Changes in the ST- and Ventricular Gradient Vectors over a Period of 25 Years

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Abstract

The ECG is a major diagnostic instrument for the detection of acute ischemia and subsequent triaging of patients after first medical contact in the setting of acute coronary syndrome. However, sensitivity and specificity of the ECG with current diagnostic criteria are limited. When a previous non-ischemic ECG is available for reference purposes, comparison of the acute and reference ECG by serial analysis is known to increase sensitivity. For acceptable specificity in serial comparison it is a prerequisite that a reference ECG remains valid (is stable) in time.

We compared, within 88 patients, 6 non-ischemic ECGs, each five years apart. The first ECG was used as a reference ECG, and each of the next 5 ECGs was compared with the initial reference ECG. We computed for each comparison the difference in the ST vector at the J point and 60 ms after the J point, and, additionally, the difference in the ventricular gradient (VG) vector. These differences were interpreted in relation to the proposed ischemia thresholds of 50 μV (ST vector) and 20 mV·ms (VG vector).

Ischemia detection thresholds were increasingly exceeded with time, varying from 26% after 5 years to 60% after 25 years, when measured 60 ms after the J point. Actually, in our study group there were many more ECGs made than those selected for our study: measured from an arbitrarily chosen point in time the most recent ECG was only 1.3 years old. Hence, the serial analyses with a time lag of 5 years was the most relevant. Our study suggests that serial ECG comparison for ischemia detection in this patient group is feasible from the point of view of dynamics in the reference ECG.

1. Introduction

In atherosclerotic disease, a stenosis in a coronary artery may cause ischemia during exercise (demand ischemia), or, when the plaque ruptures and thrombus formation causes a partly or complete occlusion, ischemia occurs during rest (supply ischemia). When supply ischemia occurs and the thrombus does not resolve spontaneously, the ischemic tissue becomes necrotic (infarction). The symptoms associated with the dynamic situation after plaque rupture are called acute coronary syndrome (ACS).

ACS may be almost symptomless and thus result in an unrecognized "silent" myocardial infarction[1]. When ACS causes more serious symptoms, medical contact is often sought. ACS associated symptoms (notably chest pain) can have many other causes, ranging between innocent and emergency diagnoses. The initial triage at first medical contact (often with ambulance personnel) obligatory involves the making of an electrocardiogram (ECG). This ECG is, together with the symptoms and the patient history, crucial in establishing the working diagnosis of ACS. When the ECG shows ST-elevation, the current guidelines recommend immediate revascularisation by percutaneous coronary intervention (PCI), preceded by thrombolysis if there is no quick access to PCI[2]. With a non-ST elevation ECG, initial antithrombotic treatment is recommended[3]. There are, however, good arguments in favour of immediate PCI as initial treatment in all ACS patients[4]. In that case, the ECG is no longer used to discriminate between different treatment modalities, but rather to demonstrate the very existence of acute ischemia, thus helping to establish the working diagnosis of ACS.

This diagnosis of ACS should have sufficient sensitivity, because false negative decisions cause delayed access to PCI and, consequently, an increased infarct size. Also, this diagnosis should have sufficient specificity, because of the huge costs involved with false positive cathlab activations.

The current criteria to detect ischemia require ST amplitudes at the J point in the order of magnitude of 100 μV. However, sensitivity is quite low at this threshold[5]. For a lower threshold, e.g., of 50 μV, specificity goes down. The latter is caused by the fact that many persons have a pre-existing nonzero J amplitude. Serial ECG analysis (comparison of the acute ECG with a previous non-ischemic ECG of the same patient) with a low threshold would likely facilitate more sensitive ischemia detection without the drawback of low specificity.

Serial ECG would also facilitate the diagnostic use of

the ventricular gradient (VG, the spatial integral of the heart vector over the QT interval[6]) for ischemia detection. Previous studies by our group have shown that ischemia detection by serial comparison of the ST amplitude and of the VG is feasible and has a high sensitivity[5,7]. This work was done in a group of patients with acute ischemia in the setting of elective PCI. A threshold for changes in VG to detect ischemia with comparable sensitivity as the threshold of 50 μV in the ST amplitude would be 20 mV·ms[5].

Knowledge about the dynamics in ST amplitude and VG in non-ischemic ECGs is pertinent to specificity assessment of ischemia detection by serial ECG analysis. Suppose a situation in which a patient has chest pain mimicking ACS, but of non-ischemic origin. When, in this case, an ECG is made, and compared with a previously made reference ECG of the same patient, differences will exist as a consequence of the ageing process, of possibly emerged or aggravated disease, of possibly instituted pharmacological treatment, etc. When these differences exceed the ischemia detection threshold, this would result in a false positive ACS diagnosis. In such a case the reference ECG is obviously no longer useful for serial comparison, and should be updated.

