International Journal of Cardiology 274 (2019) 331–336

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Borderline Q-waves in individuals without overt cardiovascular disease: Relations with adiposity, subclinical atherosclerosis and vascular stiffness

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ARTICLE INFO

Article history:
Received 22 March 2018
Received in revised form 16 August 2018
Accepted 29 August 2018
Available online 1 September 2018

Keywords:
Borderline Q-waves
Subclinical atherosclerosis
Vascular stiffness

ABSTRACT

Background: Characteristics and risk factors associated with electrocardiographic borderline Q-waves are not fully elucidated, especially in individuals without overt cardiovascular disease (CVD). Also, the relation of isolated and non-isolated borderline Q-waves with subclinical atherosclerosis and vascular stiffness is unknown.
Methods and results: We included 5746 Netherlands Epidemiology of Obesity study participants without overt CVD. Participants were divided in three groups: no Q-waves (93.7%), isolated (4.6%) and non-isolated borderline Q-waves (1.7%). Borderline Q-waves were defined as Minnesota Codes 1.2.x and 1.3.x and non-isolated as ≥1 of abnormal QRS axis, left ventricular hypertrophy or ST/T abnormalities. Several characteristics and measures of body fat were assessed. Vascular stiffness was assessed by pulse wave velocity (PWV) and subclinical atherosclerosis by carotid intima-media thickness (cIMT). Percentage of men, alcohol intake, blood pressure and fasting glucose concentrations were, compared with no Q-waves, higher in the isolated and highest in the non-isolated borderline Q-wave group. Isolated borderline Q-waves were associated with higher body mass index (difference compared with no Q-waves: 1.0 kg/m^2; 95%CI: 0.3–1.7; p-value: 0.006), waist circumference (3.4 cm; 1.0–5.8; 0.005), and visceral adipose tissue (21.9 cm^2; 7.4–36.3; 0.003) and differences were even larger for non-isolated borderline Q-waves. Compared with no Q-waves, non-isolated borderline Q-waves were associated with higher PWV (1.2 m/s; 0.4–2.0; 0.004) and cIMT (23.4 μm; 3.0–43.8; 0.024), whereas isolated borderline Q-waves were not.
Conclusion: Cardiovascular risk factors and measures of body fat, especially abdominal adiposity, were higher in participants with isolated borderline Q-waves, compared with no Q-waves, and highest in the non-isolated borderline Q-wave group. Non-isolated borderline Q-waves were associated with subclinical atherosclerosis and vascular stiffness. Future studies should investigate potential added value of borderline Q-waves in CVD prediction.

1. Introduction

The electrocardiogram (ECG) is commonly used in medical practice to assess the electrical activity in the heart, and abnormalities seen on an individual's ECG can have clinically relevant prognostic or diagnostic value for cardiovascular diseases (CVD) [1,2]. Large Q-waves on an ECG can be seen after a myocardial infarction, but can also be seen in apparently 'healthy' individuals, in whom they are thought to reflect silent ischemia [3]. Next to large Q-waves, smaller abnormalities, such as borderline Q-waves can also be found on the ECG of an individual with or without established cardiovascular disease (CVD), and may be associated with subclinical cardiovascular pathology. Without other ECG abnormalities present, these borderline Q-waves are considered isolated. However they can also be non-isolated, i.e. co-existing with other ECG abnormalities. Clinical characteristics and risk factor profiles of individuals with these borderline Q-waves are not fully elucidated, especially not in individuals without known CVD. In large cohort studies, it was observed that individuals with borderline Q-waves tended to be older, more often suffering from diabetes mellitus and hypertension and also seemed to have a worse kidney function than individuals

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[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

https://doi.org/10.1016/j.ijcard.2018.08.088
0167-5273/

without Q-waves [4–6]. Although these characteristics suggest an unfavorable metabolic profile, associations with body mass index (BMI) were not demonstrated [4,6]. Although previous studies did not observe an association between BMI and borderline Q-waves, other measures of body fat distribution, notably metabolically active visceral fat, might be associated with borderline Q-waves [7]. It is well-established that in particular abdominal adiposity is associated with CVD and mortality [7–9]. This association with abdominal adiposity could also be present for borderline Q-waves.

