Improved Electrocardiographic Detection of Hyperacute Ischemia by Difference Vector Analysis

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Abstract

Background. The ECG is important for diagnosis and triage in the hyperacute phase of acute coronary syndrome (ACS), especially during the "golden hours", when myocardial salvage possibilities are largest. An important triaging decision is whether or not a patient requires primary PCI, for which the guidelines mention ST elevation (STE) in the ECG as major criterion. This criterion has, however, a low sensitivity and specificity.

Methods. We investigated the diagnostic possibilities of ischemia detection by means of changes in the ST vector, ΔST, and/or changes in the VG (QRST-integral) vector, ΔVG. We studied vectorcardiograms (VCGs) synthesized from the ECGs of 84 patients who underwent elective PTCA. Mean ± SD balloon occlusion times were 260 ± 76 s. ECG ischemia diagnosis (STE or non-STE (NSTE), and the differences ΔST and ΔVG with the baseline ECG were measured after 3 min. of occlusion.

Results. Linear regression of ΔVG on ΔST yielded ΔVG = 324 • ΔST (r = 0.85; P < 0.0001, ΔST in mV). With ΔST thresholds of 0.025, 0.050, 0.075 and 0.100 mV and corresponding ΔVG thresholds of 8.1, 16.2, 24.3 or 32.4 mV•ms, respectively, we determined the sensitivity for ischemia detection, that varied from 55% for the STE criterion to 87 or even 99% for the one but most and the most sensitive ΔST and ΔVG criteria, respectively.

Conclusion. Differential diagnosis by ΔST and ΔVG (requiring an earlier made non-ischemic baseline ECG) could dramatically improve ECG guided detection of patients who urgently require catheter intervention.

1. Introduction

Ischemia affects action potential morphology and maximum diastolic potential[1], thus causing systolic and diastolic injury currents[2] between ischemic and surrounding healthy tissue, changing the ECG throughout the QRST interval. Amongst others, this manifests as alterations in the ST segment and in the spatial ventricular gradient (VG, spatial QRST integral)[3].

In the hyperacute phase of acute coronary syndrome (ACS), the ECG is of major importance in diagnosis of ischemia and in triaging. According to the current guidelines[4], first-choice therapy in patients with a new ST elevation (STE) pattern in the ECG is primary percutaneous coronary intervention (PCI). In case of acute coronary syndromes without ST-elevation (non-ST elevation, NSTE) the current guidelines[5] recommend antithrombotic (anticoagulant, antiplatelet) therapy rather than PCI. However, there are situations in which the ECG is non-diagnostic while there is still an urgent indication for PCI (like the ST depression without ST elevation that can be seen in left main disease). Consequently, the guidelines[4] read: "In any case, ongoing suspicion of myocardial ischemia— despite medical therapy—is an indication for emergency coronary angiography with a view to revascularization, even in patients without diagnostic ST-segment elevation." The percentage of patients with NSTE admission ECGs that require PCI may be considerable: Koyama and colleagues[6] found a completely occluded culprit artery in 47% of patients with an NSTE admission ECG (vs. 57% in patients with a STE admission ECG). These numbers clearly illustrate that there is a need to investigate if and how these ECG triaging criteria can be improved.

Reasons why the performance of the ECG criteria in separating patients who urgently need PCI from those who do not is limited, are various. Cancelation, inherent to electrocardiography, may explain how ST-changes can remain limited with relatively large areas at risk (AARs), e.g., in case of left main disease. A pre-existing non-zero ST deviation, even when not diagnostic, may either mask or exaggerate new ST changes during acute ischemia, depending on (in vectorcardiographic terms) the direction of the ischemia vector in relation to the pre-existing ST vector. Hence, it would be logical to measure and interpret the ischemic change of the ST vector with respect to its baseline value (measured in a preceding non-ischemic ECG of the same patient), instead of the ST vector in the ischemic ECG alone. The concept of such an ST difference vector was first published by Lundin et al.[7], and another Swedish research group has continued to explore the usefulness of this concept (first publication by Näslund et al.[8]), but its performance as compared with the conventional STE and NSTE ECG ischemia criteria has not been investigated so far.

