and prolongation has been associated with ventricular arrhythmias and adverse prognosis [14]. P-wave axis reflects atrial orientation and conduction and has been associated with increased (cardiovascular) mortality risk [15]. Abnormalities in T-wave axis

reflect ventricular repolarization abnormalities, which have been associated with increased risk of coronary heart disease and heart failure [16]. Abnormalities of the QRS axis, or electrical heart axis, which reflects depolarization in the heart, can have several causes. Literature regarding the prognostic value of an abnormal QRS axis is inconclusive, and associations with increased cardiovascular risk are rarely observed in individuals without cardiac disease [17,28]. The deleterious effects of VAT might be stronger for cardiac abnormalities with large metabolic influences, such as atherosclerosis and less on these ECG parameters that have more to do with cardiac activation or conduction. For example, whereas for subclinical atherosclerosis, abdominal adiposity is often described as the most important, for atrial fibrillation, similar association of waist circumference, waist:hip ratio, and BMI was shown [29]. Furthermore, epicardial adipose tissue, a specific visceral fat depot, might show stronger associations with the ECG parameters investigated in this study because of its anatomic proximity to the myocardium and conduction system [30].

A strength of our study is the large study population (n = 5939 after exclusion of participants with preexisting CVD), which made it possible to easily assess associations with sufficient statistical power. Furthermore, the NEO study has performed deep phenotyping of the participants, which made control of potential confounding factors possible. A limitation of our study is its cross-sectional design, which precludes any causal conclusions. Furthermore, adiposity measures were only investigated at 1 moment in time, not taking into account changes in the different adiposity measures in relation to the development of subclinical CVD. Moreover, self-reported variables used in this study could have been subject to information (recall) bias.

In conclusion, in a population aged 45 to 65 years without preexisting CVD, measures of both overall and abdominal adiposity were positively associated with subtle differences in ECG parameters, associated with subclinical CVD.

Adiposity measures have been proposed to aid in distinguishing people at low and high cardiovascular risk, and this study adds evidence in favor of this potential role of both measures of overall adiposity, as well as abdominal adiposity in risk stratification. The role of abdominal and overall adiposity might differ between abnormalities with large metabolic influences and activation or conduction abnormalities. Moreover, more easily determinable measures, such as BMI or waist circumference, may have greater potential for application in clinical practice than for example VAT. Future studies should evaluate the value of the inclusion of adiposity measures in ECG diagnoses, such as atrial fibrillation or left ventricular hypertrophy, and the prognostic value of adding adiposity measures to current risk prediction tools.

Acknowledgments

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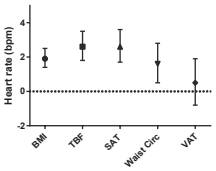
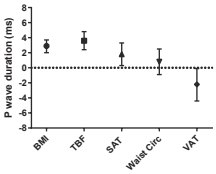
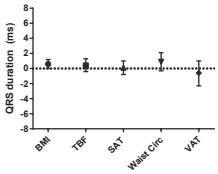
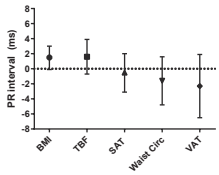
Supplementary Figure 1. Associations of standardized obesity measures with ECG parameters in subgroups of participants aged 45 to 65 years from the Netherlands Epidemiology of Obesity Study (2331 with VAT and SAT). Results were based on linear regression analyses weighed toward the BMI distribution of the general population (n = 5939), and expressed as difference in the ECG parameter (with 95% confidence interval) per standard deviation of adiposity measure. Results were based on weighted linear regression analyses adjusted for age, gender, ethnicity, smoking, alcohol intake, education level, physical activity, presence of chronic obstructive pulmonary disease, and use of digoxin, class I/III blocking medication, β blockers, calcium channel blockers, and QT-prolonging drugs. Associations with waist circumference or VAT are additionally adjusted for TBF. Standard deviations: BMI 4.4 kg/m^2; TBF 8.7%; SAT 96.6 cm^2; Waist circ 13.2 cm; VAT 55.2 cm^2. High blood pressure: ≥130 systolic/≥85 mm Hg diastolic or on antihypertensive drug treatment in a patient with a history of hypertension; high triglyceride concentration: ≥150 mg/dl or 1.7 mmol/L or use of prescription drugs to reduce serum triglyceride concentrations; high glucose concentration: ≥100 mg/dl or 5.56 mmol/L or use of prescription drugs to lower plasma glucose concentrations; high low-density lipoprotein cholesterol concentration: >160 mg/dl or 4.1 mmol/L or use of prescription drugs to reduce serum low-density lipoprotein cholesterol concentrations; low high-density lipoprotein cholesterol concentrations: <40 mg/dl or 1.03 mmol/L for men and <50 mg/dl or 1.3 mmol/L for women or use of prescription drugs to elevate serum high-density lipoprotein cholesterol. BMI = body mass index; SAT = subcutaneous adipose tissue; TBF = total body fat; VAT = visceral adipose tissue; Waist Circ = waist circumference.