Furthermore, the clinical relevance of a borderline Q-wave, especially an isolated borderline Q-wave, in an individual without previously known CVD is not clear. The literature is inconclusive on the importance of borderline, and especially isolated borderline Q-waves in individuals free of established CVD, with some studies reporting increased cardiovascular risk in individuals with borderline Q-waves [4], some reporting no increased cardiovascular risk [5] and some studies reporting increased cardiovascular risk for non-isolated borderline Q-waves only [6].

Consequently, the present study was conducted with two aims. Firstly, we aimed to investigate clinical characteristics and measures of body fat distribution in individuals without Q-waves, with isolated borderline Q-waves and with non-isolated borderline Q-waves. Secondly, we aimed to investigate measures of subclinical atherosclerosis and vascular stiffness in individuals with isolated and non-isolated borderline Q-waves compared with individuals without Q-waves.

2. Methods

2.1. Study design and population

The Netherlands Epidemiology of Obesity (NEO) study is a population-based, prospective cohort study designed to investigate pathways that lead to obesity-related diseases, in which 6671 individuals were enrolled between 2008 and 2012. Men and women aged between 45 and 65 years with a self-reported BMI of 27 kg/m^2 or higher living in the area of greater Leiden (in the Netherlands) were eligible to participate in the NEO study. In addition, all inhabitants aged between 45 and 65 years from one municipality (Leiderdorp) were invited to join irrespective of their BMI, allowing for a reference distribution of BMI. Individuals were invited to a baseline visit at the NEO study center of the Leiden University Medical Center after an overnight fast. At the time of inclusion, individuals completed a screening form, which enquired about anything that might create a health risk or that might interfere with imaging (most notably metallic devices, claustrophobia, or a body circumference of >1.70 m). Of the participants without contraindications for MRI, approximately 35% were randomly selected to undergo MRI. Prior to the study visit, participants completed a questionnaire at home with demographic, lifestyle, and clinical information. At the study center all participants underwent an extensive physical examination, including anthropometry, blood sampling, and an ECG. The present analysis is a cross-sectional analysis using the baseline measurements of the NEO study. Participants using QT-prolonging drugs, participants with a history of myocardial infarction or angina pectoris and participants with an artificial pacemaker were excluded from the study population. Furthermore, participants with large Q-waves were excluded from the present study, because we were particularly interested in the clinical relevance of borderline Q-waves. Further details of the study design and population have been described in detail elsewhere [10]. The Medical Ethics Committee of the Leiden University Medical Center approved the design of the study and all participants gave their written informed consent.

2.2. Data collection

The ethnicity of participants was self-identified in eight categories on the questionnaire and then grouped into white (>95%) and other. Level of education was reported in 10 categories according to the Dutch education system and grouped as low or high education. Tobacco smoking was categorized into current smoker, former smoker, or never smoker. Alcohol consumption was reported using a food frequency questionnaire and calculated into grams/day [11]. Participants reported the frequency and duration of their physical activity in leisure time which was expressed in hours per week of metabolic equivalents (MET-h/week) using the Short Questionnaire to Assess Health-enhancing physical activity [12]. Participants were asked to bring all the medication they were currently using to the study visit. 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., IL, USA). Blood pressure was measured three times with 5 min rest between consecutive measurements. The mean systolic and diastolic blood pressure were calculated. Blood samples were drawn after an overnight fast of 10 h. Fasting glucose, triglyceride and high-density lipoprotein concentrations as well as creatinine concentration were measured with standard methods in the central clinical chemistry laboratory of the Leiden University Medical Center [10]. Glomerular filtration rate was estimated by using the CKD-EPI formula [13].

