Journal of Electrocardiology 55 (2019) 128–132

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

Electrocardiographic definition of silent myocardial infarction in population studies: A call to standardize the standards

Elsayed Z. Soliman, MD, MSc, MS, FAHA, FACC *

Epidemiological Cardiology Research Center (EPICARE), Wake Forest School of Medicine, Winston-Salem, NC, United States of America

ARTICLE INFO

Keywords:
Silent myocardial infarction
Electrocardiogram
Population studies

ABSTRACT

According to the American Heart Association, 170,000 new silent myocardial infarctions (SMI) occur annually in the United States. Prior studies from the general population also have shown that SMI is common, but the rates varied widely. Some studies reported SMI rates as low as 4% while others reported rates as high as 57% of the total MIs. Reports on the prognostic significance of SMI compared to clinically recognized MI also have been inconsistent. Although SMI could be detected using cardiac imaging, electrocardiogram (ECG) has been the most common method for detection of SMI in both clinical and research settings due to it is low-cost and wide availability. This report highlights certain ECG methodological aspects that need to be taken into consideration when interpreting findings from population studies addressing SMI. Examples from population studies will be used in this report to show how deviation and differences in applications of the ECG standard definitions of SMI, ECG processing methods, and the frequency of ECG recording in population studies could impact the results, which may explain the wide range of rates and inconsistent conclusions about the prognostic significance of SMI. A summary of the gaps in knowledge of the SMI research is provided. By highlighting the lack of uniform approach in defining SMI despite the availability of standard definitions and pointing out the gaps in knowledge, it is hoped that a call for standardizing the use of the current standards will emerge.

Introduction

The resting 12 lead electrocardiogram (ECG) is the most commonly used investigative tools for the diagnosis and prediction of cardiovascular disease (CVD) in population studies. Among its several uses, detection of silent myocardial infarction (SMI), defined as an objective accidental finding of an MI in an individual who denies having a prior MI, has been one of the main indications to utilize ECG in these studies. Incorporating SMI as a component in the cardiovascular outcome endpoints in research studies increases the number of total MI events which increases the statistical power without increasing the sample size or study duration; all have favorable cost implications [1].

Despite the importance of SMI as a clinical endpoint in research settings, the reported incidence and prevalence of SMI varied widely among population studies, and the conclusions about its prognostic significance compared to clinically recognized MI have been inconsistent. In their literature review, Pride et al. [2] and Sheifer et al. [3] showed that some studies reported SMI rates as low as 4% while others reported rates as high as 57% of the total MIs [2,3]. Furthermore, while some studies showed that individuals with SMI have worse outcomes than those with clinically recognized MI, other studies reported different conclusions [1–5]. Differences in the populations or using different cardiac investigative modalities to detect SMI, especially if they are inherently different such as using ECG versus imaging, may explain some of the differences in SMI results among studies. To address these issues, investigators typically use statistical models adjusted for potential confounders to make their results comparable across studies, and also explicitly mention the tools by which they defined SMI.

On the other hand, the impact of the inconsistency in the application of the standard ECG methods or the definition of SMI could have a significant impact on the results which risks the appropriateness of comparing studies using what seems to be the same standard ECG methods or the definition of SMI. In this report, examples from population studies will be used to show how deviation and differences in applications of the ECG standard definitions of SMI, ECG processing methods, and the frequency of ECG recording in population studies could impact the results, which may explain the wide range of rates and inconsistent conclusions about the prognostic significance of SMI.

Purpose, terms and lexicon

Purpose

In addition to the ECG, SMI could be detected using echocardiography, nuclear imaging, or cardiac magnetic resonance imaging (c-MRI). However, ECG has been the most common method for detection of

* Epidemiological Cardiology Research Center (EPICARE), Wake Forest School of Medicine, Medical Center Blvd, Winston Salem, NC 27157, United States of America.
E-mail address: esoliman@wakehealth.edu.

https://doi.org/10.1016/j.jelectrocard.2019.05.008
0022-0736/

SMI in population studies due to it is low-cost and wide availability. The purpose of this report is not to discuss differences in SMI detection by different cardiac investigative tools since such differences are expected. Instead, the purpose is to highlight certain ECG methodological aspects that need to be taken into consideration when interpreting research from population studies which examined SMI. To fulfill this purpose, the report will focus on the definition of SMI by the Minnesota ECG Classification, the most commonly used ECG classification system in population studies [6].

