High-frequency electrocardiogram as a supplement to standard 12-lead ischemia monitoring during reperfusion therapy of acute inferior myocardial infarction.

Pettersson, Jonas; Wagner, Galen S; Sörnmo, Leif; Trägårdh, Elin; Öhlin, Hans; Pahlm, Olle

Published in:
Journal of Electrocardiology

DOI:
10.1016/j.jelectrocard.2010.04.006

2011

Original Research

High-frequency electrocardiogram as a supplement to standard 12-lead ischemia monitoring during reperfusion therapy of acute inferior myocardial infarction

Jonas Pettersson, MD, PhD,[a] Galen S. Wagner, MD[b], Leif Sörnmo, PhD,[c] Elin Trägårdh Johansson, MD, PhD[d] Hans Öhlin, MD, PhD,[e] Olle Pahlm, MD, PhD.[a]

From the [a]Department of Clinical Physiology, Lund University, Lund, Sweden, [b]Department of Cardiology, Duke Clinical Research Institute, Durham, NC, USA, [c]Electrical and Information Technology, Lund University, Lund, Sweden, [d]Clinical Physiology and Nuclear Medicine Unit, Lund University, Malmö, Sweden, and [e]Department of Cardiology, Lund University, Lund, Sweden.

This study was supported in part by The Swedish National Board for Industrial and Technical Development (NUTEK), Stockholm, Sweden, grants #P9003775 and #P9935-1.

Short title: High-frequency ECG in myocardial infarction

Address for reprints: Elin Trägårdh Johansson

Clinical Physiology and Nuclear Medicine Unit, Entrance 44

Skåne University Hospital, Lund University

SE-205 02 Malmö, Sweden

Telephone +46 40 33 87 24

Fax +46 40 33 66 20

E-mail elin.tragardh-johansson@med.lu.se

ABSTRACT

Background: Resolution of ST-segment elevation in the electrocardiogram (ECG) is used as a reperfusion sign during thrombolytic therapy in acute myocardial infarction (MI). Analysis of high-frequency QRS components (HF-QRS) might provide additional information. The study compares changes in HF-QRS (150-250 Hz) to ST-segment changes in the standard ECG during thrombolytic therapy.

Methods: Twelve patients receiving intravenous thrombolytic therapy were included. A continuous 12-lead ECG recording was acquired for 4 hours.

Results: After 1 hour of therapy 3 patients showed ST-elevation resolution as well as an increase in HF-QRS. These changes in ST and HF-QRS occurred simultaneously. No other patient showed significant changes in ST or HF-QRS after 1 hour. After 2 and 4 hours there was less concordance between the standard and high-frequency ECG.

Conclusions: In patients with early ST-elevation resolution, the standard and high-frequency ECG show similar results. Later changes are more disparate and may provide different clinical information.

Key words: high-frequency ECG, myocardial infarction

INTRODUCTION

The goal in intravenous thrombolytic therapy during acute myocardial infarction (MI) is to re-establish sufficient blood flow through the occluded, infarct-related, coronary artery and reperfuse the reversibly ischemic myocardium. It has been documented that successful therapy reduces both morbidity and mortality (1,2). Failed reperfusion therapy may be rescued by acute adjunctive therapies, e.g. percutaneous coronary angioplasty or administration of additional thrombolytic drugs (3,4). It is therefore of major clinical importance to rapidly detect failed reperfusion in the acute phase because additional interventions could then be indicated to re-establish blood flow to the myocardium in jeopardy.

The coronary angiogram has been considered the gold standard for detecting reperfusion in acute MI. The assessment is based on the blood flow in the infarct-related epicardial coronary artery. Resolution of ST-segment elevation in the electrocardiogram (ECG) is a widely used non-invasive method for detecting reperfusion. Several studies have shown that resolution of ST-segment elevation, compared to the angiographic results, provides overall fairly good diagnostic performance (5-7). Other studies have shown that the ECG provides better prognostic information than the angiogram (8). The suggested reason for these results is that the ECG is a physiologic marker of cellular ischemia (8). Even though the assessment of the ST segments provides overall fairly good diagnostic and prognostic performance, an additional electrocardiographic method that could provide more sensitive or earlier information would be of great clinical importance.

Previous studies have shown that acute myocardial ischemia is accompanied by reduced amplitude of high-frequency QRS components (HF-QRS) in the frequency range of 150-250 Hz (9-14). Studies during thrombolytic therapy, using few electrocardiographic leads, in patients with acute MI suggest that analysis of the HF-QRS also may have the ability to detect reperfusion (15,16). In these studies, reperfusion was accompanied by an increase in HF-QRS.

The present study, in patients undergoing thrombolytic therapy for acute inferior MI, was performed to investigate the feasibility of continuous monitoring of HF-QRS in the clinical environment and to compare the quantity of changes in HF-QRS and ST-segment deviation in the standard 12-lead ECG.

METHODS

Study Population

A total of 19 patients admitted to the coronary care unit, Lund University Hospital, Sweden, for receiving intravenous thrombolytic therapy in acute MI were considered for this study. Informed consent was obtained from each patient before inclusion in the study. Patients were not excluded from the study because of previous MI or coronary artery bypass surgery. In 14 of the patients, the maximal ST elevation was located in lead III and the infarction was considered to involve the inferior wall of the left ventricle. To obtain a more homogeneous study population, these 14 patients were selected for further analysis.