For the computation of an ST difference vector in suspected ACS, access to a previously made non-

ischemic ECG of the same patient is needed. We realize that this is often not possible; however, with increasing technical possibilities and the increasing use of electronic patient files, we envisage that such a comparison becomes increasingly more feasible in the near future.

Availability of a baseline ECG would also facilitate computation of an ischemic VG difference vector. Because of its non-zero[3] and highly individual[9] baseline value, the VG has until now never been used in diagnosis and triage in acute coronary syndrome. Individual comparison of the VG in an ischemic ECG and a baseline ECG is of interest because the changes in the VG during ischemia are caused by action potential morphology changes in the ischemic area, rather than the ST changes, that are strongly based on the changes in the phase 4 resting potential in the ischemic area. Moreover, VG is independent of the ventricular depolarization order[3]. Thus, ST changes and VG changes are induced by different electrophysiological processes that are, however, all related to the compromised myocardium.

In the current study, we explored the potential clinical use of ischemic ST and VG difference vectors by analyzing the ECG changes of patients during elective percutaneous transluminal coronary angioplasty (PTCA).

2. Methods

We analyzed ECGs from the STAFF III database, a collection of ECGs recorded in the setting of elective PTCA procedures performed in 1995 and 1996. These ECGs are unique because of the relatively long balloon inflation times. As such, the PTCA procedure is a model of the hyperacute phase of ACS in humans. Patients were admitted to the Charleston Area Medical Center, West Virginia, USA. Nine-lead ECGs (I, II, III, V1-V6; Mason-Likar electrode positions) were recorded at a sampling rate of 1 kHz and an amplitude resolution of 0.6 μV. A 5-minute reference ECG was made in the catheterization room prior to the PTCA procedure. ECGs were continuously recorded during PTCA. Patients were excluded when they had predominant arrhythmias (e.g., atrial fibrillation), predominant low quality ECG signal, ECG electrode misplacement, or abundant dye injections throughout the balloon occlusion episode.

2.1. ECG processing

After 100 Hz low-pass filtering to remove fluorescopy-related interference and after coarse baseline removal[10] the ECGs were processed by BEATS[11], our vectorcardiographically-oriented ECG analysis system. BEATS synthesizes a vectorcardiogram (VCG) and then interactively detects beats, defines their isoelectric points, fine-corrects the baseline by piecewise linear regression through these points, and determines landmarks in time (onset QRS, J point, peak and end of the T wave). Heart beats with low quality, incidental non-sinus beats and beats during dye injections were manually removed. In the remaining beats we computed the ST vector (magnitude, azimuth and elevation[12]) at J+60 ms, and the spatial QRST integral (a vector expressed in mV•ms), which is, by definition, the VG.

For the current study we selected a baseline and an occlusion ECG episode. As baseline we selected a stable 30-seconds episode at the end of the reference recording. As occlusion ECG we selected the period during the first balloon inflation. Reperfusion data were not studied.

2.2. Data analysis

As baseline values we computed the averaged ST and VG vectors in the baseline ECG. Dynamic ST and VG vectors during ischemia were computed as 10-beat moving averages. Dynamic ST and VG difference vectors during ischemia, ΔST and ΔVG, were computed by subtracting the baseline ST and VG vectors from these dynamic ST and VG vectors. As occlusion durations differed considerably, we report here ΔST and ΔVG values after 3 minutes of occlusion.

To investigate the relation between the 3-minute ΔST and ΔVG magnitudes we performed a linear regression forced through the origin. We adopted four cut-off values for the ΔST magnitude to detect ischemia: 0.025 mV, 0.050 mV, 0.075 mV and 0.100 mV, respectively. The cut-off value of 0.050 mV has been proposed in the setting of differential ST segment analysis[13], while the value of 0.100 mV is usually applied in conventional ischemia diagnosis. Linear regression of ΔVG on ΔST yielded corresponding ΔVG cut-off values. Thus, we determined which patients had an ECG positive for ischemia on the basis of their ST difference vector magnitude alone, their VG difference vector magnitude alone, or in either one or both.