2.3. Electrocardiography

Q-waves were assessed using the Minnesota Coding System, a system to objectively describe electrocardiographic findings [14]. This system divides Q waves into three groups based on Minnesota Codes (MC); group 1 codes: 1.1.1 to 1.1.7, group 2 codes: 1.2.1 to 1.2.8 and group 3 codes: 1.3.1 to 1.3.8. In addition, the codes are applied to three groupings of leads namely, I, aVL, V6 (anterolateral), II, III, aVF (inferior) and V1-V5 (anterior). Not every code is present in every group of leads, e.g. 1-2-4 in the inferior leads is not present in the anterior leads and no codes are based on the waveforms in the aVR lead. Examples of different Q-waves (no abnormal Q-wave, borderline Q-wave and large Q-wave) are shown in Supplementary Fig. 1. In this study, borderline Q-waves were defined as group 2 and group 3 codes and large Q-waves as group 1 codes. Abnormal QRS axis was defined as QRS axis $<-30°$ or QRS axis $>+90°$, minor ST/T abnormalities as MC 4.3, 4.4, 5.3 of 5.4, major ST/T abnormalities as MC 4.1, 4.2, 5.1 or 5.2 and left ventricular hypertrophy as MC 3.1 or 3.2. Percentages of ECG abnormalities in participants without Q-waves and with borderline Q-waves were calculated and the study population was divided in the three groups, namely participants without Q-waves, participants with isolated borderline Q-waves and participants with non-isolated borderline Q-waves. Isolated borderline Q-waves were defined as borderline Q-wave with normal QRS axis, no minor ST/T abnormality, no major ST/T abnormality and no left ventricular hypertrophy and non-isolated borderline Q-waves were defined as borderline Q-waves plus at least one of these additional abnormalities.

2.4. Measures of body fat

Height and weight were measured without shoes and 1 kg was subtracted from the weight to correct for 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. Hip circumference was measured at the maximum circumference of the buttocks. Waist-hip-ratio (WHR) was calculated by dividing the waist circumference by the hip circumference. With a bio-impedance device (TBF-310, Tanita International Division, UK) total body fat (TBF) was estimated. Abdominal subcutaneous adipose tissue (aSAT) and visceral adipose tissue (VAT) were assessed by MR imaging (1.5 Tesla MR imaging, Philips Medical Systems) using a turbo spin echo imaging protocol. 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 three slices was used.

2.5. Measures of subclinical atherosclerosis and vascular stiffness

Carotid intima-media thickness (cIMT) was assessed by ultrasonography of the far wall of the left and right common carotid arteries along a 15 mm long section 10 mm proximal of the bifurcation in recumbent position. A 7.5–10 MHz linear-array transducer (Art.Lab version 2.1, Esaote, Maastricht, The Netherlands) in B-mode setting was used to visualize the distal common carotid arteries and a wall track system was used to detect the lumen-intima and media-adventitia boundaries. The cIMT was measured in three predefined angles per side (180, 135 and 90° for the right common carotid artery and 180, 225 and 270° for the left common carotid artery) during six heartbeats. Mean cIMT was calculated for each individual by averaging all 36 cIMT measurements within each individual. Velocity-encoded magnetic resonance imaging was used for assessment of pulse wave velocity (PWV) of the aorta. The heart was imaged in short-axis view using an ECG-triggered balanced turbo-field-echo sequence. Data were analyzed using in-house software (MASS and FLOW; Leiden University Medical Center, Leiden, the Netherlands).

2.6. Statistical analysis

In the NEO study, participants with a BMI of 27 kg/m^2 or higher were oversampled. To correctly represent baseline associations in the general population [15] adjustments for the oversampling of individuals with a BMI 27 kg/m2 were made. This was done by weighting all participants towards the BMI distribution of participants from the Leiderdorp municipality [16], whose BMI distribution was similar to the BMI distribution of the general Dutch population [17]. All results are based on weighted analysis. Consequently, the results are considered to apply to a population-based study without oversampling of participants with a BMI ≥ 27 kg/m^2.