The ECG recording started in connection with the initiation of the thrombolytic therapy, and a continuous ECG recording was acquired for 4 hours whenever possible. Patients were excluded from the study if the recording started > 10 minutes after the therapy was initiated (1 patient) or if the recording was terminated after < 1 hour (1 patient). Inclusion required <20 msec changes in QRS duration during the recording. With this criterion only beats with similar QRS duration were subjected to averaging. All patients met this inclusion criterion. Thus a total of 12 patients were finally included in the study (Table I).

ECG Acquisition

The electrocardiographic recordings were performed using equipment by Siemens-Elema AB, Solna, Sweden. The signals were digitized at a sampling rate of 1000 Hz with an amplitude resolution of 0.6 μV. The recordings were stored on a PC hard disk for further analysis. The standard electrode positions were used for the precordial leads. Proximal electrode positions, using the Mason-Likar electrode configuration, were used for the limb leads (17).

Signal Processing

Signal averaging

The recordings were processed using software for ECG analysis developed by Department of Electroscience, Lund University, Lund. The 12 leads were continuously signal averaged to reduce the noise level. The averaging included beat alignment in which each beat was cross-correlated to a template (18). Beats with a cross-correlation below 0.97 were excluded from averaging. The cross-correlation was computed over the QRS interval only.

During the acute phase of MI, the ECG morphology changes over time. Therefore, an exponentially updated beat average was used (18). This procedure tracked morphologic changes during the recording while still providing sufficient noise reduction. Trend samples of the signal-averaged ECG were obtained every 10 sec. Thus, 6 trend samples were obtained each minute during the entire recording.

High-frequency ECG

The HF-QRS were extracted from the signal-averaged ECGs using a Butterworth filter (19) with a bandwidth of 150-250 Hz. Linear phase filtering was obtained by first filtering the entire signal forward and then backward (so-called forward/backward filtering) (19). The HF-

QRS during the entire QRS duration were expressed as root-mean-square values for each individual lead. The QRS onset and offset were determined from the signal-averaged ECGs in the standard frequency range (20,21).

The noise level in the 150-250 Hz frequency band, expressed as a root-mean-square value during 100 msec, starting 100 msec after QRS offset, was calculated in each lead. Trend samples of the signal-averaged ECG were excluded from the high-frequency analysis if the noise level was ≥ 0.5 μV. The mean noise level of all trend samples in all patients was calculated to compare the noise from the different lead positions.

Standard 12-lead ECG

The selected signal-averaged ECGs were analyzed in the standard frequency range. The QRS onset and offset were automatically determined. The ST-segment level above or below the PR-segment baseline at 60 msec after the J point was automatically measured in each lead in each trend sample.

ECG Analysis

Trends of the ST-segment level and the root-mean-square value were constructed in all 12 leads from the entire recordings. The trends of the root-mean-square values were produced by calculation of the mean of 12 continuous trend samples (representing a 2-minute period) using a so-called box-car filter. If 4 or more of the trend samples during the same 2-minute period were excluded, no mean value was calculated for that time period. The reason for excluding intervals was the occational presence of excessive noise, rendering analysis impossible.

The quantitative changes in the sum of ST-segment elevations and in HF-QRS in individual leads were calculated after 1, 2, and 4 hours of continuous monitoring. The ECG samples at the time of initiation of the therapy were selected for the baseline values. When the

recording started after the therapy, the first values obtained during the recording were selected as baseline. If no trend samples were obtained or if the trend samples did not have an acceptable noise level within 5 minutes from the desirable times, the patient was excluded from this part of the analysis (1-hour analysis: 1 patient, 2-hour analysis: 1 patient). The root-mean-square and ST values were calculated by taking the mean of at least 4 continuous trend samples during 1 minute of the recording.

In the high-frequency analysis, the precordial leads V1-V6 showed lower noise levels than the limb leads. Therefore, to include as many patients as possible in the analysis, the precordial leads were primarily considered when comparing the changes after 1, 2, and 4 hours. The rationale for this approach was that a previous study had concluded that in patients with maximum ST elevation in lead III (due to acute occlusion of RCA), decrease in HF-QRS was distributed among 8 leads (-aVR, II, aVF, III, V2, V3, V4, and V5) (9).

The changes in ST elevation and HF-QRS were evaluated to compare the information indicating early reperfusion. The criterion described by Dissmann et al was used for the ST-segment analysis: an ST-elevation resolution ≥ 50% after 1 hour of therapy was taken as an indication of early reperfusion (22). A change in HF-QRS exceeding 0.6 μV was considered significant (15). These cut-off values were also used for the comparison after 2 and 4 hours of recording.

Statistical methods

Comparison of the mean noise level in the precordial and limb leads was performed with Student's t-test.

RESULTS

1-hour comparison (Figure 1A)

In three of the 11 patients, the ST-elevation resolution after 1 hour of therapy met the criteria for early reperfusion (66%, 93%, and 98%). In these three patients, there was also a significant increase in HF-QRS in 2 - 5 of the precordial leads (maximal increase 0.9 µV, 1.9 µV, and 2,8 µV). All three patients showed a significant increase in lead V2, two of them also in lead V3 and V4. These patients had acceptable noise levels also in the limb leads. They all showed a significant increase in lead aVF, two of them in aVL, II and III. None of these patients had an increased root-mean-square value in I or -aVR, one of the patients even showed a decreased value in -aVR.

