Electrocardiographic predictors of cardiovascular events in patients at high cardiovascular risk: a multicenter study

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Abstract

Background There are limited data on the prevalence of electrocardiographic (ECG) abnormalities, and their value for predicting a major adverse cardiovascular event (MACE) in patients at high cardiovascular risk. This study aimed to determine the prevalence of ECG abnormalities in patients at high risk for cardiovascular events, and to identify ECG abnormalities that significantly predict MACE.

Methods Patients aged ≥ 45 years with established atherosclerotic disease (EAD) were consecutively enrolled from the outpatient clinics of the six participating hospitals during April 2011 to March 2014. The following data were collected: demographic data, cardiovascular risk factors, history of cardiovascular event, physical examination, ECG and medications. ECG was analyzed using Minnesota Code criteria. MACE included cardiovascular death, non-fatal myocardial infarction, and hospitalization due to unstable angina or heart failure.

Results A total of 2009 patients were included, 1048 patients (52.2%) had established EAD, and 961 patients (47.8%) had multiple risk factors (MRF). ECG abnormalities included atrial fibrillation (6.7%), premature ventricular contraction (5.4%), pathological Q-wave (Q/QS) (21.3%), T-wave inversion (20.0%), intraventricular ventricular conduction delay (IVCD) (7.3%), left ventricular hypertrophy (LVH) (12.2%), and AV block (12.5%). MACE occurred in 88 patients (4.4%). Independent predictors of MACE were chronic kidney disease, EAD, and the presence of atrial fibrillation, Q/QS, IVCD or LVH by ECG.

Conclusions A high prevalence of ECG abnormalities was found. The prevalence of ECG abnormalities was high even among those with risk factors without documented cardiovascular disease.

Keywords: Cardiovascular events; Electrocardiographic; High cardiovascular risk; Predictors

1 Introduction

Atherosclerosis is a highly prevalent condition that is the leading cause of death worldwide.[1] Although the trend of disease control seems to be better in developed countries, the burden of disease is increasing in developing countries[2] like Thailand.[3] The REduction of Atherothrombosis for Continued Health (REACH) registry revealed coronary artery disease (CAD), cerebrovascular disease (CVD), and peripheral arterial disease (PAD) to be common manifestations of atherosclerosis.[4] The prevalence of hypertension, diabetes, and dyslipidemia in the REACH registry was 82%, 44%, and 72%, respectively.[4] Although a decline in cardiovascular disease-related mortality was reported, the morbidity and mortality rates remain unacceptably high.[5] The prevalence of many cardiovascular risk factors is increasing, especially in developing countries.[6] The effect of the revascularization has only minimally influenced the observed reduction in cardiovascular mortality.[7,8] It cannot be proven that revascularization treatment plays a major role in reducing mortality among patients with stable disease.[9,10] Therefore, early detection of disease is essential. Electrocardiography (ECG) is a tool that can be used to study electrical abnormalities in patients with cardiac disease. Certain ECG abnormalities can be used to predict adverse events in patients with documented disease, and among those without overt disease.[11,12]

Patients at high risk for cardiovascular events are also at high risk for developing ECG abnormalities that may develop prior to the onset of serious complications.[13] Moreover, patients with risk factors that are well-controlled may have a lower probability of developing complications than...
patients whose risk factors are poorly controlled. The identification of factors that independently predict a major adverse cardiovascular event (MACE) would facilitate earlier diagnosis and treatment. However, whether the early detection of disease and earlier treatment would improve the outcome of patients needed to be proven.

Accordingly, the aims of this study were to determine the prevalence of ECG abnormalities in patients at high risk for cardiovascular events, and to identify ECG abnormalities that significantly predict a MACE.

2 Methods

The Cohort Of patients with high Risk for cardiovascular Events (CORE) registry is a prospective, multicenter, observational, longitudinal study of Thai patients with high atherosclerotic risk. Investigators in this registry include internists, cardiologists, neurologists, endocrinologists, nephrologists, and vascular surgeons. Data was collected from six centers that are located in two of Thailand’s five regions. Participating centers included four large university-based teaching hospitals, and two large provincial hospitals. The protocol for this study was approved for each participating center by the Joint Research Ethics Committee, and by the Ethics Committee of the Ministry of Public Health. Signed informed consent was obtained from all patients.