The Minnesota ECG Classification

The discussions in this report may require familiarity with the Minnesota ECG Classification [6]. Briefly, the Minnesota ECG Classification is a hierarchical coding system aimed to classify ECG abnormalities in research settings where a repeatable, valid, and quantitative method is required. The system is composed of several groups of codes which cover different types of ECG abnormalities. The Minnesota codes that pertain to myocardial infarction and ischemia are Q Codes (Minnesota Codes 1), ST Segment Depression Codes (Minnesota Codes 4) and T-wave Codes (Minnesota Codes 5). Each Minnesota code is composed of 3 numbers. The first number indicates the type of ECG abnormality the code is focused upon (e.g., Code 1 for Q codes, Code 4 for ST Segment Depression, etc.), and the other two numbers indicate severity. To avoid misclassification of abnormalities, the Minnesota ECG Classification has inherent safeguards to suppress reading/coding in the presence of certain ECG conditions that may lead to improper classification. In addition to the individual hierarchical codes for Q (Minnesota Codes 1), T (Minnesota Codes 4) and ST abnormalities (Minnesota Codes 5), MI is defined by Minnesota ECG Classification as major Q wave abnormalities (Minnesota Code (MC) 1-1-X or 1-2-X) or minor Q wave abnormalities (MC 1-3-X) with major ST-segment or T-wave abnormalities (MC 4–1, 4–2, 5–1 or 5–2) where x could be any number in the list of codes. This definition is typically used to define MI at a single point of time [6].

In longitudinal studies where there are multiple study visits, the Minnesota ECG Classification developed another method to detect new MI using what is called, significant serial changes in the Q/ST/T waves. This method takes into account significant changes in the amplitudes and the durations of Q, T and ST not only worsening of the Q, T and ST codes, and therefore it provides a more specific definition for MI. There is a different set of Minnesota Codes assigned for the significant serial changes (Q wave serial changes codes Q1 to Q 8, and ST/T serial changes STT1 to STT8). New MI using significant serial changes is defined as presence of Q1 to Q7 [7].

Silent MI versus unrecognized MI

In this report, we used the term SMI. However, there is no consensus on whether SMI or unrecognized MI (UMI) is a better term to describe the objective accidental finding of MI without a prior history of an MI. While the Task Force for the Third Universal Definition of Myocardial Infarction used the term "Silent MI" [8], the Statement for the Case Definitions for Acute Coronary Heart Disease in Epidemiology and Clinical Research Studies by the United States and European Practice Guidelines Societies used the term "UMI" [9]. On the other hand, the 2018 Fourth Universal Definition of Myocardial Infarction Task Force used both terms in the document quoted as "Silent/Unrecognized MI" [10]. It is worth noting that our current knowledge on SMI is shaped by research used both terms without distinction [2–5,11–22]. Therefore, while it may be reasonable to prefer or even to standardize the term, it is not appropriate to totally dismiss the other.

Population studies

Another term worth noting is "population studies". This is the type of studies that involve studying the health of populations—both at specific time points (cross-sectional studies) and over longer periods (longitudinal studies)—to uncover patterns, trends, and outcomes in the general population. In this report, the term population studies is used interchangeably with the term epidemiologic studies, and for this report, both terms include all designs whether observational (cohort studies) or experimental (clinical trials).

Methodological considerations on electrocardiographic SMI

Detection of SMI requires two pieces of information; excluding knowledge of a previous MI and recent objective evidence of that MI. Not uncommon, the design of the research study dictates the method by which each one those two pieces of information is obtained. This may result in heterogeneity in SMI definition and potentially conflicting results among studies, even if the intention was to use the same standard ECG definition. Using examples from population studies, the following are a few methodological aspects that need to be taken into consideration when interpreting findings from population studies addressing SMI.

Impact of variations in the application of the ECG standard definition

In cross-sectional studies where there is only baseline visit and no follow-up, SMI is typically defined as an ECG-evidence of MI in the absence of a self-reported history of MI. Excluding knowledge of a prior MI using self-reported history of a prior MI is liable to recall bias and misclassification, but it is a convenient and sometimes the only available method in population studies with such design. The ability to recall prior MI depends on the cognitive ability of that population and its access to healthcare. So the assumption that studies using self-reported history of MI as part of the definition of MI would yield comparable results may not always hold. To overcome this bias, some studies such as the Rotterdam Study [11] used baseline self-reported history supplemented by additional clinical information from the participant's physician. However, adjustment for socio-demographic factors, access to healthcare and concomitant comorbidities could lessen some of these differences among studies.