In the eight patients with ST-elevation resolution < 50%, there was no lead with a significant increase in HF-QRS. The relationship between the ST-elevation resolution and the maximal increase in HF-QRS for all 11 patients is shown in Figure 2. In two of the patients, there was increased ST elevation; one of these patients also showed a significant decrease in HF-QRS in several leads (maximal decrease -1.7 µV, lead V4).

2-hour comparison (Figure 1B)

After 2 hours of therapy there was less concordance between the standard and high-frequency ECG. In six of the patients there was ≥ 50% ST-elevation resolution. Increased HF-QRS were observed in four of these patients. In one patient there was ST-elevation resolution (58%) and decreased HF-QRS (-1.4 µV, leads V4, V5, and V6). This patient died 3 days after admission. One patient showed an ST resolution of 98% and had no significant change in HF-QRS but after 4 hours of therapy this patient had a significant increase in HF-QRS (2.0 µV, lead V2). There was increased HF-QRS also in two other patients. These patients showed slightly less ST-elevation resolution, 43% and 49% respectively.

4-hour comparison (Figure 1C)

In part disparate results from the compared ECG methods were obtained also after 4 hours of therapy. Two patients had increased ST elevation (29% and 37%). In one of these, there was a very large decrease in HF-QRS, -5.2 µV in lead V4. This patient died 1 day after the acute event.

Trend analysis

In the three patients with ST resolution indicative of early reperfusion, the trends showed that the resolution of ST elevation and increase in HF-QRS occurred at the same time (Figure 3, 4). The HF-QRS remained at a relatively high level during the rest of the recording as the ST level remained unaltered.

The patients without ST signs of early reperfusion showed varying patterns in their ST deviation during the recording; e.g. gradual resolution of the ST elevation or alternating ST level with or without complete resolution after 4 hours. The HF-QRS showed in some of these patients variable development and no stable increase of the HF-QRS (Figure 5).

Noise level analysis

The mean noise level in the precordial leads ranged from 0.27 µV (V2) to 0.34 µV (V5). The noise levels were significantly higher in the limb leads compared to the precordial leads ($p=0.01$). The mean noise level in the limb leads ranged from 0.39 µV (-aVR) to 0.47 µV (III).

DISCUSSION

During thrombolytic therapy in acute MI it is of major clinical importance to rapidly detect failed reperfusion as additional acute interventions could re-establish blood flow to the myocardium in jeopardy. The coronary angiogram has been considered the gold standard for detecting reperfusion in acute MI but previous studies have shown that ST-elevation resolution provides better prognostic information than the angiogram (8). Electrocardiographic methods provides bedside information and continuous monitoring is possible. The assessment of ST segments provides overall fairly good diagnostic and prognostic performances but an additional electrocardiographic method that further would increase the reliability would be of great clinical importance.

Comparison between standard and high-frequency ECG

Previous studies have indicated that reperfusion in patients with acute MI is accompanied by an increase in HF-QRS (15,16). The results of the present study support these previous findings. After 1 hour of therapy there was complete agreement regarding early reperfusion between the standard and high-frequency ECG in all of the 11 patients. The changes indicative of reperfusion observed in 3 patients, both in the standard and high-frequency range, occurred at the same time during the continuous recordings. These results suggest that early, rapid resolution of the myocardial ischemia might be detected with similar performance with standard and high-frequency ECG.

After 2 and 4 hours of therapy there were more disparate results from the standard and high-frequency ECG, e.g. some of the patients showed ST-elevation resolution but no increase in HF-QRS and vice versa. The discrepancy between standard and high-frequency ECG in these patients could in part be explained by the ST-elevation resolution due to cellular death in the infarcted area. This cellular death is not expected to result in an increase in HF-QRS.

Interesting observations were made regarding the 2 patients who died within a few days from the acute event. Those patients had the largest observed decrease in HF-QRS from the initial values. Contrary to the high-frequency results, 1 of these patients showed a significant ST-elevation resolution (58%) after 2 hours of therapy.

Previous studies have shown that there are marked location-specific electrophysiologic differences in acute myocardial ischemia and infarction, due primarily to variations in the anatomic relationships between the myocardium and its Purkinje supply (23). The central points of the commonly involved inferior myocardial region and the distribution of the posterior fascicle of the left bundle branch almost exactly coincide (24). Abboud et al. have suggested that the HF-QRS might be associated with the number of branches in the conduction system (13). When the myocardium where the posterior fascicle inserts is ischemic the conduction from the Purkinje fibres to the myocardium is impaired. The marked increase in HF-QRS seen in some of the patients during reperfusion in the present study might be explained by a resolution of the ischemia and a re-establishment of the conduction from the Purkinje fibres to the myocardium.

Noise level analysis

This study shows that continuous monitoring of HF-QRS is possible in patients receiving thrombolytic therapy in acute MI. The electrodes were placed by the regular staff and no specific instructions were given to the patients. The signal processing was performed off-line but the analysis could be made on-line with an appropriate ECG device.