2.1 Study population

Patients aged 45 years or older with established atherosclerotic disease (EAD), which is defined as CAD, CVD, or PAD, or having at least three atherosclerosis risk factors [multiple risk factors (MRF)], were consecutively enrolled from the outpatient clinics of the six participating hospitals during the April 2011 to March 2014 enrollment period. Only patients with available ECG data during six months prior to study enrollment were included in this study. Patients with cardiac implantable electronic devices (CIED) were excluded from the analysis. Documented CAD was defined as satisfying one or more of the following criteria: stable angina with documented CAD, history of unstable angina with documented CAD, history of percutaneous coronary intervention (PCI), history of coronary artery bypass graft (CABG) surgery, or previous myocardial infarction (MI). Documented CVD was defined as hospitalization with a diagnosis of transient ischemic attack or ischemic stroke. Documented PAD was defined as meeting one or both of the following criteria: current intermittent claudication with ankle-brachial index (ABI) of less than 0.9 and/or previous history of surgery or intervention, such as angioplasty, stenting, peripheral arterial bypass graft (PABG), or other vascular intervention, including amputation. Atherosclerosis risk factors consisted of those that were documented in the medical record and/or those for which patients were receiving treatment at the time of study enrollment. Those risk factors are listed, as follows: diabetes mellitus (DM); hypertension [systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg or current treatment with antihypertensive agents]; dyslipidemia, which could be hypercholesterolemia (total cholesterol > 200 mg/dL or LDL-cholesterol > 130 mg/dL) or hypertriglyceridemia (> 150 mg/dL) or low HDL cholesterol (< 40 mg/dL) or current treatment with lipid modifying agents; chronic kidney disease (CKD) defined as the presence of proteinuria or estimated glomerular filtration rate (GFR) less than 60 mL/min; current smoker of at least one cigarette per day; men aged 55 years or older, or women aged 65 years or older; and family history of premature atherosclerosis.

Patients with one or more of the following conditions were excluded: acute atherosclerotic event within three months, large aortic aneurysm indicated for surgery, current participation in a blinded clinical trial, limited life expectancy due to a non-cardiovascular condition, such as cancer or documented human immunodeficiency virus (HIV) infection, and/or those who could not commit (for any reason) to returning for all follow-up visits.

2.2 Data collection

Data collected at baseline included height, weight, waist circumference, seated SBP and DBP, ankle brachial index (ABI), and medications. Patients were reevaluated at 6, 12, 24, 36, 48, and 60 months. Clinical data and cardiovascular events were prospectively recorded and analyzed. MACE was defined as a composite of cardiovascular death, MI, stroke, unstable angina requiring hospital admission, and heart failure hospitalization. In this study, only subjects who had complete one-year visit data were analyzed.

Data were locally collected using a standardized case report form. Patient data was then forwarded to the data management group of the Medical Research Network of the Consortium of Thai Medical Schools (MedResNet). Data was checked for quality and completeness prior to data analysis. Random site monitoring was performed annually.

2.3 ECG data collection and analysis

Twelve-lead ECG data that was in the medical record within six months prior to enrollment in the CORE registry was collected and recorded. ECG was analyzed using Minnesota Classification of the ECG for population studies. Based on Minnesota Code ECG classification, the following
ECG data was recorded in the case record form: abnormal rhythm, such as atrial fibrillation/atrial flutter (AF/AFL) and premature ventricular contraction (PVC); Q or QS wave abnormality (Q/QS) (code 1.1, 1.2); T-wave inversion (TWI) (code 5.1, 5.2); intraventricular conduction delay (IVCD), including left bundle branch block (LBBB), right bundle branch block (RBBB), and non-specific IVCD (code 7.1, 7.2, and 7.4); left ventricular hypertrophy (LVH) by either Sokolow-Lyon criteria\(^\text{[10]}\) or Cornell criteria\(^\text{[17]}\); and atrioventricular conduction delay/block (AVB), including 1\(^{\text{st}}\), 2\(^{\text{nd}}\), and 3\(^{\text{rd}}\) degree AV block (code 6.1-6.3).