Baseline characteristics are presented as mean (SD), median (25th, 75th percentiles) or as percentage, for the three specified groups. Next, means (se) of measures of body fat were calculated for each group. Differences with 95% confidence intervals were estimated for the groups with Q-waves compared to the group without Q-waves using linear regression analysis. If differences in BMI, TBF or aSAT were observed between groups, these were adjusted for VAT and if differences in waist circumference or VAT were observed, these were adjusted for TBF. Finally, subclinical atherosclerosis and vascular stiffness were investigated in the three groups and again, differences with 95% confidence intervals were estimated compared with the group without Q-waves. No adjustment for confounding was made since our two study aims were mostly of a descriptive nature. Data were analyzed using STATA (Statacorp, College Station, Texas, USA), version 14.

3. Results

3.1. Study groups

681 participants using QT-prolonging drugs were excluded. Similarly, 129 participants with a history of myocardial infarction, 61 with angina pectoris and 6 participants with an artificial pacemaker were excluded. Also, 48 participants with large Q-waves (MC 1.1.x) were excluded. The total number of participants included in this study was 5746, of which 43% were men. Participants were then divided in participants without Q-waves, with isolated borderline Q-waves and with non-isolated borderline Q-waves. Percentages of other ECG abnormalities in participants without and with borderline Q-waves are shown in Fig. 1. Other ECG abnormalities were more prevalent among participants with borderline compared with no Q-waves. In 16% of participants without Q-waves and in 27% of participants with borderline Q-waves, at least one of the other ECG abnormalities was present. Of the study population, 93.7% did not have Q-waves, 4.6% had isolated borderline Q-waves and 1.7% had non-isolated borderline Q-waves.

3.2. Baseline characteristics

Baseline characteristics of the three groups (no Q-waves, isolated borderline Q-waves and non-isolated borderline Q-waves) are presented in Table 1. Several risk factors were, compared with participants without Q-waves, higher in participants with isolated borderline Q-waves and highest in participants with non-isolated borderline, namely age (55.6, 55.7 and 59.0 years respectively), percentage of men (43, 52 and 61% respectively), systolic (129.9, 131.1 and 137.5 mmHg respectively) as well as diastolic blood pressure (83.1, 83.1 and 86.9 mmHg respectively), use of antihypertensive therapy (20, 23 and 32% respectively), fasting glucose (5.4, 5.6 and 5.7 mmol/l respectively), triglycerides (1.0, 1.0 and 1.2 mmol/l respectively) and use of lipid lowering therapy (8, 13 and 14% respectively). Furthermore, participants with non-isolated borderline Q-waves were less often highly educated (47, 51 and 36% respectively) and had the highest alcohol intake out of the three groups (9.9, 8.8 and 19.2 g/day respectively). No relevant differences were observed in triglyceride, LDL-cholesterol or HDL-cholesterol concentrations or estimated glomerular filtration rate between the groups.

3.3. Borderline Q-waves and measures of body fat

Table 2 reports measures of body fat in the three groups. For measures of body fat, participants with isolated borderline Q-waves had a higher BMI (difference: 1.0 kg/m^2; 95% confidence interval: 0.3–1.7; p-value: 0.006), higher waist circumference (3.4 cm; 1.0–5.8; 0.005), and more VAT (21.9 cm^2; 7.4–36.3; 0.003) compared with participants without Q-waves. The difference of measures of body fat for participants with non-isolated borderline Q-waves compared with participants without Q-waves was even larger (BMI: 1.7 kg/m^2; 0.7–2.8; 0.001; waist circumference: 5.5 cm; 2.2–8.8; 0.001; VAT: 29.3; 7.8–50.7; 0.007; WHR: 0.03; 0.01–0.05; 0.001). There were no differences between participants with isolated or non-isolated borderline Q-waves and participants without Q-waves for TBF and aSAT. Furthermore, the difference in BMI between groups disappeared after adjusting for VAT (isolated borderline Q-waves compared with no Q-waves: −0.2 kg/m^2; −0.9–0.6; 0.620 and non-isolated borderline Q-waves compared with no Q-waves: 1.1 kg/m^2; −0.3–2.4; 0.134), while the difference in waist circumference and VAT between groups remained after adjusting for TBF.