Limitations of the present study

The major limitations of the present study are the small study population and the lack of a non-ECG method as a gold standard, i.e. coronary angiogram or myocardial scintigraphy. These limitations make it impossible to draw definitive conclusions about the performance regarding reperfusion and prognosis of the two investigated ECG methods.

Only acute inferior MIs were studied. A previous study during elective percutaneuous coronary transluminal angioplasty showed that the sensitivity for the detection of acute myocardial ischemia was highest during ischemia due to occlusion of the left anterior descending coronary artery, both with standard- and high-frequency ECG (9). The results could therefore be different when investigating other patients groups with acute MI in other areas of the left ventricle.

In the study, patients with previous MI were included. Previous studies have shown that patients with ischemic heart disease have reduced HF-QRS compared to normal individuals (25). In the present study, however, only changes over time were investigated, and no absolute values of HF-QRS were used.

Conclusions

Continuous monitoring of HF-QRS is feasible in patients undergoing intravenous thrombolytic therapy in acute MI. The standard and high-frequency ECG seem to show similar results in patients with an early, rapid ST-elevation resolution. Later changes seem to be more disparate. A non-ECG method and a larger study population are necessary to determine the performance of the two ECG methods regarding reperfusion and the ability to provide prognostic information.

REFERENCES

1. GUSTO-I angiographic Investigators. The effects of tissue plasminogen activator, streptokinase, or both on coronary artery patency, ventricular function and survival after acute myocardial infarction. N Engl J Med 1993;329:1615-22.
2. Kennedy JW. Optimal management of acute myocardial infarction requires early and complete reperfusion. Circulation 1995;91:1905-6.
3. Simoons ML, Arnout J, van den Brand M, et al. Retreatment with alteplase for early signs of reocclusion after thrombolysis. The European Cooperative Study Group. Am J Cardiol 1993;71:524-8.
4. White HD, Cross DB, Williams BF, et al. Safety and efficacy of repeat thrombolytic treatment after acute myocardial infarction. Br Heart J 1990;64:177-81.
5. Hogg KJ, Hornung RS, Howie CA, et al. Electrocardiographic prediction of coronary artery patency after thrombolytic treatment in acute myocardial infarction: use of the ST-segment as non-invasive marker. Br Heart J 1988;60:275-80.
6. Klootwijk P, Cobbaert C, Fioretti P, et al. Noninvasive assessment of reperfusion and reocclusion after thrombolysis in acute myocardial infarction. Am J Cardiol 1993;72:75G-84.
7. Clemmensen P, Ohman M, Sevilla DC, et al. Changes in standard electrocardiographic ST-segment elevation predictive of successful reperfusion in acute myocardial infarction. Am J Cardiol 1990;66:1407-11.
8. Shah A, Wagner GS, Granger CB, et al. Prognostic implications of TIMI flow grade in the infarct related artery compared with continuous 12-lead ST-segment resolution analysis. Reexamining the "gold standard" for myocardial reperfusion assessment. J Am Coll Cardiol 2000;35:666-72.

9. Pettersson J, Pahlm O, Carro E, et al. Changes in high-frequency QRS components are more sensitive than ST segment deviation for detecting acute coronary artery occlusion. J Am Coll Cardiol 2000;36:1827-34.
10. Pettersson J, Lander P, Pahlm O, et al. Electrocardiographic changes during prolonged coronary artery occlusion in man: comparison of standard and high-frequency recordings. Clin Physiol 1998;18:179-86.
11. Abboud S, Cohen RJ, Sadeh D. A spectral analysis of the high frequency QRS potentials observed during acute myocardial ischemia in dogs. Int J Cardiol 1990;26:285-90.
12. Abboud S, Cohen RJ, Selwyn A, et al. Detection of transient myocardial ischemia by computer analysis of standard and signal-averaged high-frequency electrocardiograms in patients undergoing percutaneous transluminal coronary angioplasty. Circulation 1987;76:585-96.
13. Abboud S, Berenfeld O, Sadeh D. Simulation of high-resolution QRS complex using a ventricular model with a fractal conduction system. Effects of ischemia on high-frequency QRS potentials. Circulation Research 1991;68:1751-60.
14. Mor-Avi V, Shargorodsky B, Abboud S, et al. Effects of coronary occlusion on high frequency components of the epicardial electrogram and body surface electrocardiogram. Circulation 1987;76:237-43.
15. Aversano T, Rudicoff B, Washington A, et al. High frequency QRS electrocardiography in the detection of reperfusion following thrombolytic therapy. Clin Cardiol 1994;17:175-82.
16. Abboud S, Leor J, Eldar M. High frequency ECG during reperfusion therapy of acute myocardial infarction. IEEE Comput Soc, Comput Cardiol 1990;351-3.
17. Mason RE, Likar I. A new system of multiple-lead exercise electrocardiography. Am Heart J 1966;71:196-205.