For Q wave, deflection should be at least 0.1 mV (1 mm in amplitude). Q/QS was defined as follows: (1) anterolateral site (I, aVL, and V6), Q/R amplitude ratio \(\geq \frac{1}{3}\) plus Q duration \(\geq 0.03\) s, Q duration \(\geq 0.04\) s in lead I or V6, Q duration \(\geq 0.04\) s plus R amplitude \(\geq 3\) mm in lead aVL, Q/R amplitude ratio \(\geq \frac{1}{3}\) plus Q duration \(\geq 0.02\) s and \(< 0.03\) s in lead I or V6, Q duration \(\geq 0.03\) s and \(< 0.04\) s in lead I or V6, or QS pattern in lead I in the absence of LBBB; (2) inferior (posterior) site (leads II, III, aVF), Q/R amplitude ratio \(\geq \frac{1}{3}\) plus Q duration \(\geq 0.03\) s in lead II, Q duration \(\geq 0.04\) s in lead II, Q duration \(\geq 0.05\) s in lead III, plus a Q-wave amplitude \(\geq 1.0\) mm in lead aVF, Q duration \(\geq 0.05\) s in lead aVF, Q/R amplitude ratio \(\geq \frac{1}{3}\) plus Q duration \(\geq 0.02\) s and \(< 0.03\) s in lead II, Q duration \(\geq 0.03\) s and \(< 0.04\) s in lead II, QS pattern in lead II in the absence of LBBB, Q duration \(\geq 0.04\) s and \(< 0.05\) s in lead III plus a Q-wave \(\geq 1.0\) mm amplitude in lead aVF, Q duration \(\geq 0.04\) s and \(< 0.05\) s, in lead aVF, or Q amplitude \(\geq 5.0\) mm in lead III or aVF; and (3) anterior site (leads V1-V5), Q/R amplitude ratio \(\geq \frac{1}{3}\), plus Q duration \(\geq 0.03\) s in any of leads V2-V5, Q duration \(\geq 0.04\) s in any of leads V1-V5, QS pattern when initial R wave is present in adjacent lead to the right on the chest in any of leads V2-V6, QS pattern in all of leads V1-V4 or V1-V5, Q/R amplitude ratio \(\geq \frac{1}{3}\) plus Q duration \(\geq 0.02\) s and \(< 0.03\) s, in any of leads V2-V5, Q duration \(\geq 0.03\) s and \(< 0.04\) s in any of leads V2-V5, or QS pattern in all leads V1-V3 in the absence of LBBB.

T-wave inversion was defined as follows: (1) anterolateral site (I, aVL, and V6), T amplitude negative 5.0 mm or more in either of leads I, V6, or in lead aVL; (2) inferior (posterior) site (leads II, III, aVF), T amplitude negative 5.0 mm or more in lead II or in lead aVF when QRS is mainly upright; and (3) anterior site (leads V1-V5), T amplitude negative 5.0 mm or more in any of leads V2-V5.\(^{[15]}\)

### 2.4 Statistical analysis

All statistical analyses were performed using SPSS Statistics version 20 (SPSS, Inc., Chicago, IL, USA). Demographic and clinical data were summarized using descriptive statistics. Continuous data are presented as mean \(\pm\) SD, and categorical data are given as count and percentage. Continuous data were compared using Student’s t-test for unpaired data, and categorical data were compared using chi-square test. Baseline characteristics were compared between patients with EAD and patients with MRF. Univariate and multivariate analyses were performed to identify ECG abnormalities significantly associated with a future MACE. A P-value of less than 0.05 was considered statistically significant.