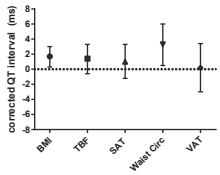
Normal blood pressure (40%)

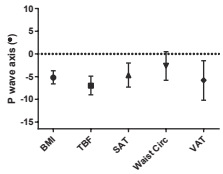


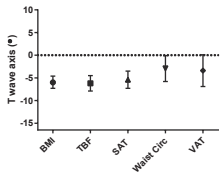


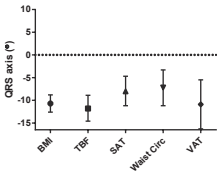




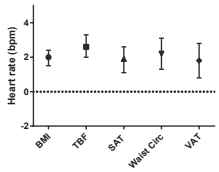


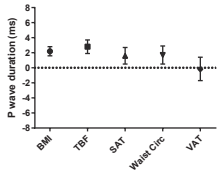


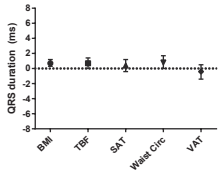


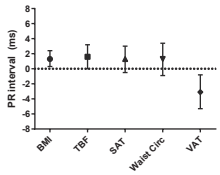


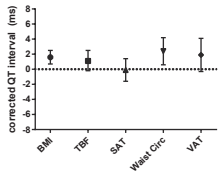
↑ blood pressure (60%)

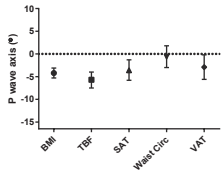


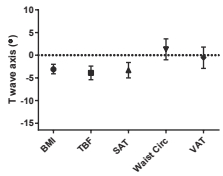


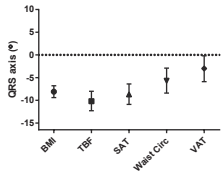




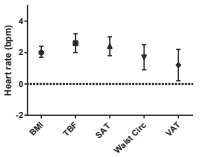


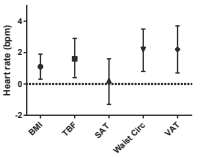


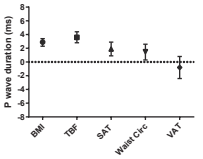


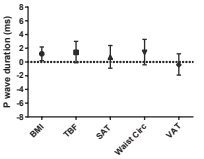


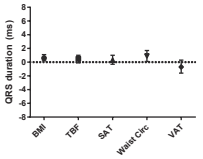
Normal triglyceride concentration (83%) **↑ triglyceride concentration (17%)**