In our current study, we sought to answer the question how long a non-ischemic ECG can be used as a reference ECG for the detection of acute ischemia, by studying the dynamics of the ST amplitude and of VG in a group of patients followed over a period of 25 years.

2. Methods

Data were selected from our Departmental ECG database, comprising more than 800,000 ECGs. Only electively ECGs made in the outpatient clinic were selected; ECGs made during a hospital admission or at the emergency department were excluded. Six successive 5-year periods were defined, beginning 1985-1989 (pentad 0), and ending 2010-2014 (pentad 5). A computerized algorithm selected all patients who had at least 1 elective ECG made in each of the pentads. Only ECGs of sufficient technical quality and with regular sinus rhythm were included. When more than one ECG was available in a pentad, the ECG best positioned in time was selected, thus creating, per patient, a set of 6 ECGs, ECG0 … ECG5, that were as much as possible evenly spaced in time.

2.1. Clinical diagnosis

For each ECG the associated cardiologic diagnosis was noted by checking a set of diagnostic statements in the digital patient file.

2.2. ECG interpretation

To characterize the ECG in general, all ECGs were analysed by the Glasgow ECG Analysis Program[8], and categorized into abnormal and normal as to QRS duration, QT interval, etc.

2.3. ECG analysis

ECGs were analyzed by our vectorcardiographically-oriented research tool LEADS [9], using the Kors matrix for vectorcardiogram (VCG) synthesis. After computation of an averaged beat, the automatically determined onset-QRS, J-point end end-T settings were manually verified by two observers, and when necessary they were corrected. The J point was localized according the procedure mentioned in the Minnesota code[10]. The end of the T wave was defined in the vector magnitude signal as the time instant where the tangent to the point with the steepest slope of the descending limb of the T wave intersects the baseline. Then, three variables were computed: the ST vectors at the J point and 60 ms after the J point (ST(J+0) and ST(J+60)), and the ventricular gradient vector (VG).

Finally, for each patient, five serial comparisons were done, by computing the difference vectors ΔST(J+0), ΔST(J+60) and ΔVG between the pentad 1-5 ECGs on one hand, and the pentad 0 reference ECG on the other hand.

2.4. Statistics

Data are described as numbers, percentages, means and standard deviations. Trends over time (a monotonous increase or decrease over time) were detected by a sign test. Comparisons between data series were made by paired t-tests.

3. Results

A total of 88 patients (58/30 male/female, mean±SD age at the reference ECG 40.4±12.3 years) fitted all prerequisites to be included in the study group. The body mass index at the time of the reference ECG was 24.3±3.4 $kg \cdot m^{-2}$; and 25 years thereafter, the body mass index of the study group had increased to 27.0±5.0 $kg \cdot m^{-2}$ ($P<0.01$).

3.1. Clinical Diagnosis

The major diagnostic categories at the time of the reference ECG are listed in Table 1.

Table 1. Major diagnoses of the study group at the time of the reference ECG. The sum of the diagnoses exceeds the number of patients in the study group because more than one diagnosis can apply to a single patient.

Diagnosis	N	%
Systemic Hypertension	34	38.6
Valvular Heart Disease	26	29.5
Diabetes Mellitus	16	18.2
Myocardial Infarction	13	14.8
Stable Angina	12	13.6
Non-ischemic Myopathy	11	12.5
Conduction Disorders	9	10.2
Arrhythmia / Channelopathy	8	9.1
M. Marfan	2	2.3
Pulmonary Hypertension	1	1.1
Total	132	

3.2. ECG interpretation

According to the Glasgow ECG interpretation program, 38/88 (43%) of the ECGs were classified as abnormal or borderline abnormal. An overview of categories of ECG abnormalities is given in Table 2.

Table 2. Major categories of ECG abnormalities in the reference ECGs, according to the Glasgow ECG interpretation program.

Category of ECG abnormality	N	%
Sinus tachycardia and bradycardia	21	23.9
Abnormal P wave	7	8.0
Abnormal AV conduction	2	2.3
Abnormal frontal QRS axis	12	13.6
Prolonged QRS duration	14	15.9
High QRS amplitude	9	10.2
Abnormal ST segment	24	27.3
Abnormal T wave	21	23.9
Long QT	2	2.3
Abnormal or borderline abnormal ECG	38	43.2

3.3. ECG Analysis

Figure 1 shows the histograms of ΔST(J+0), ΔST(J+60) and ΔVG as a function of time. Table 3 shows that our proposed thresholds for serial detection of ischemia, 50 μV for ΔST and 20 mV·ms for ΔVG were most often exceeded for ΔVG, and least often for ΔST(J+60) (P<0.01). All percentages show an increasing trend with time (P<0.01).