### 3 Results

A total of 2009 patients were included. The average age of patients was 66.5 \(\pm\) 9.6 years, and 1068 patients (53.2%) were male. Of all included patients, 1048 patients (52.2%) had EAD, and 961 patients (47.8%) had MRF. Baseline demographic and clinical characteristics, medications, and ECG findings compared between EAD patients and MRF patients are shown in Table 1. Patients with EAD were more likely to be male and to be taking cardiovascular medication than MRF patients, and MRF patients had more cardiovascular risk factors than EAD patients. The prevalence of ECG abnormalities was significantly higher in patients with EAD compared to those with MRF for AF/AFL, PVC, Q/QS, TWI, LVH, and AVB. The overall prevalence of ECG abnormalities was 6.7% for AF/AFL, 5.4% for PVC, 21.3% for Q/QS, 20.0% for TWI, 7.3% for bundle branch block (BBB) or IVCD, 12.2% for LVH, and 12.5% for AVB. Among 135 patients with AF/AFL, 129 patients were AF and 6 patients were AFL.

Among the 524 patients with history of MI, ECG showed Q/QS in 194 patients (37.0%). Among the 427 patients with Q/QS in ECG, only 194 patients (45.4%) had history of MI.

By the one-year follow-up, 88 patients (4.4%) had developed MACE, including cardiovascular death in 11 patients (0.5%), MI in 21 patients (1.0%), stroke in 14 patients (0.7%), hospitalization due to unstable angina in 14 patients (0.7%), and hospitalization due to heart failure (HF) in 41 patients (2.0%). Table 2 shows comparisons of variables in patients with and without MACE. Patients with MACE had a significantly older, being male, having CKD, lower body mass index, EAD, using antiplatelet, statin, and beta-blocker. ECG abnormalities that had a higher prevalence in patients with MACE were AF/AFL, Q/QS, BBB or IVCD, and LVH.

Univariate and multivariate analysis based on variables with a P-value < 0.2 from univariate analysis are shown in Table 3. Independent predictors of MACE were CKD, EAD, and the presence of AF/AFL, Q/QS, BBB or IVCD, or LVH.
Table 1. Baseline demographic and clinical characteristics, medications, and ECG findings compared between patients with EAD and patients with MRF.

| Characteristics                              | Total (n = 2009) | EAD (n = 1048) | MRF (n = 961) | P-value  |
|----------------------------------------------|------------------|---------------|---------------|----------|
| Age, yrs                                     | 66.51 ± 9.7      | 67.0 ± 9.9    | 66.0 ± 9.5    | 0.021*   |
| Male gender                                  | 1068 (53.2%)     | 644 (61.5%)   | 424 (44.1%)   | < 0.001* |
| Male > 55 yrs or female > 65 yrs             | 1502 (74.8%)     | 820 (78.2%)   | 682 (71.0%)   | < 0.001* |
| Diabetes                                     | 1148 (57.1%)     | 456 (43.5%)   | 692 (72.0%)   | < 0.001* |
| Hypertension                                 | 1778 (88.5%)     | 868 (82.8%)   | 910 (94.7%)   | < 0.001* |
| Dyslipidemia                                  | 1782 (88.7%)     | 869 (82.9%)   | 913 (95.0%)   | < 0.001* |
| Current smoker                               | 63 (3.1%)        | 43 (4.1%)     | 20 (2.1%)     | 0.090*   |
| Family history of premature atherothrombosis | 178 (8.9%)       | 98 (9.4%)     | 80 (8.3%)     | 0.419    |
| CKD                                          | 504 (25.1%)      | 257 (24.5%)   | 247 (25.7%)   | 0.542    |
| WC, cm                                       | 88.7 ± 11.5      | 88.6 ± 11.5   | 88.8 ± 11.4   | 0.710    |
| BMI, kg/m²                                    | 25.2 ± 4.4       | 24.8 ± 4.2    | 25.7 ± 4.6    | < 0.001* |
| Obese or overweight                          | 905 (45.0%)      | 532 (44.4%)   | 473 (50.8%)   | 0.006*   |
| Medications                                  |                  |               |               |          |
| Antiplatelet                                  | 1504 (74.9%)     | 1027 (98.0%)  | 477 (49.6%)   | < 0.001* |
| Statin                                       | 1809 (90.0%)     | 973 (92.8%)   | 836 (87.0%)   | < 0.001* |
| Beta-blocker                                  | 1162 (57.8%)     | 832 (79.4%)   | 330 (34.3%)   | < 0.001* |
| ACEI                                         | 686 (34.1%)      | 398 (38.0%)   | 288 (30.0%)   | < 0.001* |
| ARB                                          | 648 (32.3%)      | 288 (27.5%)   | 360 (37.5%)   | < 0.001* |
| CCB                                          | 904 (45.0%)      | 359 (34.3%)   | 545 (56.7%)   | < 0.001* |
| Diuretic                                     | 616 (30.7%)      | 312 (29.8%)   | 304 (31.6%)   | 0.366    |
| Antidiabetic agents                          | 954 (47.5%)      | 357 (34.1%)   | 597 (62.1%)   | < 0.001* |
| ECG findings                                 |                  |               |               |          |
| AF                                           | 135 (6.7%)       | 83 (7.9%)     | 52 (5.4%)     | 0.025*   |
| PVC                                          | 108 (5.4%)       | 80 (7.6%)     | 28 (2.9%)     | < 0.001* |
| Q/QS                                         | 427 (21.3%)      | 323 (30.8%)   | 104 (10.8%)   | < 0.001* |
| TWI                                          | 401 (20.0%)      | 315 (30.1%)   | 86 (8.9%)     | < 0.001* |
| IVCD                                         | 147 (7.3%)       | 87 (8.3%)     | 60 (6.2%)     | 0.077    |
| LVH                                          | 245 (12.2%)      | 165 (15.7%)   | 80 (8.3%)     | < 0.001* |
| AVB                                          | 251 (12.5%)      | 152 (14.5%)   | 99 (10.3%)    | 0.004*   |