The situation is more complicated with ECG definition of MI even if the intention is using the same standard. In both the REasons for geographic and racial differences in stroke (REGARDS) study [12], and the United Kingdom Prospective Diabetes Study (UKPDS) study, SMI [13] was defined as ECG-evidence of MI using the Minnesota ECG Classification [6] in the absence of a self-reported history of MI. Despite citing the same standard definition of ECG-MI (the Minnesota ECG Classification), there were inherent differences in the application of the definition.

In the REGARDS study, ECG-MI was defined in 16,653 participants using the typical definition of MI by the Minnesota ECG classification at one point of time (major Q wave abnormalities (Minnesota Code (MC) 1-1-X or 1-2-X) or minor Q wave abnormalities (MC 1-3-X) with major ST-segment or T-wave abnormalities (MC 4–1, 4–2, 5–1 or 5–2)) [12]. On the other hand, in the UKDPS study modified this definition and defined ECG-MI as only major Q wave abnormalities (Minnesota code (MC) 1-1-X or 1-2-X) omitting the rest of the definition [13]. The authors justified omitting minor Q waves plus major ST/T wave abnormalities claiming that these are non-specific. Whether this is a justified argument or not, this decision resulted in marked variation in the reported SMI rates between the REGARDS and UKPDS although both, assumingly, used the same ECG classification. While REGARDS study showed that SMIs contributed 32.4% of the total MIs, SMI rate was only half of that in the UKPDS (16.6% of the total MI) [12,13].

In the UKPDS study participants with SMI were also more likely to be women [13]. However, in the Action to Control Cardiovascular Risk in Diabetes (ACCORD), men were found to have a higher prevalence of silent MI on baseline ECGs than women [14]. Notably, the ACCORD study used the same Minnesota codes defining ECG-MI definition as those used in the REGARDS [12]. These differences in the prevalence rates

and gender differences in cross-sectional studies triggered by deviations in the applications of the standard definition, whether justified or not, create uncertainty and confusion.

Different approaches and modifications in using the Minnesota ECG Classification have been utilized in longitudinal studies as well. When multiple exam visits are available in longitudinal studies, some studies defined SMI in a follow-up visit as presence of ECG evidence of MI by the Minnesota ECG Classification (major Q wave abnormalities with or minor Q wave plus major ST-segment or T-wave abnormalities) in that visit without evidence of a clinical MI in a prior visit. This approach was utilized in a recent publication from the Atherosclerosis Risk in the Communities (ARIC) Study [15] where SMI was examined in 9498 participants. The ARIC participants included in this analysis underwent biennial three follow-up visits with ECG recording in each visit after the baseline exam which also included an ECG recording. ECG-MI was defined in each visit using the standard Minnesota Code while hospital admissions were reviewed to document clinical MIs during the same follow-up period. The study showed that SMI contributed over 45% of the total MIs [15]. This approach is supposed to be less specific and hence would yield more SMI cases.

A more specific approach that also utilizes the Minnesota ECG Classification is the Q/ST/T serial changes. This approach takes into account not only developing new ECG-MI by Minnesota Code as previously defined in a follow-up visit but also requires significant changes in the amplitude and duration of the Q/ST/T waveforms. This approach is used mainly in the clinical trials to improve specificity. In the Multiple Risk Factor Intervention Trial (MRFIT), for example, SMI was defined in 12,866 participants as significant Q wave changes (Minnesota serial changes Q1 code to Q7 code) [16]. In MRFIT, SMI contributed 25% of the total MIs, which is notably much lower than that reported in the ARIC study.

Because MI definition using the Minnesota ECG Classification significant serial changes Q/ST/T is specific and yields a smaller number of MIs, Q1 to Q8 instead of Q1 to Q7 has been used occasionally define MI. This approach was used in a prior analysis from the Women Health Initiative [17] study and the Strategies for Management of Antiretroviral Therapy (SMART) trial [18].

Differences in the application the standard MI definition could explain some of the differences in the variations in the reported rates and conflicting sex results among population studies. Without taking into account the method by which SMI is defined, our interpretation of the SMI research would not be complete and comparing studies would not be appropriate. The lack of a uniform approach in applying the standard definition of SMI could hinder our ability to improve our understanding of SMI.