In addition, we compared the diagnostic performance of ΔST and ΔVG with the standard ECG ischemia diagnosis (STE, NSTE) after 3 minutes of ischemia. Ten-second ECG segments from the baseline ECGs and from the occlusion ECGs after 3 minutes of ischemia were transferred to our departmental ECG management system and analyzed by the University of Glasgow ECG Analysis Program[14]. Thus, an ECG diagnosis was generated, and STE / NSTE classification was established of the baseline and ischemic ECGs, by using the measurement matrix data of the Glasgow program. STE was diagnosed as an elevation at the J-point of ≥ 0.2 mV in two or more contiguous leads in leads V1 or V2, and of ≥ 0.1 mV in other contiguous leads. Contiguity in the frontal plane is defined in the lead sequence aVL, I, inverted aVR, II, aVF, III. Also, a depression of ≥ 0.1 mV in leads V2 or V3 was counted as STE. When the ECG did not qualify as STE, it qualified as NSTE.

3. Results

The STAFF database comprises 104 patients; after exclusion, 84 patients (54/30 male/female, mean ± SD age 60 ± 11years) constituted our study group. Three patients had aberrant conduction and two had a pre-existing STE ECG. Occlusion sites of the first inflation were: left main in 2, LAD in 25, LCx in 16, and RCA in 41 patients. Mean ± SD duration of the initial inflation was 260 ± 76 seconds; in 13 of 84 patients (15%) the duration of the initial inflation was shorter than 180 seconds (mean ± SD 145 ± 29 seconds). In those 13 patients, ΔST and ΔVG were measured at the end of balloon inflation.

3.1. Ischemia thresholds

Figure 1 is a scatterplot of the 3-minute ΔST and ΔVG magnitudes. The equation of the linear regression forced through the origin was ΔVG = 324 • ΔST (ΔVG in mV•ms, ΔST in mV). The ΔST and ΔVG magnitudes correlated significantly (r = 0.84; P < 0.0001). The ΔVG magnitude cut-off values that correspond to the ΔST cut-off values 0.025, 0.050, 0.075 and 0.100 mV are 8.1, 16.2, 24.3 or 32.4 mV•ms, respectively. Hence, either a minimal ΔST magnitude of 0.025 / 0.050 / 0.075 / 0.100 mV or a minimal ΔVG magnitude of 8.1, 16.2, 24.3 or 32.4 mV•ms would signify the presence of ischemia in hyperacute complete coronary occlusion.

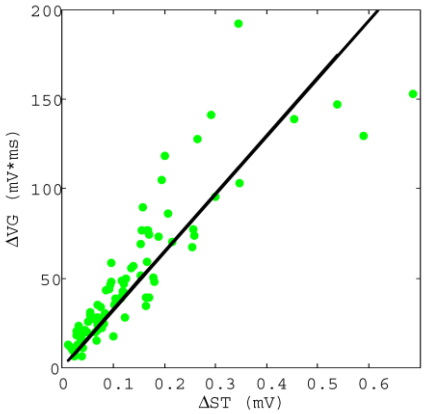

Figure 1. Scatterplot of ΔST versus ΔVG after 3 minutes of balloon occlusion with linear regression forced through the origin: ΔVG = 324 • ΔST (ΔVG in mV•ms, ΔST in mV, r = 0.84; P < 0.0001).

3.2. Diagnostic performance

Table 1 shows the sensitivities of the conventional 12-lead ECG ischemia diagnosis, the four ΔST and the four ΔVG four combined threshold criteria (one or both of the thresholds should be reached), respectively.

In 46/84 (55%) of the patients, the ischemic ECG showed a pattern of new STE. Eleven of the 13 (85%) patients who had occlusions <3 minutes had a new STE ECG, demonstrating that the patients with the briefer occlusions were not the reason of the limited percentage (55%) of patients who had a new STE ischemic ECG. ΔVG performed slightly better than ΔST, and the combination of ΔVG and ΔST performed slightly better than ΔVG alone for all threshold categories.