Data are presented as means ± SD or n (%). *P-value < 0.05 indicates statistical significance. Obese or overweight is defined as BMI ≥ 25 kg/m². ACEI: angiotensin converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; AVB: atrio-ventricular block; BMI: body mass index; CCB: calcium channel blocker; CKD: chronic kidney disease; EAD: established atherosclerotic disease; ECG: electrocardiogram; IVCD: intraventricular conduction delay; LVH: left ventricular hypertrophy; MRF: multiple risk factor; PVC: premature ventricular contraction; Q/QS: Q-wave or QS-wave; TWI: T-wave inversion; WC: waist circumference.

by ECG. BBB or IVCD was the strongest predictor for MACE following by the presence of EAD. There were 92 patients of RBBB, 29 patients of LBBB and 26 patients of IVCD in our study. RBBB, LBBB, and IVCD had a hazard ratio (95% confidence interval) for the prediction of MACE from the Cox-proportional analysis of 3.66 (2.02–6.65), 6.39 (2.95–13.84), and 3.64 (1.33–9.93). The P-values for RBBB, LBBB, and IVCD for the prediction of MACE were < 0.001, < 0.001, and 0.012, respectively.

Among 251 patients with AVB, 244 patients (97.2%) were 1st degree AVB, 7 patients (2.8%) were 2nd or 3rd degree AVB. AVB was demonstrated in 15% and 9.1% of patients with and without beta-blockers (P < 0.001). The use of beta-blocker was associated with MACE from univariate analysis, but the association disappeared during multivariate analysis. Although beta-blocker might be a cause of AVB, there was no significant interaction between beta-blocker and AVB on the association with MACE from Cox-proportional regression analysis (P-value for interaction test was 0.802).