18. Pahlm O, Sörnmo L. Data processing of exercise ECGs. IEEE Trans Biomed Eng 1987;34:158-65.
19. Proakis JG, Manolakis DG. Digital signal processing – principles, algorithms, and applications. Upper Saddle River, New Jersey: Prentice-Hall; 1996.
20. Jonson B, Lundh B, Pahlm O, et al. Determination of QRS onset and end in orthogonal and scalar ECGs. A new approach. IEEE Computer Society, Computers in Cardiology 1984;459-62.
21. Xue Q, Reddy S, Aversano T. Analysis of high-frequency signal-averaged ECG measurements. J Electrocardiol 1995;28 Suppl:239-45.
22. Dissmann R, Goerke M, von Ameln H, et al. Detection of early reperfusion and prediction of left ventricular damage from the course of increased ST values in acute myocardial infarct with thrombolysis. Z Kardiol 1993;82:271-8.
23. Grant RP, Dodge HT. Mechanism of QRS complex prolongation in man: left ventricular conduction disturbance. Am J Med 1956;20:834-52.
24. Startt/Selvester RH, Wagner GS, Ideker RE. Myocardial infarction. In: Macfarlane P, Lawrie TDV, editors. Comprehensive Electrocardiology: Theory and Practice in Health and Disease. New York: Pergamon Press, 1989;1:565-629.
25. Trägårdh E, Pahlm O, Wagner GS, Pettersson J. Reduced high-frequency QRS components in patients with ischemic heart disease compared to normal subjects. J Electrocardiol 2004;37:157-62.

FIGURE LEGENDS

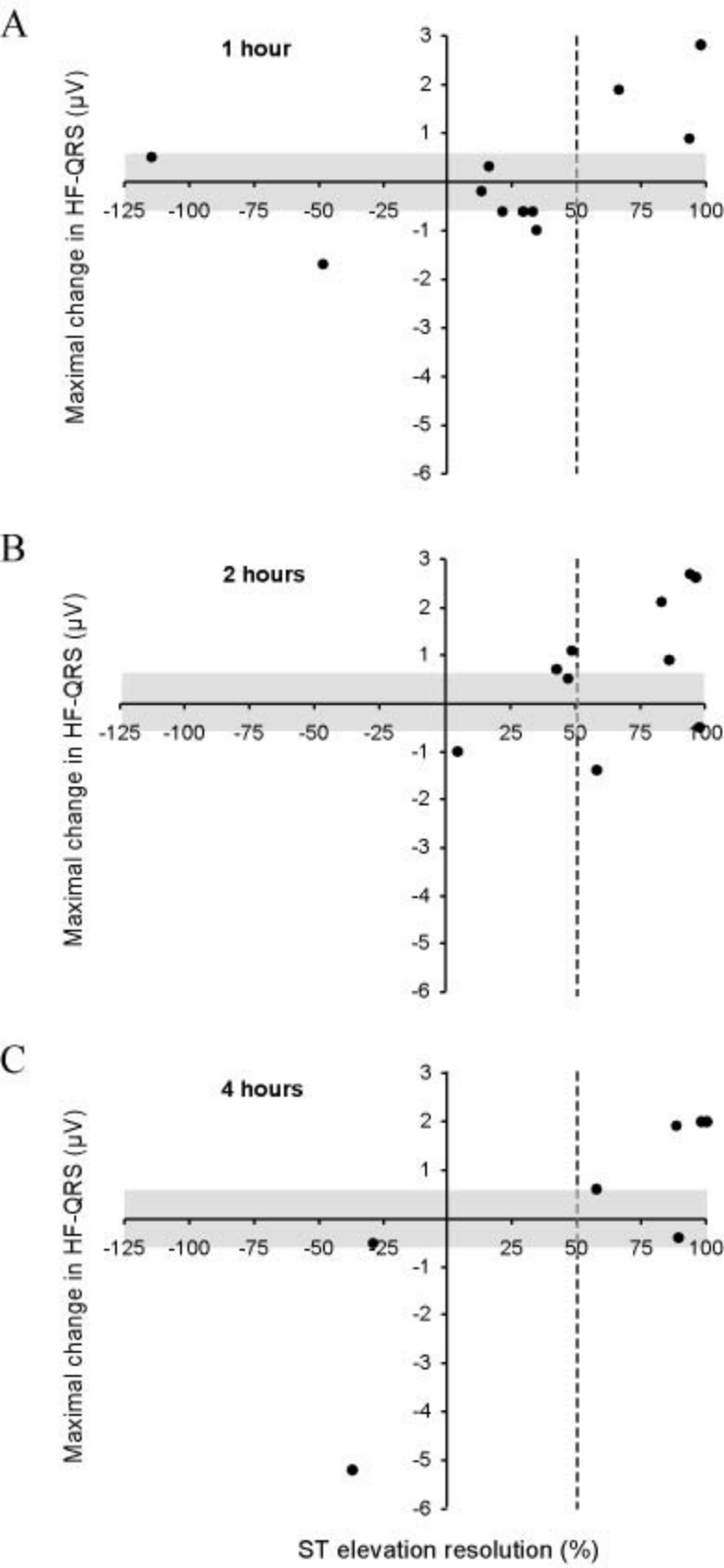
Figure 1. The maximal change in HF-QRS (µV) in any lead after 1 (upper panel, A), 2 (middle panel, B), and 4 (lower panel, C) hours of therapy vs. the summed ST-elevation resolution (%). The grey area indicates a non-significant change in HF-QRS (± 0.6 µV) and the dashed line the ST criteria for reperfusion (50%). For example, the patient represented by the dot furthest to the right, had a almost 100 % ST segment resolution, and a significant increase in HF-QRS, measuring almost 3 µV.