Impact of the nature and processing of the ECG tracings

The Minnesota ECG Classification has been incorporated into several computer algorithms to enable automated classification of ECG abnormalities from digital ECG signals acquired from electrocardiographs. Ammar et al. reviewed data from fourteen major population studies, most of them used the Minnesota ECG Classification, and concluded that computerized ECG analysis is superior to visual reading in defining SMI due to better reliability, speed and cost [19]. However, their conclusion was based on the predictive ability of SMI not based on comparison with a gold standard of accurate diagnosis of MI. Also, they assumed that the wide range of SMI rates observed in their analysis (4% to 44%) is due to underestimation of visual compared to computerized automated detection of SMI using the Minnesota ECG Classification. However, the opposite could also be true; computerized Minnesota ECG Classification might be over-estimating SMI.

In another study that highlights differences among automated and visual reading, Kors et al. compared two computer programs incorporating the Minnesota ECG Classification with the visual reading standard [23]. Those two programs were the Minnesota Code-Modular ECG Analysis System (MC-MEANS) and the NOVACODE program. The agreement between the visual and the computer MC ECG interpretation was greater than 90% for all of the Minnesota codes except the Q code, which was 77% for MC-MEANS and 81% for NOVACODE. The less agreement in the assignment of Q codes between automated processing of ECG and visual reading, which is the single most important step in the detection of SMI, indicates inherent differences between automatic and manual detection of MI even if both utilize the Minnesota code. Lack of exact agreement between the two computerized systems is also worth noting.

Although automatic interpretation has the advantage of enhancing reproducibility, which is of critical importance in population studies, absolute dependence on software is not free of the risk of overestimating detection of a serious condition like MI. Contemporary software, regardless of their capabilities, cannot detect certain artifacts or arrhythmias which may distort the ability to measure Q waves correctly. Therefore, a hybrid approach of automated processing of ECG supplemented with human editing of extreme global onsets and offsets of ECG waveforms, and detection of artifacts and arrhythmias may have the potential to improve quality. The challenge is (and has been) is standardizing the levels of human interference to ensure consistency.

Impact of the frequency of recording ECG in population studies

The pathological Q waves after acute MI may regress or disappear in as many as 25% to 63% of patients [24]. This represents a challenge in the detection of SMI using ECG which depends on the presence of these Q waves. Results from the Framingham Heart studies have shown that 10% of the anterior and 25% of inferior MIs lose their ECG signs within two years [25]. This means that many of the cases of SMI, especially inferior SMI, would go undetected with long intervals between ECG visits.

Regression of Q waves could be explained by periinfarct positive remodeling, varying activation of the superior and inferior walls, functional recovery of stunned or hibernating myocardium in the infarcted area and the opposite wall MI [24]. These factors may differ from one population to another, depending on their coexisting comorbidities and their age distribution. Different population studies used different schedules to collect ECG data. Budgetary issues, the life expectancy of the population and the expected number of events are some of the factors involved in deciding the frequency of recording ECG in population studies.

In the ARIC study, which included middle-aged community-based population, ECG tracings were recorded every two years for a total of four visits between 1987 and 1998 until they decided to have another visit later in 2010 [15]. On the other hand, in the Cardiovascular Health Study (CHS) which enrolled a cohort of seniors older than 65 years, ECG recording was done annually [20]. Using the same SMI definition including the Minnesota ECG Classification, recording ECG every two years in ARIC yielded 317 incident SMI events detected in 9498 participants during 8.9 years follow up [15]. On the other hand, recording ECG every year in the CHS yielded more incident SMI events (459 SMI events), although the number of participants in the CHS (4355 participants) was just half of that in the ARIC study and the follow-up was shorter (6 years follow up) [20]. Obviously, the old age of the CHS participants might have played a role in the excess number of SMI, but the impact of the frequent ECG recording cannot be ignored.

Although understanding the progression of coronary heart disease including SMI requires more frequent visits and ECG data collection, the cost of these visits in population studies could be prohibitive. Nevertheless, infrequent visits can lead to missing the opportunity to detect SMI which is a major contributor to the burden of coronary heart disease. Identifying the ideal frequency of recording ECG in different populations is needed for better planning of the studies.