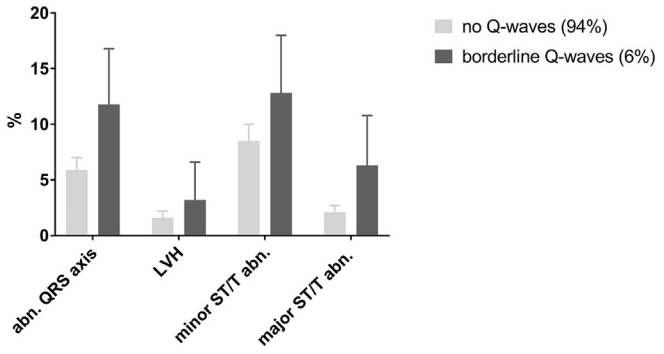

Fig. 1. ECG abnormalities in participants without and with borderline Q-waves. Data are presented as percentages and 95% confidence intervals. Results are based on analyses weighted towards the body mass index distribution of the general population (n = 5746). Abnormal QRS axis: <−30/>+90; LVH: MC 3.1, 3.2; minor ST/T abnormality: MC 4.3, 4.4, 5.3, 5.4; major ST/T abnormality: MC 4.1, 4.2, 5.1, 5.2.

3.4. Borderline Q-waves and subclinical atherosclerosis and vascular stiffness

In Table 3 measures of subclinical atherosclerosis and vascular stiffness are shown in the three groups. The differences between participants with isolated borderline Q-waves and participants without Q-waves were small for both PWV (−0.2 m/s; −0.5–0.1; 0.139) as for cIMT (2.7 μm; −11.2–16.5; 0.704). However, participants with non-isolated borderline Q-waves had a higher PWV (difference: 1.2 m/s; 95%CI: 0.4–2.0; 0.004) as well as higher cIMT (23.4 μm; 3.0–43.8; 0.024) compared with participants without Q-waves.

4. Discussion

In this cross-sectional analysis of 5746 participants of the NEO study, we observed, compared with participants without Q-waves, a worse cardiovascular risk profile in participants with isolated borderline Q-waves, that was even worse in participants with non-isolated borderline Q-waves. Participants with non-isolated borderline Q-waves, compared with participants without Q-waves were older, more often male, had a higher alcohol intake and also higher blood pressure and fasting glucose concentrations. For participants with isolated borderline Q-waves, compared with participants without Q-waves, cardiovascular risk factors were more often present, however, less evident than for participants with non-isolated borderline Q-waves. This association between cardiovascular risk factors and borderline Q-waves is in line with literature, although reports vary in the exact risk factors associated with borderline Q-waves [4–6]. Borderline Q-waves could be the result of scar tissue, in which no electrical activity is present, representing damage to the heart tissue.

We observed higher values of several measures of body fat (BMI, waist circumference, VAT and WHR) in participants with isolated borderline Q-waves and the highest values in participants with non-isolated borderline Q-waves, compared with participants without Q-waves. No differences were observed for TBF or aSAT. Two previous studies report no differences in BMI between individuals with borderline Q-waves and without [4,6]. In the general population-based 4th Copenhagen City Heart Study mean BMI in 5267 individuals without Q-waves was 25.7 kg/m^2, whereas this was 26.3 kg/m^2 in 114 individuals with Q-waves (defined as MC 1.1.X to 1.3.X) [4]. Despite this difference not being statistically significant, similar to our study, individuals with Q-waves have a higher BMI than individuals without Q-waves. Furthermore, a study in the general Japanese population did not observe differences in BMI between individuals without abnormal Q-waves (men: 22.5 kg/m^2, women: 22.8 kg/m^2), individuals with mild abnormal Q-waves (defined as MC 1-3-X; men: 22.9 kg/m^2, women: 23.0 kg/m^2) and individuals with moderate/severe abnormal Q-waves (defined as MC 1-2-X or 1-1-X; men: 22.1 kg/m^2, women: 24.4 kg/m^2) [6]. In this Japanese population the BMI of individuals is generally lower than the BMI of Dutch individuals included in the NEO study, which makes it difficult to compare these results to our study. Our results are plausible,

Table 1
Characteristics of 5746 participants aged 45 to 65 years from the Netherlands Epidemiology of Obesity study.