We performed additional analysis by using conventional risk factors and clinical data in the prediction of MACE with and without ECG data to explore how adding ECG data might improve the risk prediction for MACE. The
Table 2. Clinical and ECG characteristics compared between patients with and without MACE.

| Characteristics                        | MACE (n = 88) | No MACE (n = 1921) | P-value |
|----------------------------------------|---------------|--------------------|---------|
| Age, yrs                               | 69.8 ± 10.0   | 66.4 ± 9.7        | 0.001*  |
| Male gender                            | 51 (58.0%)    | 1017 (52.9%)      | < 0.001*|
| Male > 55 yrs or female > 65 yrs       | 75 (85.2%)    | 1427 (74.3%)      | 0.021*  |
| Diabetes                               | 51 (58.0%)    | 1097 (57.1%)      | 0.875   |
| Hypertension                           | 75 (85.2%)    | 1703 (88.7%)      | 0.325   |
| Dyslipidemia                           | 75 (85.2%)    | 1707 (88.9%)      | 0.293   |
| Current smoker                         | 1 (1.1%)      | 62 (3.2%)         | 0.523   |
| Family history of premature atherothrombosis | 8 (9.1%)    | 170 (8.8%)        | 0.938   |
| CKD                                    | 39 (44.3%)    | 465 (24.2%)       | < 0.007*|
| WC, cm                                 | 87.4 ± 11.2   | 88.8 ± 11.5       | 0.298   |
| Obese or overweight                    | 24 (31.6%)    | 881 (48.2%)       | 0.004*  |
| EAD                                    | 72 (81.8%)    | 976 (50.8%)       | < 0.001*|

Data are presented as means ± SD or n (%). *P-value < 0.05 indicates statistical significance. Obese or overweight is defined as BMI ≥ 25 kg/m². ACEI: angiotensin converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; AVB: atrio-ventricular block; BMI: body mass index; CCB: calcium channel blocker; CKD: chronic kidney disease; EAD: established atherosclerotic disease; ECG: electrocardiogram; IVCD: intraventricular conduction delay; LVH: left ventricular hypertrophy; MACE: major adverse cardiovascular event; PVC: premature ventricular contraction; Q/QS: Q-wave or QS-wave; TWI: T-wave inversion; WC: waist circumference.

results of the analysis was added in the results section. We demonstrated that the area under the curve for the prediction of MACE by using conventional risk factors was 0.735, which is increased to 0.823 when adding ECG data (Figure 1). Comparison of receiver operating characteristic curves of using conventional risk factors with and without ECG data showed that the area under the curve of adding ECG data was significantly greater than that without using ECG data (P = 0.002).

4 Discussion

Prevalence of ECG abnormalities is higher in patients with EAD compared to those with MRF. Many ECG findings, including AF, Q/QS, IVCD, and LVH are independent predictors for future cardiac events.

The rate of PVC in our study population may be underestimated due to the snapshot nature of ECG collection. Put another way, patients may have PVC even though it is not shown or detected on a single ECG test. However, the 5.3% prevalence of PVC in this study is higher than the 1.2% rate that was previously reported in Thai population.[18] Healthy subjects with PVC had a good prognosis.[19] However, PVC may increase risk of death in patients with CAD.[20] In our study, PVC was more common in patients with EAD than in those with MRF, which suggests a relationship between of
### Table 3. Univariate and multivariate analysis for factors significantly associated with increased risk of MACE.