Other factors impacting standardization of the definition of SMI by ECG

Central processing of ECG data at specialized ECG core laboratories using standard methods with pre-specified quality control protocols is the preferred approach in research. There are several factors that could impact standardized ECG coding include ECG coder training, data acquisition, patient preparation, technician training, and the nature of quality control. Although several studies used the Minnesota ECG Classification as part of their definition of SMI, it is uncommon for these studies to provide details about the quality measures of processing and coding the ECG data. Knowledge on its own is not enough when it comes to the Minnesota ECG Classification, but the repeatable and consistent application which requires continuous training and quality control measures of the staff which unlikely to achieve outside centralized units.

Gaps in knowledge

Regardless of the uncertainty about the precise rates of SMI by ECG and how its prognostic significance compares to clinically recognized MI, all studies agree that it is common, and it is associated with poor outcomes including coronary heart disease, heart failure, and mortality [2,3,6,10,12,14,17–20]. However, still, there are several gaps in knowledge that need to be addressed to understand better, diagnose, and treat SMI, and ultimately prevent SMI. Some of these gaps are:

- Lack of standard approaches for defining SMI by ECG in research and clinical settings. Despite the existence of standard definitions to detect SMI using ECG, lack of uniform approaches to applying these standards in different situations hinders the ability to appropriately compare results from different studies.
- ECG and cardiac imaging provide different information, and therefore each modality could be useful to understand parts of the natural history of SMI. Studies are needed to explore how ECG and imaging could be integrated rather than replacing each other to advance our understanding of SMI.
- There is an opportunity to develop more precise ECG-based models for estimating SMI size and prediction of the risk of SMI using more sophisticated ECG models. This opportunity is possible given the availability of digital ECG data which provide hundreds of waveform measurements, imaging data that provide actual size of infarct area which could serve as a gold standard and the availability of fast computers that could handle large volumes of information and complex computations.
- Studies are needed to investigate the cost-effectiveness of screening for SMI as part of coronary heart disease prevention, especially in high-risk groups such as those with diabetes or old age.
- There is a need for better understanding of risk factors specific to SMI that are different from clinical MI and exploring optimal modifications of these risk factors. Investigating the potential reasons for the reported sex and race differences in SMI would be part of this.

Concluding remarks

Currently, the most common method for detecting SMI in population studies is ECG. Despite its wide use and the appearance of using standard definitions, the methodology is far from being standardized or consistent. This includes deviation from applying the standard definitions, differences in the approaches of processing the ECG data and lack of information on the ideal frequency of recording ECG. Whether some of these issues are dictated and justified by study design and logistics, most of the studies do not directly address the rationale behind their decisions. The net result is inconsistent and occasionally conflicting reports which hinder progress. Even the terms referring to accidental finding of an MI without prior knowledge of the patient have been used inconsistently; some prefer SMI while others use UMI or both.

There is no doubt that SMI is common, even if the exact rate is unclear, and there is no denying that it is associated with poor prognosis, whether this association is similar or more than clinically recognized MI. Therefore, we need to enhance our understanding and develop optimal management strategies for the prevention and management of SMI. The first step, however, is to have a uniform approach(s) for detection of SMI which builds on the available standard definitions but fits different research scenarios.

Declaration of Competing Interest

None.