	No Q-waves, 93.7%	Isolated borderline Q-waves, 4.6%	Non-isolated borderline Q-waves, 1.7%
Age, years	55.6 (6.0)	55.7 (6.6)	59.0 (6.5)
Sex, men, %	43	52	61
Ethnicity, white, %	95	99	99
Education level, high, %	47	51	36
Alcohol intake, g/day	9.9 (2.9–21.1)	8.8 (3.2–20.8)	19.2 (7.7–25.0)
Physical activity (MET-hour/week)	30.0 (16.0–50.5)	26.9 (14.0–45.5)	29.0 (17.8–52.0)
Smoking, %			
Never	39	39	22
Former	45	44	68
Current	16	16	10
Body mass index, kg/m^2	25.6 (23.1–28.1)	26.7 (23.7–29.0)	27.4 (24.9–29.9)
Systolic blood pressure, mmHg	129.9 (16.9)	131.1 (18.5)	137.5 (20.3)
Diastolic blood pressure, mmHg	83.1 (10.2)	83.1 (11.6)	86.9 (11.4)
Use of antihypertensive therapy, %	20	23	32
Fasting plasma glucose, mmol/l	5.4 (0.9)	5.6 (1.2)	5.7 (1.3)
Diabetes mellitus, %	5	10	7
Triglycerides, mmol/l	1.0 (0.7–1.4)	1.0 (0.7–1.7)	1.2 (0.7–1.8)
LDL, mmol/l	3.6 (0.9)	3.5 (1.1)	3.6 (1.2)
HDL, mmol/l	1.6 (0.5)	1.5 (0.5)	1.5 (0.6)
Use of lipid lowering therapy, %	8	13	14
eGFR, ml/min/1.73m^2	86.3 (12.3)	86.6 (12.5)	84.9 (13.5)

eGFR, estimated glomerular filtration rate (CKD-EPI); HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein; MET, metabolic equivalent of task during leisure time.
Data are presented as mean(SD), median(25th, 75th percentiles), or percentages.
Results were based on analyses weighted towards the BMI distribution of the general population.
Borderline Q-wave: Minnesota codes 1.2.X, 1.3.X.
No Q-waves, n = 5294; isolated borderline Q-waves, n = 317; non-isolated borderline Q-waves, n = 135.

since overweight/obesity is an important cardiovascular risk factor. Since both waist circumference and VAT are measures of abdominal adiposity and no differences were observed for TBF between groups, we also investigated whether differences in BMI between groups were mainly due to differences in abdominal adiposity. Indeed, the difference in BMI between groups disappeared after adjustment for waist circumference or VAT, indicating that differences in abdominal adiposity between the three groups are also responsible for the observed BMI difference.

Finally, we observed that PWV and cIMT, measures of subclinical atherosclerosis and vascular stiffness, were higher in participants with non-isolated borderline Q-waves than in participants without Q-waves, but that this was less clear for isolated borderline Q-waves. This association of non-isolated borderline Q-waves with more subclinical atherosclerosis and vascular stiffness is in line with the increased prevalence of cardiovascular risk factors, the presence of other ECG abnormalities, and more abdominal adiposity.