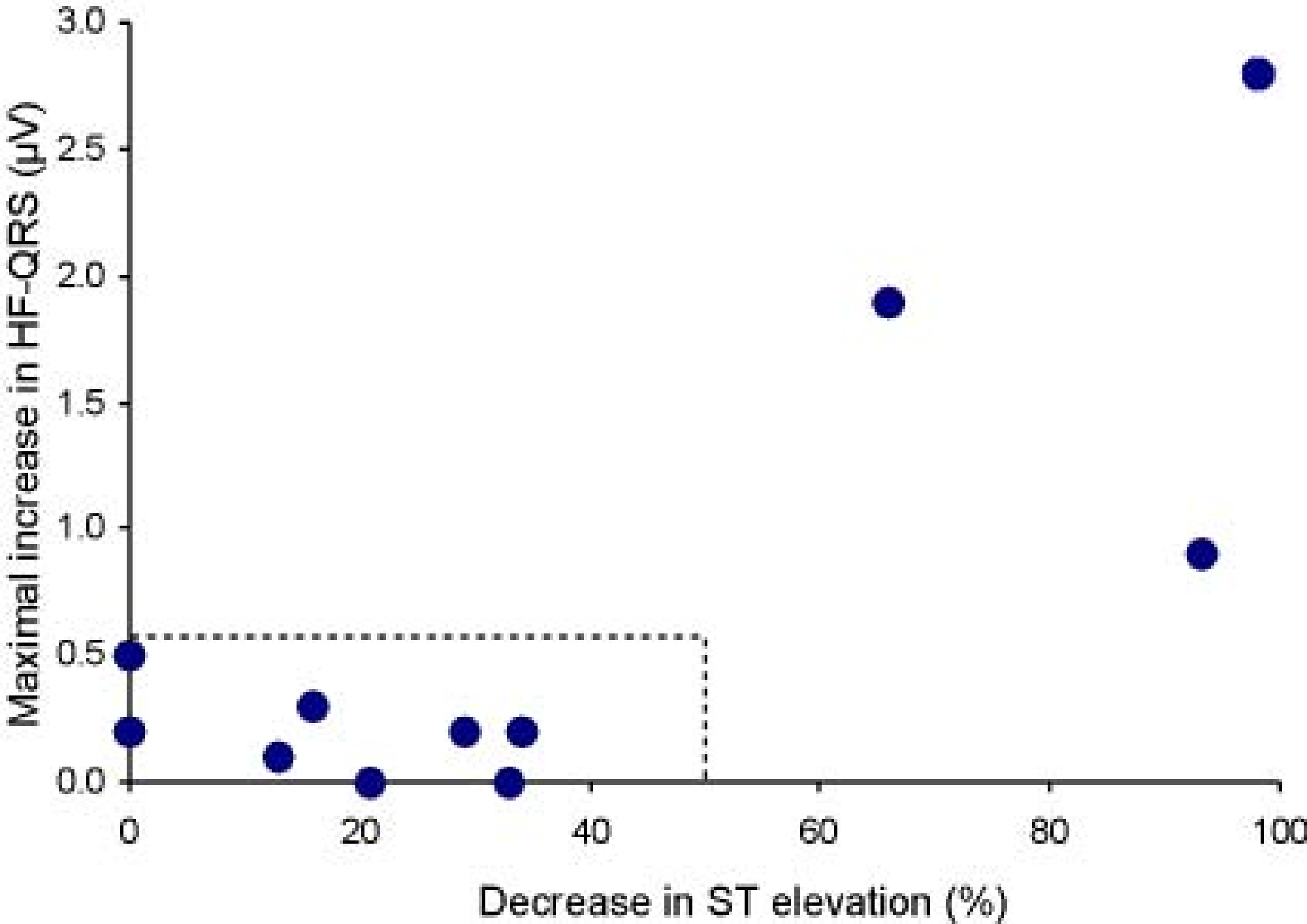
Figure 2. The relationship between the summed ST-elevation resolution (%) and the maximal increase in HF-QRS (µV) in any lead after 1 hour of therapy. The dashed lines indicate the ST and HF-QRS criteria for reperfusion.