| Variables                                      | Univariate analysis |          | Multivariate analysis |          |
|------------------------------------------------|---------------------|----------|-----------------------|----------|
|                                                | HR (95% CI)         | P-value  | HR (95% CI)           | P-value  |
| Age > 65 yrs                                    | 1.65 (1.06–2.59)    | 0.028    | 2.38 (1.50–3.79)      | < 0.001  |
| Male gender                                    | 1.22 (0.80–1.85)    | 0.350    |                       |          |
| Male > 55 yrs or female > 65 yrs                | 1.95 (1.08–3.52)    | 0.026    |                       |          |
| Diabetes                                       | 1.02 (0.67–1.56)    | 0.940    |                       |          |
| Hypertension                                   | 0.72 (0.40–1.29)    | 0.264    |                       |          |
| Dyslipidemia                                    | 0.71 (0.39–1.27)    | 0.247    |                       |          |
| Current smoker                                 | 0.36 (0.05–2.59)    | 0.311    |                       |          |
| Family history of premature atherothrombosis   | 1.02 (0.49–2.10)    | 0.965    |                       |          |
| CKD                                            | 2.39 (1.57–3.64)    | < 0.001  | 2.38 (1.50–3.79)      | < 0.001  |
| WC                                             | 0.52 (0.34–0.81)    | 0.004    |                       |          |
| Obese or overweight                            | 0.49 (0.30–0.79)    | 0.004    |                       |          |
| EAD                                            | 4.35 (2.51–7.46)    | < 0.001  | 3.49 (1.89–6.44)      | < 0.001  |
| Medications                                    |                     |          |                       |          |
| Antiplatelet                                   | 4.70 (2.05–10.78)   | < 0.001  |                       |          |
| Statin                                         | 1.34 (0.62–2.92)    | 0.454    |                       |          |
| Beta-blocker                                   | 3.01 (1.79–5.05)    | < 0.001  |                       |          |
| ACEI                                           | 0.91 (0.58–1.42)    | 0.670    |                       |          |
| ARB                                            | 0.66 (0.40–1.07)    | 0.091    |                       |          |
| CCB                                            | 0.68 (0.44–1.05)    | 0.083    |                       |          |
| Diuretic                                       | 1.39 (0.91–2.14)    | 0.132    |                       |          |
| Antidiabetic agents                            | 0.91 (0.60–1.39)    | 0.669    |                       |          |
| ECG findings                                    |                     |          |                       |          |
| AF                                             | 2.81 (1.61–4.92)    | < 0.001  | 2.78 (1.53–5.05)      | 0.001    |
| PVC                                            | 1.33 (0.58–3.04)    | 0.506    |                       |          |
| Q/QS                                           | 2.00 (1.29–3.11)    | 0.002    | 1.84 (1.14–2.97)      | 0.012    |
| TWI                                            | 2.11 (1.35–3.29)    | 0.001    |                       |          |
| IVCD                                           | 4.86 (3.03–7.79)    | < 0.001  | 3.71 (2.22–6.23)      | < 0.001  |
| LVH                                            | 2.46 (1.52–3.99)    | < 0.001  | 2.06 (1.24–3.45)      | 0.006    |
| AVB                                            | 1.26 (0.70–2.26)    | 0.449    |                       |          |

Data are presented as means ± SD or n (%). *P*-value < 0.05 indicates statistical significance. Variables with a *P*-value < 0.2 in univariate analysis were included in multivariate analysis. Obese or overweight is defined as BMI ≥ 25 kg/m². ACEI: angiotensin converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; AVB: atrio-ventricular block; CCB: calcium channel blocker; CI: confidence interval; CKD: chronic kidney disease; EAD: established atherosclerotic disease; ECG: electrocardiogram; HR: hazard ratio; IVCD: intraventricular conduction delay; LVH: left ventricular hypertrophy; MACE: major adverse cardiovascular event; PVC: premature ventricular contraction; Q/QS: Q-wave or QS-wave; TWI: T-wave inversion; WC: waist circumference.

PVC to the myocardial pathology of patients with established disease. Although PVC was presence in 6.8% of patients with MACE and 5.8% of those without MACE, it was not statistically significant. The number of patients with PVC may be too small to detect the difference. The presence of PVC that has been shown to predict clinical outcomes usually came from ambulatory monitoring data.[21]

Q/QS abnormality is one of the diagnostic criteria for MI according to the universal definition of MI.[22] The significance of and criteria for Q/QS in each ECG lead may be different.[15,23] We previously reported a comparison between Q/QS from ECG and myocardial scar by cardiac magnetic resonance (CMR), which indicated a healed MI.[11]