The fact that borderline Q-waves are associated with specifically higher amounts of VAT gives more insight into the cardiovascular risk associated with these borderline Q-waves. Several underlying pathways are thought to be involved in these associations. Visceral adipocytes have high lipolytic activity and cause an increased amount of free fatty acids to be released into the portal circulation, leading to hepatic insulin resistance and adverse cardiovascular effects [18–20]. Furthermore, VAT is a metabolically active tissue, secreting several cytokines, chemokines and hormones, and has been linked to several unfavorable conditions, such as insulin resistance, impaired lipid and glucose metabolism, CVD and mortality [21–24]. More VAT is also accompanied by higher concentrations of pro-inflammatory factors, such as interleukin 6, tumor necrosis factor-α and C-reactive protein, that can enhance a local pro-inflammatory environment, but also can have more systemic effects, promoting atherosclerotic disease and arterial stiffness [7,25–30]. Also, associations between VAT and more subclinical atherosclerosis and vascular stiffness have been shown in the literature and abdominal adiposity has been described as a stronger risk factor for subclinical atherosclerosis and vascular stiffness than overall adiposity [31–33].

In current practice, borderline isolated Q-waves are often considered as non-pathological. However, the appearance of a borderline isolated Q-wave on the ECG of an individual without known CVD could represent electrical damage, an unrecognized myocardial infarction, and be associated with a worse prognosis [34]. Especially the presence of a 1.2 coded borderline Q-wave together with T wave changes, could be the result of an unrecognized myocardial infarction, which was associated with poor prognosis previously [35,36]. The borderline Q-wave could also just be a positional variant, without any prognostic consequences, which makes clinical decision making particularly complicated. Borderline Q-waves could possibly improve current risk prediction scores for CVD. In 6991 individuals from the Copenhagen Heart Study aged 65 years and over, ECG changes among which

Table 2
Relations between borderline Q-waves and measures of body fat.

	No Q-waves [1], 93.7%	Isolated borderline Q-waves [2], 4.6%	Non-isolated borderline Q-waves [3], 1.7%	Difference 2 vs 1 (95%CI)	p-value*	Difference 3 vs 1 (95%CI)	p-value**
BMI, kg/m^2	26.1 (0.1)	27.1 (0.4)	27.8 (0.5)	1.0 (0.3–1.7)	0.006	1.7 (0.7–2.8)	0.001
TBF, %	31.5 (0.2)	31.6 (0.7)	31.3 (1.2)	0.2 (−1.3–1.6)	0.828	−0.2 (−2.6–2.1)	0.855
aSAT, cm^2	232.0 (2.5)	238.9 (12.8)	254.0 (21.8)	7.0 (−18.5–32.5)	0.593	22.1 (−21.0–65.1)	0.315
Waist circ., cm	91.4 (0.2)	94.8 (1.2)	96.9 (1.7)	3.4 (1.0–5.8)	0.005	5.5 (2.2–8.8)	0.001
VAT, cm^2	86.6 (1.5)	108.5 (7.2)	115.9 (10.8)	21.9 (7.4–36.3)	0.003	29.3 (7.8–50.7)	0.007
WHR	0.88 (0.00)	0.90 (0.01)	0.92 (0.01)	0.01 (−0.00–0.03)	0.098	0.03 (0.01–0.05)	0.001

aSAT, abdominal subcutaneous adipose tissue; BMI, Body Mass Index; TBF, total body fat; VAT, visceral adipose tissue; Waist circ., waist circumference; WHR, waist:hip ratio.
Data are presented as mean (se) and difference (95% confidence interval). Results are based on linear regression analyses weighted towards the BMI distribution of the general population.
For VAT and aSAT: no Q-waves n = 2099; isolated borderline Q-waves n = 121; non-isolated borderline Q-waves n = 50.
* 2 vs 1, ** 3vs 1.

Table 3
Relations between borderline Q-waves and subclinical atherosclerosis and vascular stiffness.