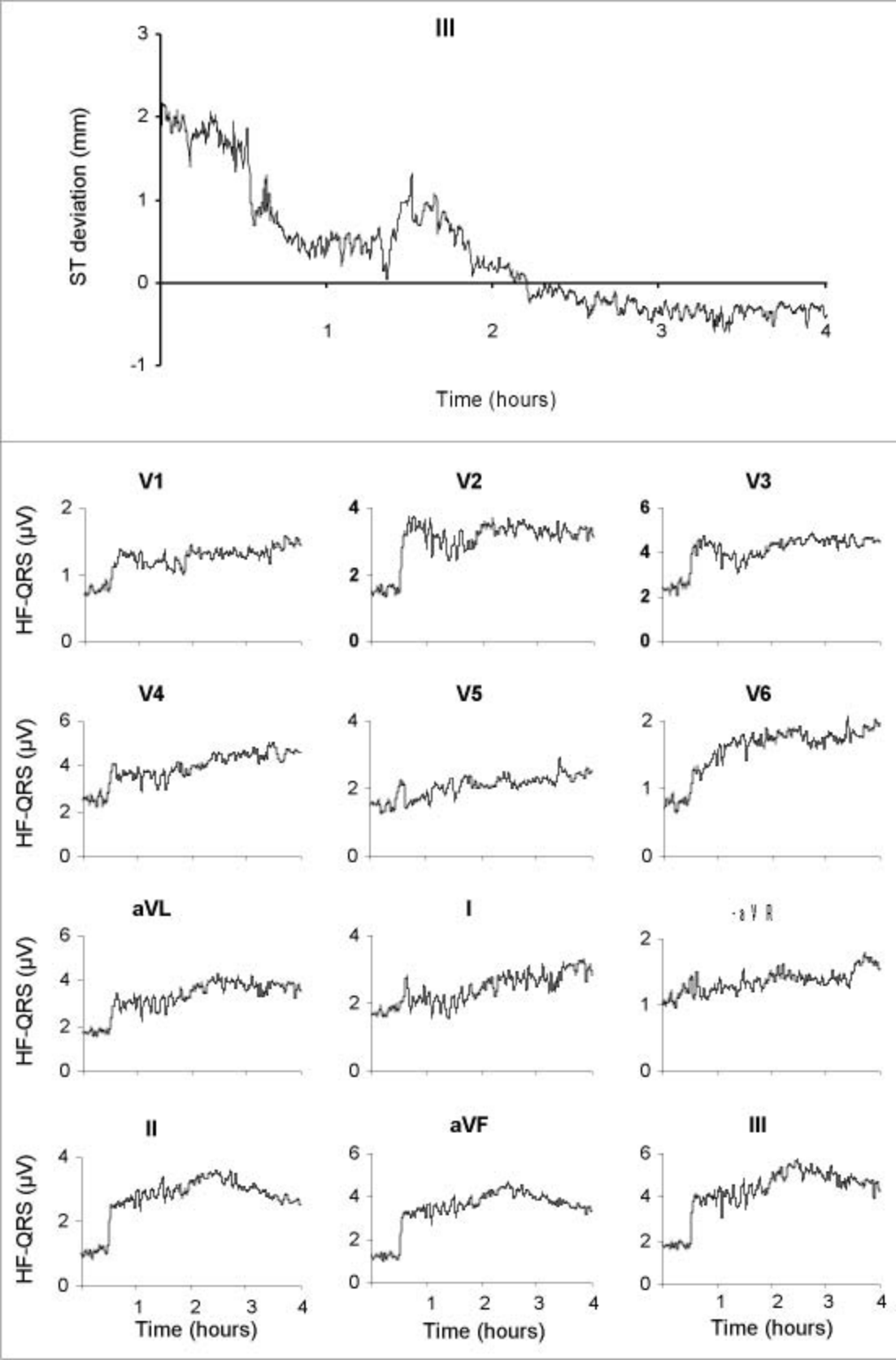
Figure 3. Trends of ST deviation (mV) in lead III and HF-QRS (µV) in all 12 leads during 4 hours of continuous ECG monitoring after thrombolytic therapy. A patient meeting the ST criteria for reperfusion is shown (# 7).

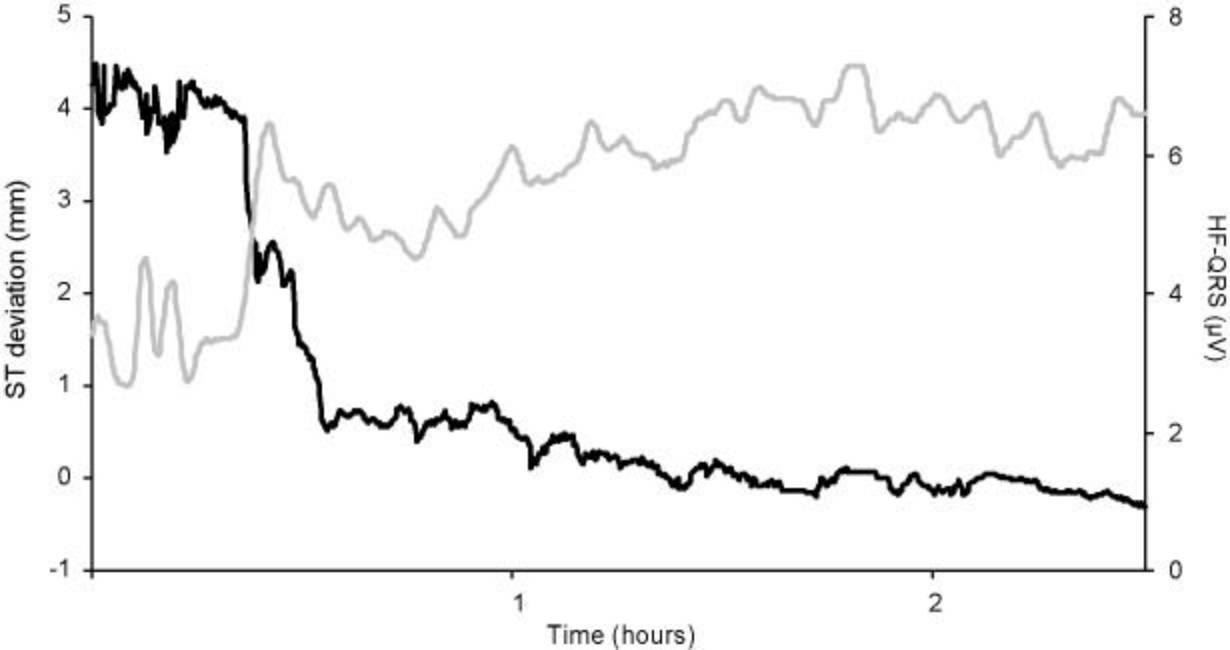
Figure 4. The ST deviation in lead III (black line, left vertical axis) and HF-QRS in lead V2 (grey line, right vertical axis) in a patient meeting the ST criteria for reperfusion (patient # 1). Recording duration 2.5 hours.