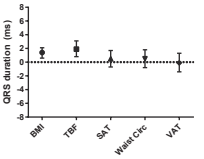


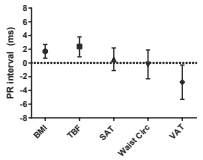


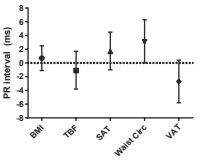


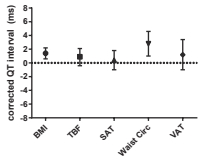


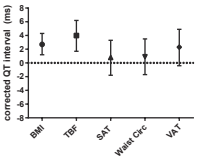


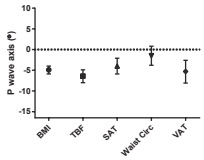


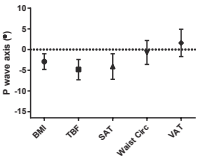


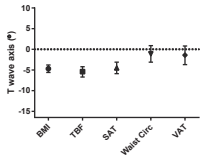


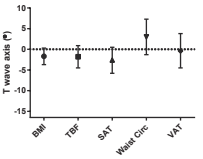


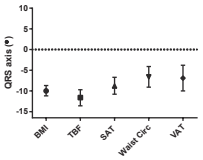


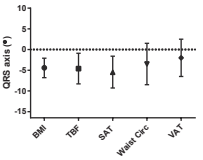




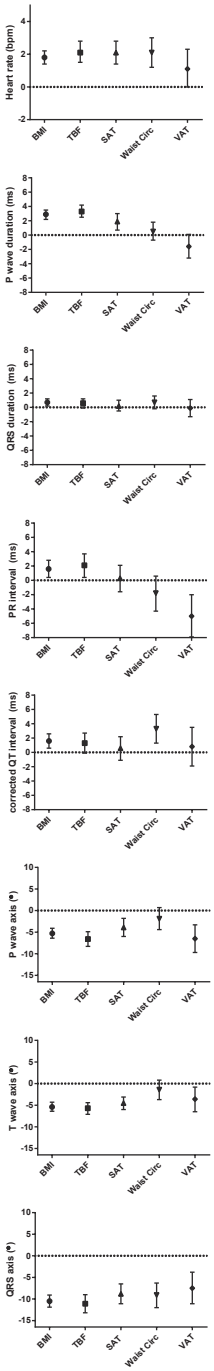




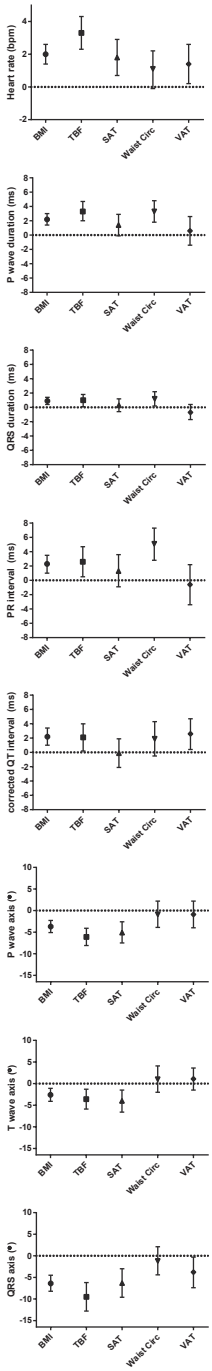




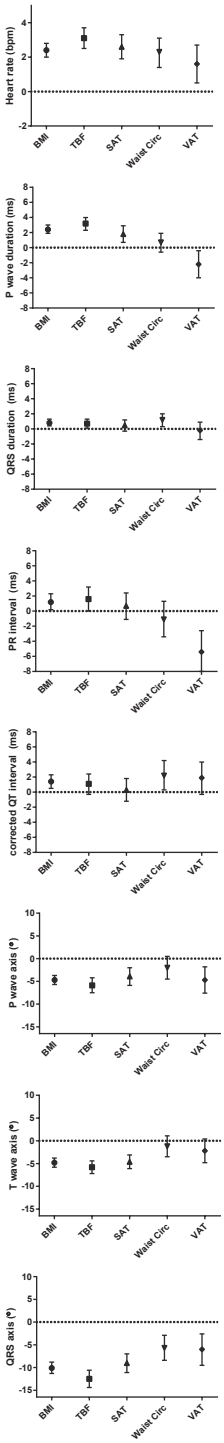
Normal glucose concentration (70%)