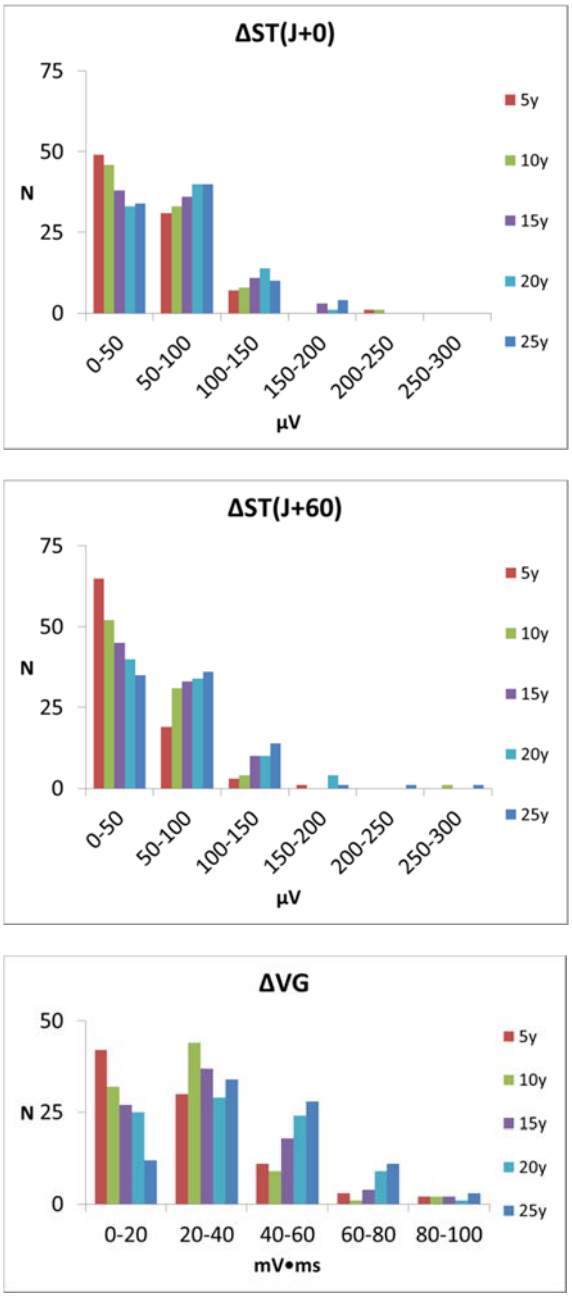

Figure 1. Histograms of ΔST(J+0), ΔST(J+60) and ΔVG as a function of time.

Table 3. Serial comparison percentages in which the difference vector size exceeded the low differential thresholds of 50 μV for ΔST and 20 mV·ms for ΔVG.

Compared Pentads	ΔST(J+0)	ΔST(J+60)	ΔVG
0–1	44	26	52
0–2	48	41	64
0–3	57	49	69
0–4	62	54	72
0–5	61	60	86

4. Discussion

We measured the changes in the ST(J) and ST(J+60) vectors and in the VG vector as a function of time in a study group consisting of patients who have been visiting the cardiology outpatient clinic for at least 25 years. Purpose was to investigate how stable the J amplitude and the ventricular gradient are in time, because of the potential use of these ECG variables in ischemia detection by serial ECG analysis.

It is according to expectation that the ECG changes in our study group are larger than those in a population of normals, in whom J amplitudes appear hardly to change with age[11] (we are not aware of any report describing changes of the ventricular gradient with age in normals). Indeed, patients who regularly visit the cardiology outpatient clinic suffer *de facto* from various diseases (see Table 1) and the progression of disease and associated changes in the medication regimen are likely to affect the heart and its electrical function. Obviously, the more distant in time from the reference ECG, the larger the differences (see Table 3 and Figure 1).

Especially in the first 3 pentads, the ST vector changes seems to be smaller when measured 60 ms after the J point than at the J point itself. This finding can have practical consequences for the decision where, relative to the J point, to measure ST amplitudes in ACS diagnosis[12].

Our results show that an electively-made non-ischemic ECG cannot serve during 25 years as a reference ECG for the purpose of ischemia detection by serial analysis. However, clinical practice caused many more ECGs to be made in our patients than those with 5-year time laps that we included for serial analysis. We have taken an arbitrary point in time, January 1, 2000, and interrogated our Departmental ECG database for the most recent ECG. That most recent ECG was found at an average of 1.3 years back in time. Hence, even the serial analysis for the first pentad, with an average delay of 5 years, gives already a too pessimistic estimate of the amount of ECG dynamics that we have to take into account in order to assess specificity of ischemia detection by serial ECG analysis.

In conclusion, our study suggests that serial ischemia detection from the point of view of specificity may be well feasible, however, we should study shorter time delays as well to corroborate this conclusion. This, and a further investigation which clinical events and medication changes caused the major ECG changes in our study group will be next topics of research.

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