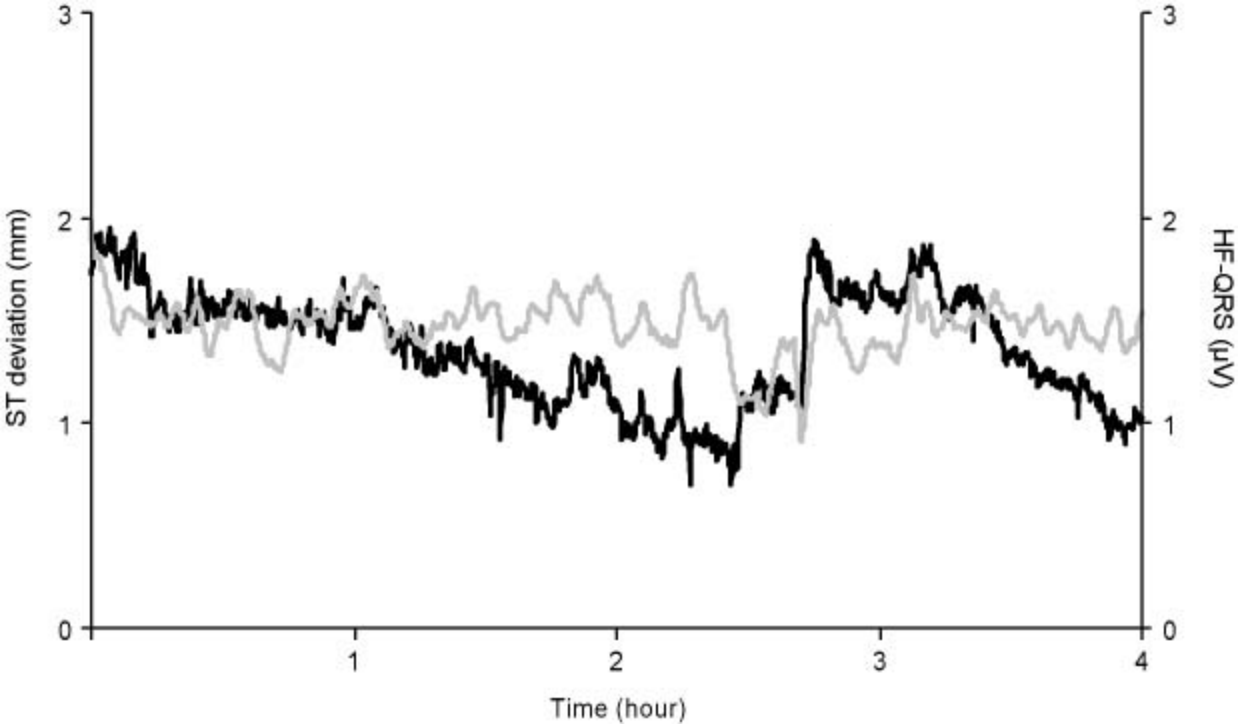
Figure 5. The ST deviation in lead III (black line, left vertical axis) and HF-QRS in lead V2 (grey line, right vertical axis) in a patient not meeting the ST criteria for reperfusion (patient # 3).


A
1 hour
Maximal change in HF-QRS (µV)
B
2 hours
Maximal change in HF-QRS (µV)
C
4 hours
Maximal change in HF-QRS (µV)
ST elevation resolution (%)


Maximal increase in HF-QRS (μV)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
20
40
60
80
100
Decrease in ST elevation (%)


III
ST deviation (mm)
3
2
1
0
-1
1
2
3
4
Time (hours)
V1
V2
V3
V4
V5
V6
aVL
I
aVR
II
aVF
III
HF-QRS (μV)
Time (hours)


ST deviation (mm)
HF-QRS (μV)
Time (hours)
5
4
3
2
1
0
-1
8
6
4
2
0
1
2


3
2
1
0
ST deviation (mm)
HF-QRS (μV)
1
2
3
4
Time (hour)

TABLES

Table 1. Characteristics of the included patients.

Patient #	Sex	Age	Recording duration (hour)	Maximal initial ST elevation	
				Lead	(mm)
1	m	48	2.5	III	4.1
2	f	76	2.6	III	3.2
3	m	59	4	III	1.9
4	f	71	4	III	4.4
5	f	71	4	III	2.1
6	m	92	4	III	2.5
7	m	54	4	III	2.1
8	f	79	4	III	2.6
9	m	71	1.7	III	2.5
10	m	55	4	III	3.5
11	f	80	2.1	III	5.5
12	m	64	2.1	III	3.8

f – female, m – male