	New STE			
N				46
%				55
	ΔST (mV)			
Δ	0.025	0.050	0.075	0.100
N	77	68	54	45
%	92	81	64	54
	ΔVG (mV·ms)			
Δ	8.1	16.2	24.3	32.4
N	82	72	61	50
%	98	86	73	60
	Combined ΔST and ΔVG			
Δ	*see above for Δ values*			
N	83	73	62	52
%	99	87	74	62

Table 1. Sensitivity to detect ischemia after 3 minutes of total occlusion by the conventional ECG criteria ("New STE"), by the ST difference vector ΔST, by the VG difference vector ΔVG and by their combination.

4. Discussion

In the current study, we compared conventional ECG ischemia diagnosis with ST and VG difference vector diagnosis. Measured during PTCA, the cause of ischemia was a complete coronary occlusion in all patients. If a similar complete occlusion had spontaneously occurred in these patients, this should have led to the triaging decision of cardiac catheterization. In the guidelines this decision is taken for patients with STE ECGs. Patients with NSTE ECGs may also get an indication for PCI; however, such patients should then pass more diagnostic tests or be considered urgent by the responsible physician[5]. This might take extra time and thus might lead to more necrotic myocardium, and would thus have a

negative impact on the prognosis of these patients. In our study, only 55% of the patients had a STE ECG after 3 minutes of occlusion, 45% of the ECGs remained NSTE.

The difference vector magnitudes performed better: at the conventional STE threshold ($\Delta ST > 0.100$ mV; corresponding $\Delta VG > 32.4$ mV·ms), this combination could identify 62% of the cases. With $\Delta ST > 0.050$ mV and $\Delta VG > 16.2$ mV·ms, 87% of the cases was detected. As mentioned in the Methods section, the ΔST threshold of 0.050 mV was earlier proposed in the setting of differential ST segment analysis (14). A further decrease to $\Delta ST > 0.025$ mV and $\Delta VG > 8.1$ mV·ms allowed identification of nearly all ischemic ECGs.

Our study demonstrates that appropriate sensitivity of ECG-based ischemia detection during complete coronary occlusion requires a much lower ST threshold than currently applied in clinical routine. However, the lower the ST threshold, the more pre-existing non-zero ST amplitudes would hamper such a diagnosis. When a non-ischemic reference ECG of the same patient is at disposition, differential vectorcardiographic analysis can potentially solve this problem.

The good linear relationship ($r=0.84$) between the ΔST and ΔVG suggests that a potential solution for patients with pre-existing conduction disturbances can be found in difference vector analysis of the ventricular gradient (as mentioned earlier, VG is independent of the ventricular depolarization order). Again, a requirement is that a non-ischemic reference ECG of the patient is at disposition.

As the STAFF III database contains no false positive cases, our study offers no insight in the specifity of ischemia detection by ECG difference vector analysis. Further research should be done to assess spontaneous short and long term intra-subject ST and VG variability and the effects of medication on ST and VG. Also, intra-individual ST and VG changes with ACS-alike symptoms (e.g., pulmonary embolism) should be assessed.

During the first two hours of ACS, when most of the myocardial AAR is still salvageable and when point-of-care biomarker tests are not yet conclusive because of the still limited amount of necrosis, the ECG is nearly the sole objective source of information. Because the limited diagnostic performance of the current ECG criteria for ischemia detection hampers hyperacute ACS triaging, continuing efforts should be done to improve ECG-based ischemia detection.

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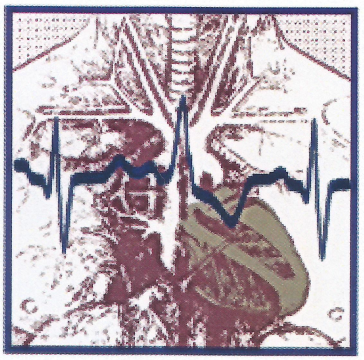

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