References

[1] Gibson CM, Nafee T, Kerneis M. Silent myocardial infarction: listen to the evidence. J Am Coll Cardiol 2018;71:9–11.
[2] Pride YB, Piccirillo BJ, Gibson CM. Prevalence, consequences, and implications for clinical trials of unrecognized myocardial infarction. Am J Cardiol 2013;111:914–8.
[3] Sheifer SE, Manolio TA, Gersh BJ. Unrecognized myocardial infarction. Ann Intern Med 2001;135:801–11.
[4] Conti CR, Bavry AA, Petersen JW. Silent ischemia: clinical relevance. J Am Coll Cardiol 2012;59:435–41.
[5] Valensi P, Lorgis L, Cottin Y. Prevalence, incidence, predictive factors and prognosis of silent myocardial infarction: a review of the literature. Arch Cardiovasc Dis 2011;104:178–88.
[6] Prineas RJ, Crow RS, Blackburn H. The Minnesota code manual of electrocardiographic findings. Littleton, MA: John Wright–PSG; 1982.
[7] Prineas RJ, Crow RS, Zhang ZM. The Minnesota code manual of electrocardiographic findings. London: Springer Science & Business Media; 2009.
[8] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. Circulation 2012;126:2020–35.
[9] Luepker RV, Apple FS, Christenson RH, Crow RS, Fortmann SP, Goff D, et al. Case definitions for acute coronary heart disease in epidemiology and clinical research studies: a statement from the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; the European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; and the National Heart, Lung, and Blood Institute. Circulation 2003;108:2543–9.
[10] Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Circulation 2018;138:00. https://doi.org/10.1161/CIR.0000000000000617.
[11] Leening MJ, Elias-Smale SE, Felix JF, Kors JA, Deckers JW, Hofman A, et al. Unrecognised myocardial infarction and long-term risk of heart failure in the elderly: the Rotterdam Study. Heart 2010;96:1458–62.
[12] Levitan EB, Safford MM, Kilgore ML, Soliman EZ, Glasser SP, Judd SE, et al. Assessment tools for unrecognized myocardial infarction: a cross-sectional analysis of the REasons for Geographic and Racial Differences in Stroke population. BMC Cardiovasc Disord 2013;13:23.
[13] Davis TM, Coleman RL, Holman RR, Group UKPDS. Prognostic significance of silent myocardial infarction in newly diagnosed type 2 diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS) 79. Circulation 2013;127:980–7.
[14] Stiles MC, Seaquist ER, Yale JF, Green JB, Katz LA, Kempainen S, et al. Is silent myocardial infarction more common in women with type 2 diabetes than in men? J Diabetes Complications 2012;26:118–22.
[15] Zhang ZM, Rautaharju PM, Prineas RJ, Rodriguez CJ, Loehr L, Rosamond WD, et al. Race and sex differences in the incidence and prognostic significance of silent myocardial infarction in the Atherosclerosis Risk in Communities (ARIC) Study. Circulation 2016;133:2141–8.
[16] Grimm Jr RH, Tillinghast S, Daniels K, Neaton JD, Mascioli S, Crow R, et al. Unrecognized myocardial infarction: experience in the Multiple Risk Factor Intervention Trial (MRFIT). Circulation 1987;75:116–8.
[17] Zhang ZM, Prineas RJ, Soliman EZ, Baggett C, Heiss G, ARIC Research Group. Prognostic significance of serial Q/ST-T changes by the Minnesota Code and Novacode in the Atherosclerosis Risk in Communities (ARIC) study. Eur J Prev Cardiol 2012;19:1430–6.
[18] Gupta M, Miller CJ, Baker JV, Lazar J, Bogner JR, Calmy A, et al. Biomarkers and electrocardiographic evidence of myocardial ischemia in patients with human immunodeficiency virus infection. Am J Cardiol 2013;111:760–4.
[19] Ammar KA, Kors JA, Yawn BP, Rodeheffer RJ. Defining unrecognized myocardial infarction: a call for standardized electrocardiographic diagnostic criteria. Am Heart J 2004;148:277–84.
[20] Stacey RB, Zgibor J, Leaverton PE, Schocken DD, Peregoy JA, Lyles MF, et al. Abnormal fasting glucose increases risk of unrecognized myocardial infarctions in an elderly cohort. J Am Geriatr Soc 2019;67:43–9.
[21] Qureshi WT, Zhang Z-M, Chang PP, Chang PP, Rosamond WD, Kitzman DW, et al. Silent myocardial infarction and long-term risk of heart failure: the ARIC study. J Am Coll Cardiol 2018;71:1–8.

[22] Rautaharju PM, Prineas RJ, Wood J, Zhang Z-M, Crow R, Heiss G. Electrocardiographic predictors of new-onset heart failure in men and in women free of coronary heart disease (from the Atherosclerosis in Communities [ARIC] Study). Am J Cardiol 2007;100:1437–41.
[23] Kors JA, Crow RS, Hannan PJ, Rautaharju PM, Folsom AR. Comparison of computer assigned Minnesota codes with the visual standard method for new coronary heart disease events. Am J Epidemiol 2000;151:790–7.
[24] Michael MA, El Masry H, Khan BR, Das MK. Electrocardiographic signs of remote myocardial infarction. Prog Cardiovasc Dis 2007;50:198–208.
[25] Vasan RS, Benjamin EJ, Levy D. Prevalence, clinical features and prognosis of diastolic heart failure: an epidemiologic perspective. J Am Coll Cardiol 1995;26:1565–74.