From this comparison study, Q/QS had a sensitivity, specificity, and accuracy of approximately 50%, 93%, and 77%, respectively.[11] In the present study, Q/QS was detected in 21.4% of our study population, which is very high compared to the previous population study survey in Thailand, which showed Q/QS in 2.2% in men and 0.8% in women.[22] The prevalence of Q/QS was not different between EAD patients and MRF patients, which indicated a very high prevalence of Q/QS among those who did not have a history of MI. Our study showed that Q/QS was demonstrated in 24.2% of patients with a history of MI, which indicated a
limited sensitivity for its use to diagnose prior MI. In addition and importantly, Q/QS may disappear in 20% of patients 3–4 years after myocardial infarction.[24] Interestingly, 74% of patients with Q/QS in our study had no history of MI. If we excluded other potential causes of Q/QS that can mimic MI, this group may be called ‘unrecognized MI’. The prevalence of unrecognized MI from the previously reports was approximately 23%.[25] The prognosis of recognized and unrecognized MI seems to be similar.[11,25] Since the Q/QS pattern may overestimate the prevalence of MI in the very low risk group, imaging to confirm a diagnosis of MI may be useful.[11,26]

TWI may be a non-specific ECG abnormality or may be a marker for MI or ischemia.[27] It may also be a marker for other disease that mimics CAD, such as hypertrophic cardiomyopathy.[28] In our study, the prevalence of TWI was 20%. A previous study from a population survey in Thai population found TWI in 1.4% of men and in 9.6% of women.[23] In our study, there was a trend toward an increased prevalence of TWI in patients with EAD when compared to those with MRF. If we exclude TWI that might be secondary from LVH, the number of patients with TWI would be 308 patients (15.3%). Ischemia-related T-wave inversion was identified by the presence of concomitant horizontal or downsloping ST-segment depression of at least 1 mm. In our study, 31.2% of patients with TWI have significant ST-segment depression. However, there was no significant interaction in the effect of TWI with and without ST-segment depression on MACE. The criteria that we used to define TWI is a negative T-wave amplitude of at least 5 mm. This criterion selects patients that should have some cardiac pathology more than non-specific changes and may explain why there was no significant interaction between patients with TWI with and without ST-segment depression. We also found an increased prevalence of AVB in patients with EAD. However, among 251 patients with AVB, 2nd degree and 3rd degree was found in only three and four patients, respectively.

The prevalence of LVH in our study was 12.4%, and the rate was similar between EAD and MRF. LVH usually related to uncontrolled hypertension, and was found to be a marker for increased risk of cardiovascular event,[13,29] especially when associated with ST-T changes or strain pattern.[29]

Many studies have reported the predictive value of ECG variables on cardiovascular outcome.[30–32] Our group previously report the prognostic value of ECG among patients with suspected CAD who were referred for CMR imaging for the assessment of myocardial ischemia.[11,29] In those reports, we demonstrated that ECG Q/QS diagnosed by Minnesota Code criteria or by universal definition had an increased risk of death and non-fatal MI.[11] LVH by voltage criteria and by strain pattern also showed independent prognostic value for cardiovascular event in the same group of patients.[29] Previous study showed increased QRS duration to be associated with poor cardiovascular outcome.[30] AF/AFL can lead to not only ischemic stroke, but also to death and HF.[33] The results of our study revealed 4 ECG variables (i.e., AF/AFL, Q/QS, IVCD, and LVH by voltage) to be independent predictors of adverse cardiovascular outcome. TWI was found to be associated with an increased risk of MACE in univariate analysis, but it did not remain statistically significant in multivariate analysis.

4.1 Limitations

This study has some mentionable limitations. Firstly, the ECG data included in this study was single-time ECG data, which means that it cannot be used to evaluate or determine a trend relative to the relationship between treatment and the long-term control status of risk factors. Secondly, although a significant proportion of patients with ECG abnormality had a good control of risk factors, we should not conclude from these findings that control of risk factors cannot improve ECG abnormality. We should perhaps instead conclude that control of these risk factor may be even more important for preventing cardiac and ECG abnormalities before they develop. Last but not least, we may miss the detection of PAF in our study, since we did not use long-term monitors.

4.2 Conclusions

A high prevalence of ECG abnormalities was found in
both EAD patients and MRF patients, and the prevalence of ECG abnormalities was high even among those with risk factors without documented cardiovascular disease. Many ECG abnormalities are markers for increased risk of cardiovascular event.

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