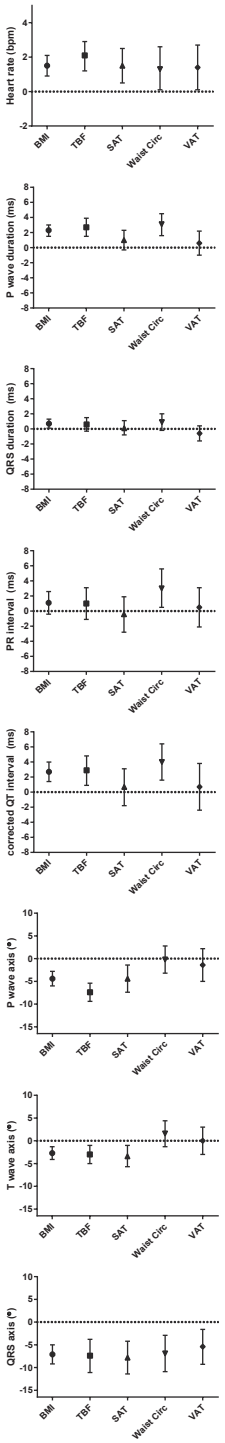
↑ glucose concentration (30%)



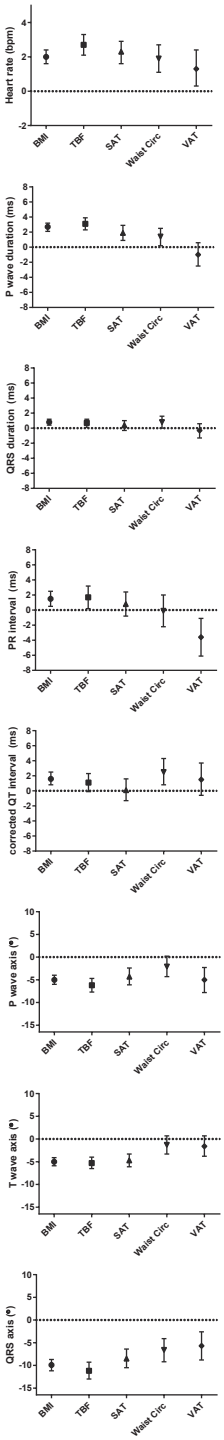
Normal LDL concentration (66%)



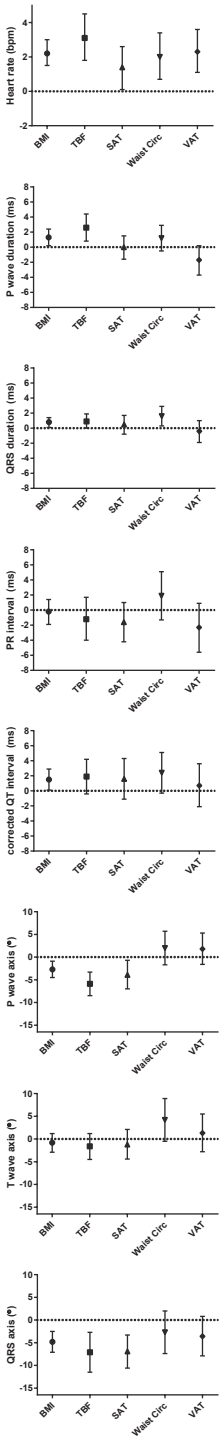
↑ LDL concentration (34%)



Normal HDL concentration (84%)



↓ HDL concentration (16%)



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