	No Q-waves [1], 93.7%	Isolated borderline Q-waves [2], 4.6%	Non-isolated borderline Q-waves [3], 1.7%	Difference 2 vs 1 (95%CI)	p-value *	Difference 3 vs 1 (95%CI)	p-value **
PWV, m/s	6.6 (0.0)	6.3 (0.1)	7.8 (0.4)	−0.2 (−0.5–0.1)	0.139	1.2 (0.4–2.0)	0.004
cIMT, μm	614.7 (1.9)	617.4 (6.8)	638.1 (10.2)	2.7 (−11.2–16.5)	0.704	23.4 (3.0–43.8)	0.024

cIMT, carotid intima media thickness; PWV, pulse wave velocity.
Data are presented as mean (se) or difference (95% confidence interval) Results are based on linear regression analyses weighted towards the BMI distribution of the general population.
For PWV: no Q-waves n = 2032; borderline isolated Q-waves n = 119; non-isolated borderline Q-waves n = 45.
For cIMT: no Q-waves n = 5233; borderline isolated Q-waves n = 313; non-isolated borderline Q-waves n = 135.
* 2 vs 1, ** 3vs 1.

abnormal Q-waves, showed added value in the prediction of fatal and non-fatal cardiovascular events [37]. Future studies should further elucidate the role of borderline Q-waves in cardiovascular risk prediction. In this study we observed a worse cardiovascular risk factor profile as well as higher waist circumference and VAT in participants with isolated borderline Q-waves, which was even more pronounced in participants with non-isolated borderline Q-waves, compared with participants without Q-waves. We also observed non-isolated, but not isolated borderline Q-waves to be associated with more subclinical atherosclerosis and vascular stiffness, compared with no Q-waves. Therefore it would be of great interest to investigate the association of borderline Q-waves with cardiovascular risk within certain subgroups of individuals with increased cardiometabolic risk. Future studies should be investigated whether it might be indicated to further investigate borderline Q-waves when found on an individuals' ECG, especially in individuals with increased waist circumference or VAT, who already are at higher cardiovascular risk.

4.1. Strengths and limitations

The largest strength of this study is the extensive phenotyping of a large number of participants, which made it possible to investigate several different measures of body fat and subclinical atherosclerosis and vascular stiffness in relation to borderline Q-waves. There are also some limitations of this study that need to be considered. In this study, only 4.6% of participants displayed isolated borderline Q-waves on the ECG and 1.7% of participants non-isolated borderline Q-waves [4,6]. Subgroups of participants with increased cardiovascular risk, or increased waist circumference or VAT were too small and therefore we did not have enough statistical power to investigate the association of borderline Q-waves with subclinical atherosclerosis and vascular stiffness within subgroups. However, the prevalence of borderline Q-waves observed in this present study is similar to the prevalence in other population-based studies [4,6]. Also, it should be noted that coding ECGs according to the Minnesota Coding system is not error-free. Measurement error is likely to be also present in this study, e.g. if wrongly measured, a 1.2 code could actually be a 1.1 or 1.3 code.

5. Conclusion

The results of this study show an unfavorable cardiometabolic risk factor profile in participants with isolated borderline Q-waves that is even more unfavorable in participants with non-isolated borderline Q-waves. Furthermore, measures of abdominal adiposity, namely waist circumference and VAT, were higher in participants with isolated borderline Q-waves and highest in participants with non-isolated borderline Q-waves, compared with participants without Q-waves. Also, non-isolated borderline Q-waves were associated with more subclinical atherosclerosis and vascular stiffness, results for isolated borderline Q-waves are less clear, despite the less favorable cardiometabolic risk factor profile.

Borderline Q-waves can be identified on an easily obtainable ECG, which makes them a possibly useful addition to cardiovascular risk assessment. The possible added value of borderline Q-waves to current risk prediction scores for CVD should be further investigated in future studies. Furthermore, the prognostic significance of borderline Q-waves within subgroups of individuals with increased cardiovascular risk or with more body fat could be investigated in longitudinal studies.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.08.088.

Funding

This work was supported by the participating Departments; the Division and the Board of Directors of the Leiden University Medical Centre, and by the Leiden University, Research Profile Area 'Vascular and Regenerative Medicine'.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Acknowledgements

We express our gratitude to all individuals who participate in the Netherlands Epidemiology in Obesity study. We are grateful to all participating general practitioners for inviting eligible participants. We furthermore thank P.R. van Beelen and all research nurses for collecting the data, P.J. Noordijk and her team for sample handling and storage, and I. de Jonge, MSc for data management of the NEO study.

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